

A Mother's Heart Beats for Two: To Explore the Current Provision of Evidence-based Practice and Clinical Outcomes for Women with Cardiovascular Disease during Pregnancy

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Abstract

Background

As an increasingly recognised causal factor in maternal and neonatal mortalities and morbidities, cardiovascular disease in the mother provides the impetus for research that may then translates to improved quality improvement measures in clinical practice. The South Australia Perinatal Pregnancy Guidelines (SAPPG) for women with cardiac conditions during pregnancy were developed and available since 2010. Although regularly revised, no evaluation of the uptake of the guidelines and their impact on clinical outcomes has occurred. Therefore, the aim of this thesis was to perform the first assessment of adherence to SAPPGs in South Australia and determine both predictors of adherence and association with clinical outcomes for mother and baby.

Objectives

1. Measure the adherence to SAPPG for pregannt women with preexisting and acquired cardiac disease during pregnancy in SA from 2003 to 2013
2. Identify the predictors and associated factors for adherence.
3. Determine the disparities between the three major obstetric hospitals in SA as regards to adherence to the guidelines?
4. Determine the association between clinical outcomes and guideline adherence scores.

Methods

1. A retrospective cross-sectional observational study analysed medical records data collected via an online data abstraction tool (DAT). Adherence measured across the hospital sites within the ten-year timeframe (2003-2013) used a scoring system for 40 variables and included two cardiac cohorts of women with preexistent and newly acquired cardiac disease.
2. Multivariable logic regression analysis examined correlations of predictors, factors and guideline adherence. The analysis yielded an odds ratio (OR) for greater or lesser adherence scores that influenced the uptake of guideline recommendations.
3. Clinical outcomes analysed were categorised into cardiac, obstetric, and neonatal groups for multivariate regressional analysis and correlated to the adherence score.

Results

1. Overall adherence to the SAPPGs was normally distributed, with a mean score of 16.3, SD±6.7.
2. The preexisting cardiac group reported a higher mean score of 17 ±6.5 compared to the 'newly acquired group' with a mean score of 15 ±6.8. Factors and predictors that were associated with a higher adherence score predicted included the occurrence of preconception cardiac consultation (OR 18.5:95% CI 2.0, 168) and a comprehensive antenatal initial assessment.
3. The state's high-risk quartenary referral centre was associated with increased adherence to guidelines as compared with other sites (OR 3.9, 95% CI 2.3, 5.6, p <0.001).

4. Women with a compication of heart failure, elective LSCS and babies requiring admission to intensive care or special baby care were the most statistically significant clinical outcomes with increased adherence scores (MD= 3.546, 95% CI:1.689, 5.403), (MD=3.197, 95% CI:3.584, 6.811) and (MD=3.581, 95% CI:1.822, 5.340) respectively.

Conclusion

SAPPG's recommendations of preconception counselling, and initial comprehensive antenatal assessment by appropriately skilled health professionals are pivotal to a multidisciplinary approach to preparation and anticipation of managing and preventing adverse clinical outcomes in women with preexisting cardiac conditions. In acquired cardiac conditions, SAPPGs guideline informed care from the moment of cardiac diagnosis during pregnancy resulted in lower adherence overall. But once recognised, appropriate management of adverse outcomes were similarly associated with adherence to SAPPPG.

Thesis declaration

This thesis is submitted to the University of Adelaide to fulfil the Doctor of Philosophy's requirements. This thesis represents my original work towards this research degree. I certify that this work does not contain material accepted for an award or any other degree or diploma in my name at any other university or tertiary institution. My conviction is that there is no content previously published or written by another person except where due referenced in the text.

Also, I certify that no part of this work will, in future, be used in a submission in my name for any other degree or diploma from any university or tertiary institution without prior approval of the University of Adelaide. Likewise, for the partner institution responsible for the joint award of this degree.

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Signed: Dated : 6th November 2021

Publications and presentations

Peer-reviewed journal articles related to the thesis.

Millington S, Magarey J, Dekker G, Clark R. Cardiac conditions in pregnancy and the role of midwives: A discussion paper. *Nurs Open*. 2019;6(3):722-732. DOI: 10.1002/nop2.269

Millington S, Arstall M, Magarey J, Clark R, Dekker G. Adherence to clinical practice guidelines for South Australian pregnant women with cardiac conditions between 2003 and 2013. Original research *PLoS One*. 2020;15(3):e0230459. DOI: 10.1371/journal.pone.0230459

Millington S, Edwards S, Clark R, Dekker G, Arstall M. The association between guidelines adherence and clinical outcomes during pregnancy in a cohort of women with cardiac comorbidities. Original research *PLoS One*. 2021; 16(7): e0255070. DOI:/ journal. pone.0255070.

Conference presentations

Millington S, Magarey J, Clark R. Mother's heart beats for two: exploring the current continuum of care for women with cardiac disease during pregnancy. Poster presented at: Translating evidence into practice, NHF 4th Heart Foundation Conference Prevention of Cardiovascular Disease; 16-18 May 2013; Adelaide, Australia.

Millington S, Magarey J, Clark R. A mother's heart beats for two: exploring the current continuum of care for women with cardiac disease during pregnancy. Moderated poster presented at: welcome reception, Bridging the Divide: focusing on the inequalities or gaps in the experience and treatment of cardiovascular disease, ACRA ASM National Conference; 12-14 August 2013; Albert Park, Australia.

Invited presentations

Millington S, Magarey J, Dekker GA, Clark R. (2014) A Mother's heart beats for two: To explore the current provision of evidence-based practice, outcomes, and 'lived experience' for women with cardiovascular disease during pregnancy. Oral presentation: 3 December, Gawler Hospital, South Australia.

Millington S, Magarey J, Dekker GA, Clark, R. (2016) A Mother's heart beats for two: To explore the current provision of evidence-based practice, outcomes, and 'lived experience' for

women with cardiovascular disease during pregnancy. Oral presentation at: Regional Health Services, 21 September, Gawler Hospital, South Australia.

Millington S, Magarey J, Dekker GA, Clark R. (2017) 'Snapshot view of pregnant women journey at three metropolitan hospitals' oral presentation of preliminary data analysis. Oral presentation at: Research Conversazione; September 2017; Adelaide Nursing **S**chool, University of Adelaide.

Millington S, Magarey J, Dekker GA, Clark R. (2018) An evaluation of the quality of care of pregnant women with preexistent & newly acquired heart conditions. Moderated e-poster presentation: Day 2; Research Conversazione; 2018; Adelaide Nursing School, University of Adelaide.

Millington S, Arstall M, Dekker GA, Clark, R. (2019). Adherence to clinical practice guidelines for South Australian pregnant women with cardiac conditions between 2003 and 2013. Oral presentation at: Monthly researchers' meeting; December 2019; Lyell McEwin Hospital Robinson Research Institute, Adelaide, Australia.

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Key abbreviations

ACS	Acute coronary syndrome
AF	Atrial fibrillation
AHA	American Heart Association
AMI	Acute myocardial infraction
ANRQ	Antenatal Psychosocial Risk Questionnaire
ARVD	Arrhythmogenic right ventricular dysplasia
ARVNT	Atrioventricular nodal re-entry tachycardia
AS	Aortic stenosis
ASD	Atrial septal defect
AVD	Assisted vaginal delivery
BAV	Bicuspid aortic valve
BMI	Body Mass Index
BMV	Bag-mask ventilation
BrS	Brugada syndrome
CAD	Coronary artery disease
CHD	Congenital heart disease
CIED	Cardiac internal electrical device
CMP	Cardiomyopathies
CoA	Coarctation of aorta
CPGs	Clinical Practice Guidelines
CPAP	Continuous positive pressure ventilation
CT	Computed tomography
CTPA	Computed tomography pulmonary angiogram
CVD	Cardiovascular disease
ECMO	Extracorporeal membrane oxygenation
EP	Electrophysiology studies
EPDS	Edinburgh Postnatal Depression Scale
FTP	Failed to progress in labour
GDM	Gestational diabetes mellitus
GH	Gestational hypertension
HCM	Hypertrophic cardiomyopathy
HF	Decompensated heart failure
HELLP	Haemolysis, elevated liver enzymes and low platelets syndrome
IABP	Intra-aortic balloon pump

IC	Ischaemic cardiomyopathy
ICD -10-AM	The International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification
IUFD	Intrauterine fetal death >20 weeks
IUGR	Intrauterine growth restriction
IPPV	Intermittent positive pressure ventilation
LBBB	Left bundle branch block
LCE	Late cardiac events (> 6 months post-delivery)
LSCS	Lower segment caesarean section
LVEF	Left ventricular ejection fraction
LVH	Left ventricular hypertrophy
LVOT	Left ventricular outflow tract
MACE	Major adverse cardiac event
MMD	Maternal myotonic muscular dystrophy
MR	Mitral regurgitation
MS	Mitral valve stenosis
MVD	Mixed valve disease
MVP	Mitral valve prolapse
NICU	Neonatal Intensive Care Unit
NSTEMI	Non-elevated ST-segment myocardial infarction
NVD	Normal vaginal delivery
NYHA	New York Heart Association
PDA	Patent ductus arteriosus
PET	Preeclampsia
PCCM	Peripartum cardiomyopathy
PCI	Percutaneous coronary intervention
PFO	Patent foramen ovale
PH	Pulmonary hypertension
PIH	Pregnancy-induced hypertension
RDS	Respiratory distress syndrome
RHD	Rheumatic heart disease
SAPPGS	South Australian Health Perinatal Practice Guidelines
SBCU3	Special Baby Care Unit level 3
SFD	Small for gestational age
STEMI	ST-segment myocardial infarction

SVT	Supraventricular tachycardia
TIC	Tachycardiomyopathy
TOF	Tetralogy of Fallot
TOP	Termination of pregnancy
VHD	Valvular heart disease
VSD	Ventricular septal defect
VT	Ventricular tachycardia
VF	Ventricular fibrillation
WPW	Wolff-Parkinson-White syndrome

Chapter 1: Introduction

1.1 Background and rationale

Although cardiac disease complications occur in few pregnancies, it is a leading cause of maternal morbidity and mortality; therefore, research to improve maternal care and clinical outcomes needs to be prioritised.[1,2] Up to 15% of maternal mortalities during pregnancy have been attributed to cardiac conditions.[3] However, the World Health Organization (WHO) recently recommended severe maternal morbidities (SMM) were better indicators of the quality of care, given the declining maternal mortality ratio in high-income countries.[4, 5] SMM rates complicate up to 8% of hospital-based deliveries in lower- and middle-income countries but are trending upwards.[4] Common preventable factors were provider-related, i.e. failure to identify 'high risk' status, delay in diagnosis and treatment.[4] Globally, there is an emerging pattern of substandard maternal health care and suboptimal use of best practice strategies to prevent and treat morbidities which may occur across countries regardless of wealth , contributing to the burden of SMM with an Australia perspective included.[4] Therefore, research that monitors the continuum of care and evaluates health care providers' adherence to cardiac explicit clinical practice guideline (CPG) recommendations has the potential to improve clinical outcomes for both mother and baby but has not been previously published. This research project utilised a novel approach to comprehensively examine cardiac-specific CPGs, allocating a score for adherence to the CPGs components and determining any association between the overall adherence score and clinical outcomes.

1.1.1 Global perspective on cardiac disease in pregnancy

In 2017, the prevalence of adult congenital heart disease (ACHD) was estimated globally at 12 million.[6] ACHD continues to be the most common maternal cardiac condition seen in pregnancy; with advanced medical and cardiac surgical care enabling women to survive to reproductive years [7,8], the number of women with CHD aspiring to pregnancy is increasing. The Registry of Pregnancy and Cardiac Disease (ROPAC) global prospective observational studies show an increasing trend of high-risk pregnancies, from 0.7% in 2007–2010 to 10.9% in 2015–2018.[3]

Women diagnosed with structural heart disease, CHD, VHD, cardiomyopathy (CMP), ischaemic heart disease (IHD), aortic pathology (AOP) or pulmonary hypertension are included in the registry and are predominantly (60%) from developing countries.[3] Women with CHD made up 3,295 (57.4%) of the total pregnancies in ROPAC 5,739, with a mean age of 29 years.[3] One in five women experienced a cardiac event during pregnancy or postpartum, particularly those with preexisting structural heart disease.[3,9] Heart failure and/or maternal mortality was the primary composite endpoint observed in 629 pregnancies (11%) with maternal death in 34 women (0.6%).[3] But recent ROPAC data (2020)

reflects an increasing trend of women of childbearing age with acute coronary syndrome (ACS) and ischaemic heart disease (IHD).[9]

The prospective Canadian Cardiac Disease in PREGnancy (CARPREG) study encompassed preexisting and pregnancy-acquired cardiac conditions seen in pregnancy. Similarly, 13% of pregnancies experienced decompensated heart failure and 11% arrhythmias requiring treatment. [10,12]. Maternal cardiac disease was also associated with neonatal complications such as fetal loss, preterm birth, growth restriction and low birth weight (<10th percentile).[12] Therefore, women with complex corrected congenital heart disease or who develop pregnancy-acquired cardiac conditions are at increased risk of adverse pregnancy outcomes.[13-17] The translational perspective of this research was the need for additional research on the specific components of cardiovascular and obstetric care that will improve outcomes for these women.[17]

Australia and New Zealand report low maternal mortality rates due to the lack of valid population-based estimates of the prevalence and aetiology of maternal cardiac disease.[11] Therefore, the burden and the broader impact are underestimated and limit appropriate health service planning.[11] Parsonage et al. found that emerging cardiac causes for maternal deaths are reported in developed countries, i.e. Australia and New Zealand.[11] they advocate a nationally agreed strategy to deliver the best obstetric and neonatal outcomes for women with cardiac disease in pregnancy in both nations. The process should include carefully coordinated multidisciplinary care and ongoing research that identifies optimum care models and emphasises continuous quality improvement with patient-reported outcomes.[11] There are no national guidelines or strategies for managing women with cardiac disease during pregnancy.

In South Australia, the broad spectrum of cardiac disease in pregnant women encompasses rheumatic and congenital heart disease, ischaemic heart disease, heart failure and arrhythmias as indicated in the statewide guidelines.[18] The annual SA health preganacy outcome reports do not include this data within the listed medical conditions of preganancy, therefore there is a paucity of data. Pregnant women with underlying cardiac conditions have increased susceptibility to acute pulmonary oedema (APO), pulmonary hypertension (PH), infective endocarditis, thromboembolism, fulminating peripartum cardiomyopathy, aortic dissection and cardiac arrhythmias.[2] The South Australian Perinatal Guidelines (SAPPG) specific to cardiac disease in pregnancy, first developed and implemented in 2010, are accessible to all SA Health public university-affiliated teaching hospitals providing obstetric services (see Appendix D). However, there is no reported evaluation of adherence to the cardiac-specific CPGS in South Australia except for this research project. The SAPPGs have been revised and updated in 2012, 2014, 2018 and 2021.

1.1.2 Clinical Practice Guidelines and gaps in research

Clinical practice guidelines (CPGs) are defined as ‘statements that include recommendations intended to optimise patient care that are informed by a systematic review of evidence and assessment of the

benefits and harms of alternative care'.[19] SAPPGs referred to in this thesis is a version of CPGs, a clinical practice guideline developed in SA for SA clinicians during the time frame leading up to and after birth.[18] Developers and clinicians expect CPGs to be informed by rigorous methodological evidence, such as randomised control trials (RCT) or observational research. However, given the ethical complexities, and a lack of such trials is a challenge in the combined cardiology and obstetric context. Moreover, CPGs pertinent to cardiac disease in pregnancy, as do all CPGS translate quality research findings into recommendations to assist clinicians in decision-making and improved care. [20]Due to the lack of qulaity research as regards cardiac problems in pregnancy , the level of evidence used often does not include random controlled trials (RCTS). Adherence to best practice CPGs, such as preconception counselling, risk assessment and interdisciplinary team collaboration in high-risk pregnancies, are pivotal in mitigating mortalities and morbidities in women with cardiac conditions.[21] Clinical expertise and patient preferences are important considerations in clinical decision-making.[11]

The international CPGs for managing CVD during pregnancy were first published in 2011 by the European Society of Cardiology (ESC), with the proviso that health professionals were responsible for individualised care. The ESC also emphasised the need for surveillance and for registries to evaluate clinical care benchmarked against CPGs to complete the loop between clinical research, writing guidelines and implementation.[22] Suboptimal adherence to CPGs may reflect inadequate implementation processes and should be easily correctable. Research gaps exist in verifying real-life clinical practice and evaluating adherence to pertinent CPGs and their association with clinical outcomes in diverse contexts.

In 2018, the ESC revision of CPGs for managing CVD during pregnancy [2] proposed new concepts, enforcing the 'modified World Health Organization' classification of maternal risk and implementing the 'pregnancy heart team' and focusing more on assisted reproductive therapy and not allowing women with heart disease to continue pregnancy beyond 40 weeks.[2,23] The ROPAC findings reiterate the updated ESC CPGs, particularly multidisciplinary team management of high-risk pregnant women in specialised tertiary centres and identifying women who require additional care with existing conditions such as CVD.[2]

Although generic, the revised Australian national CPGs for pregnancy care [24] emphasise the importance of the initial antenatal assessment, including a comprehensive history within the first ten weeks, continuity of care, multidisciplinary management in high-risk pregnancies and clinical evaluation in late and prolonged pregnancy, [24,25] as well as the importance of identifying women who require additional care with existing conditions such as CVD and have yet to be assessed. Although there are no national cardiac-specific CPGs for pregnant women in Australia, some states have developed policies. In addition to the SAPPGs for cardiac disease in pregnancy, the King Edward Memorial Hospital (KEMH) Obstetrics and Gynaecology Department in Western Australia

independently developed their own statewide clinical practice guidelines on cardiac disease in pregnancy (see Appendices D). [18,26]

These guidelines prescribe additional care to the standard for all pregnant women outlined in the shared care handheld records, plus the clinical pathways for vaginal or caesarean section delivery options. Cardiac-specific SAPPGs prescribe preconception care, including CVD screening, obstetric history with previous cardiac events and interventions, a comprehensive antenatal assessment, physical assessment, pertinent cardiac investigations, appropriate multidisciplinary team members, and maternal and fetal risk assessments. Additionally, the model of care (i.e., obstetrician or midwife group), level of hospital, and detailed management plans for labour and delivery modes are recommended according to the pregnant woman's cardiac status.

1.2 Research aim and objectives

1.2.1 Aim

The overarching theme of this research project was to explore the continuum of care for women with cardiac conditions during pregnancy benchmarked against the available cardiac-specific clinical practice guidelines in South Australia.

The following specific research questions and research objective underpinned the process.

1. What is the spectrum of cardiac disease in pregnancy, namely preexisting, congenital and newly acquired cardiovascular conditions?
2. What current cardiac-specific evidence-based CPGs inform the continuum of care for women with cardiac disease in pregnancy?
3. Do health practitioners adhere to the SAPPGS for these women across the SA Health metropolitan hospitals with obstetric services?
4. What are the predictors and factors for adherence to the statewide cardiac-specific CPGs?
5. How do the three major obstetric hospitals in SA vary in adherence to the guidelines?
6. Does the improved adherence (total score) to the CPGs determine the clinical outcomes for mothers and babies?

This thesis is not intended to determine ethnic disparities in adherence to the guidelines.

1.3 Scope, significance and intended outcomes

Cardiac conditions in pregnancy are under-resourced and under-researched areas because maternal heart disease burden is not quantifiable in Australia and New Zealand. In South Australia there has been no published audit or research into cardiac problems in pregnancy therefore the significance of this research is that it produces new evidence that verifies real-life practices for a cohort of women with cardiac disease during pregnancy in South Australia; identifies both disparities and gaps in the

recommended care and exemplars of practice and determines any correlation with clinical outcomes. Although international experience and clinical registries are important, Australian research contextualises the unique challenges of women within health care delivery services.[11] The significance of this research is that it produces new evidence that verifies real-life practices for a cohort of women with cardiac disease during pregnancy in South Australia; identifies both disparities and gaps in the recommended care and exemplars of practice and determines any correlation with clinical outcomes. The ultimate goals of the research are to improve the uptake of established statewide best practice guidelines through audit and feedback, and to emphasise the need for continuous quality improvement to prevent severe morbidities and mortalities in these women. The intended outcome of this work is to promote the adoption CPGs for women with cardiac disease in pregnancy that will enhance mother and baby clinical outcomes.

1.4 Thesis overview

This thesis consists of five chapters that include three published manuscripts (Table 1). The subsequent chapters present each study's aims and an expanded description of the materials and methods discussed in the accompanying papers (three published). Chapter 2 consists of a published discursive paper describing the spectrum of cardiac conditions and physiological changes during pregnancy for midwives and addresses their important role in the heart health team. It also provides an updated literature review with contemporary evidence on cardiac disease in pregnancy and clinical practice guidelines. Chapter 3 provides additional information on the methodology for the second publication. The first study is original research reporting on the evaluation of adherence to SAPPGs, using logistic regression analysis for the CPGs variables and making comparisons across the hospital sites and between the cardiac groups. Chapter 4 presents the second study, which describes the clinical variables' frequencies and determines their association with the overall adherence score, using linear regression analysis. Chapter 5 provides discussion and conclusion and encompasses a critical review of the doctoral work, summarising key findings, strengths and limitations. Additionally, clinical implications and recommendations arising from the thesis and future research are addressed.

Table 1 Thesis review

Chapter	Content	Research Objectives
Chapter 1	Introduction	Describes the background of thesis topic. Outlines the rationale, aims, and objectives of the thesis. Provides the overview of the thesis.

Chapter 2	Literature review and Manuscript 1: Cardiac conditions in pregnancy and the role of midwives: A discussion paper	The discursive paper describes the spectrum of cardiac conditions seen in pregnancy, associated complications, and management. Also, it explores the role of midwives in the pregnancy heart team. An updated literature review describes and evaluates recent evidence on cardiac conditions in pregnancy and related CPGs.
Chapter 3	Adherence to clinical practice guidelines for South Australian pregnant women with cardiac conditions between 2003 and 2013.	The first report on the evaluation adherence to statewide perinatal guidelines for pregnant women with cardiac conditions, with an overall adherence score out of possible 40. Identifies the predictors of adherence to SAPPGs with stratification of both the factors and the prior predictors of cardiac groups and three practice settings.
Chapter 4	Manuscript 3: The association between guidelines adherence and clinical outcomes during pregnancy in a cohort of women with cardiac comorbidities	Describes the frequency of clinical variables and determines their association with the SAPPGs adherence score. Describes the clinical variables, including maternal cardiac, obstetric, and neonatal outcomes, interventions, and complications.
Chapter 5	Discussion and Conclusion	A critical review of doctoral work that summarises the key findings, strengths, and limitations. It outlines the clinical implications, recommendations arising from the thesis and future research.

Chapter 2: Updated literature review

2.1 Overview of Chapter 2

Chapter 1 provided an overview of cardiac disease in pregnancy and noted that pertinent CPGs for cardiac disease in pregnancy translate complex research findings into recommendations to assist clinicians in decision-making. Additionally, adherence to CPGS can improve care and mitigate mortalities and morbidities. Chapter 1 introduced the research gap in reported evaluation of real-life practice adherence to CPGs recommendations. An initial literature review commenced in 2012 that aimed to identify and summarise available knowledge, opinions, and issues on the research topic, given the paucity of data available locally. The review was conducted through electronic databases using key terms. An orthodox systematic and Cochrane review was not feasible nor undertaken due to insufficient high-level evidence at the commencement of research. A review of international evidence and computerised databases informed the published manuscript included in this chapter, that outlines the spectrum of cardiac disease in pregnancy and describes cardiovascular physiological changes in pregnancy. The discursive paper highlights the greater potential role of midwives within the pregnancy heart team. Since midwives provide a therapeutic relationship and care throughout pregnancy, they are well placed to facilitate the integration of appropriate CPGs care.

2.1.1 Procedure

The researcher undertook the Joanna Briggs Institute (JBI) systematic review training and was assisted by the University's specialist librarian in health care at the outset of the research program with search strategy due to the paucity of literature available. The librarian appraised the search results to validate the appropriateness of search terms, databases, and fields and methodology.

2.1.2 Databases searches

An initial search of computerised databases included CLINICAL KEY, SCOPUS, PubMed/MEDLINE, Cumulative Index of Nursing and Allied Health Literature (CINAHL), PubMed and EMBASE. The review was commenced in February–March 2012 with broad search parameters of cardiovascular disease in pregnancy, but those yielded 55,964 articles incorporating the previous ten years (2012–2002). Therefore, a refined search using cardiac or heart disease in pregnancy was conducted. The final articles included in the initial literature review was 1,126. Ongoing review of the literature occurred throughout research project supported by library email alerts. Targeted search methods included using key terms that described the disease or conditions and used the Boolean 'OR 'operator, e.g., 'cardiac' OR 'heart' OR 'Congenital heart disease' OR 'acquired heart disease'. The search was narrowed by combining terms using the operator 'AND.' For example' heart disease,' 'cardiac,' 'adult congenital heart disease,' AND 'pregnancy outcomes" as well as 'risk assessment'. Cross-referencing based on

citations and bibliographies of retrieved articles yielded additional papers. The following research questions assisted the researcher in the search strategy to explore information that will provide insight on the proposed research for women with cardiac disease during pregnancy in South Australia.

7. What is the spectrum of cardiac disease in pregnancy?
8. What is the current evidence-based practice to support the continuum of care for women with cardiac disease in pregnancy?
9. What are the components CPGs, i.e. risk assessment, management and follow-up plan, for these women?
10. Who are the healthcare teams involved in the continuum of care of this cohort of women?
11. What is the role of midwives in caring for these women?

Additional search strategies, quality assessment process, and results not included in the following publication are available in Appendices A.

2.2 Manuscript, Paper One – Cardiac conditions in pregnancy and the role of midwives: a discussion paper

The following paper, 'Cardiac conditions in pregnancy and the role of midwives: A discussion paper', was published in *Nursing Open* February 2019.

Statement of authorship and publication 1

Statement of Authorship

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Principal Author

Name of Principal Author (Candidate)	Sandra Millington
Contribution to the Paper	Performed scoping of international literature and electronic data bases, interpreted findings, wrote manuscript, and acted as corresponding author
Overall percentage (%)	90%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	Date 21/04/2021

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate in include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	Judith Magarey
Contribution to the Paper	Supervised development of work, editing and manuscript evaluation
Signature	Date 3 4 21

Name of Co-Author	Gustaaf A Dekker

Contribution to the Paper	Conceptualisation, interpretation of data and critical revision of the manuscript for pertinent intellectual content
Signature	[redacted] Date 3 8 21
Name of Co-Author	Judith Magarey
Contribution to the Paper	Conceptualisation of original draft manuscript, interrater reliability and validation of Data abstraction tool (DAT)
Signature	[redacted] Date 4/8/21
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DISCURSIVE ARTICLE

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Cardiac conditions in pregnancy and the role of midwives: A discussion paper

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Abstract

Aim: This paper provides an overview of the two broad categories of cardiac conditions observed in pregnancy (congenital and acquired). It also identifies the midwives' role in the childbirth continuum and includes assessment, track and trigger systems and management during labour and delivery.

Design: Discussion paper.

Methods: Data were collected by reviewing international evidence and by searching computerized databases.

Results: Research has identified that women with associated risk factors of a cardiac condition who delay pregnancy have an increased risk of experiencing cardiovascular complications in pregnancy with poorer outcomes. The Three Ps in a Pod clinical initiative in the United Kingdom highlights working as a team in multidisciplinary programmes to improve mothers' care and save lives. Midwives play a key role during pregnancy and need to be appraised in relation to cardiovascular disease observed in pregnancy, its potential risks and anticipated problems and within the continuum of care.

KEYWORDS
advanced midwifery education, cardiovascular diagnosis, heart disease, pregnancy complications

1 | INTRODUCTION

In 2018, the European Society of Cardiology reported a greater risk of cardiovascular disease (CVD) in pregnancy in the Western world. This was attributed to increasing age at first pregnancy and pregnancies in the late reproductive years (or between ages 40–50) that included comorbidities (Regitz-Zagrosek et al., 2018). Historically, rheumatic heart disease (RHD) was a contributing factor for cardiac complications in pregnancy; however, today women who have undergone surgery for complex congenital heart disease (CHD) or have who have acquired cardiac disease are at high risk (Johns, 2013). This does not imply that expectant women with heart disease cannot achieve an uncomplicated pregnancy; many women do so. Good care is facilitated through appropriate preconception counselling and evaluation, when potential risks can be identified and discussed and, in some cases, through therapeutic interventions implemented to optimize the clinical status of mother and unborn child (Zöllner, Curry, & Johnson, 2013). However, accurate diagnosis of cardiac disease in pregnancy remains complex, as the physiological changes in the cardiovascular system during pregnancy mimic disease and, therefore, present a confusing clinical picture (Arafeh & Baird, 2006; Merrigan, 2009). Women with pre-existent or newly diagnosed cardiac conditions during pregnancy require both physiological and psychological support to achieve the best outcome for both mother and baby (Revell, 2016).

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The psychological state of a mother may influence transient changes in their cardiovascular system during labour and delivery, with emotions such as anxiety and fear linked to hypertension and increased vasoactive hormones (Nicholson et al., 2016; Revell, 2016). Current research has identified that perinatal depression is an important risk factor for pregnancy-associated CVD, particularly heart failure, and contributes to poorer outcomes, in turn (Nicholson et al., 2016). These women often require complex counselling, multidisciplinary team follow-ups and referral to a high-risk maternity hospital. As such, midwives have an important educational and supportive role throughout a woman's pregnancy (Revell, 2016).

What does this paper contribute to the wider global clinical community?

Cardiac disease remains a major global cause of maternal mortality and morbidity. Accurate diagnosis of cardiac disease in pregnancy remains complex, since physiological changes in the cardiovascular system during pregnancy mimic disease and, therefore, present a confusing clinical picture. This paper highlights the following:

- Midwives play a key role during pregnancy and need to be appraised of the CVD observed in pregnancy, its potential risks, anticipated problems and in terms of their role within the continuum of care.
- Midwives will often be the first healthcare providers to see pregnant women with cardiac disease and can facilitate risk assessment and detection of these problems to ensure optimal management.
- There is also a potential role for midwives within the childbirth continuum to collaborate in multidisciplinary teams with ongoing surveillance; perform risk assessments; and ensure parental health education, maternal awareness and self-management to optimize outcomes for both mother and baby.

2 | AIMS OF THE STUDY

The aim of this paper was to update midwives with an overview of the cardiovascular conditions observed in pregnancy, highlight management and consider their role with the health of mother and baby. Indeed, it is a challenge for midwives to reconcile a culture of risk and the changing profile of women giving birth with the philosophy of midwifery and midwifery education, as advocated by the International Confederation of Midwives (ICM) (Bharj et al., 2016). Although the phenomena of respectful care and over-medicalization reported in Bharj et al. (2016) are acknowledged, it will not be discussed in the context of this paper. Instead, the focus is on midwives as among the first healthcare providers to see pregnant women and their role in conducting risk assessment and facilitating optimal management for women-centred care (International Confederation of Midwives & Global Standards for Midwives Education, 2010). Research Ethics Committee approval was not required for this discussion paper.

3 | BACKGROUND

3.1 | The significance of cardiovascular disorders in pregnancy

Cardiac conditions typically seen in pregnancy fall into two broad categories: congenital and acquired (Johns, 2013). Corrected CHD is the most prevalent cardiac condition and is generally well tolerated, although this is dependent on the specific type of cardiac defect. Factors that influence how well a mother and her baby tolerate pregnancy include the maternal heart's functional status (i.e. the ventricular function), the severity of valvular disease and the presence of cyanosis or pulmonary hypertension (Johns, 2013). Cyanotic CHD in pregnant women also poses a significant risk for both mother and foetus, with a high incidence of stillbirth, preterm delivery and intrauterine growth restriction (IUGR) (Yu-Ling Tan, 2010).

During 2009 and 2014 in the UK, 189 women reportedly died from heart disease associated with or aggravated by pregnancy (Knight et al., 2016). Sudden arrhythmic cardiac death with normal hearts was the most common cause of heart disease-related deaths ($N = 53$, 35%), with ischaemia following ($N = 34$, 22%). Women who died and had pre-existing cardiac problems comprised 17% of that sample, while 77% of women were not known to have cardiac problems. This is a reminder to be cognizant of the possibility of undiagnosed cardiac disease in pregnant or recently delivered women (Knight et al., 2016).

The same "confidential" report on acquired heart disease found that 34 women died from ischaemic-related heart conditions, representing 22% of 153 cardiac deaths between 2009–2014 (Cantwell et al., 2011; Knight et al., 2016). Further, there were 16 deaths as a result of atherosclerosis and 11 due to coronary artery dissection (Cantwell et al., 2011; Knight et al., 2016). Increased maternal age and pre-existent risk factors such as stress, smoking, obesity, high cholesterol, diabetes, hypertension and a family history of heart disease all contribute to the increased risk of atherosclerotic coronary artery disease (CAD) associated with death in pregnancy (Burchill et al., 2015; Cantwell et al., 2011; Johns, 2013). Acquired cardiac conditions such as acute coronary syndrome (ACS), cardiomyopathies and arrhythmias also contribute to the global cause of complications in pregnancy and between 10 and 15% of indirect maternal mortality (Babic, Gabric, & Pintaric, 2011; Cantwell et al., 2011; Elkayam et al., 2014; Smith, Young, & Greer, 2008; Turitz & Friedman, 2014; Westhoff-Bleck, Podewski, Hilfiker, & Hilfiker-Kleiner, 2013). RHD remains a challenge in developing countries as a major cause of maternal mortality, mostly from severe mitral stenosis, with a mortality rate of up to 5% (Yu-Ling Tan, 2010). The latest Australian maternal data (dated between 2008–2012) reported 16 deaths from CVD, four of which were from dissection of the aorta, four were due to cardiomyopathy and two were a consequence of myocardial infarction (Humphrey et al., 2015).

With significant changes to midwifery education programmes and clinical practice in Australia (which advocate the ICM philosophy of midwifery and that pregnancy and childbirth are normal physiological processes), it is no longer routine practice for midwives to undertake a comprehensive antenatal physical examination for pregnant women (Chalmers, Mangiaterra, & Porter, 2001; Tierney, Sweet, Houston, & Ebert, 2018). However, it is beneficial to provide additional education for midwives on cardiac history, as well as assessment to address specific clinical issues for RHD for Indigenous women and recent migrants, as a component of culturally sensitive antenatal care (Bharj et al., 2016; Clarke & Boyle, 2014). The following sections detail the physiological cardiovascular adaptations during normal pregnancy, the track and trigger systems and labour and delivery information for midwives to consider in their practice.

3.2 | Cardiovascular adaptations during normal pregnancy

The following physiological changes present unique challenges for women who may be cardiac compromised in pregnancy (Ruys, Cornette, & Roos-Hesselink, 2013):

1. The increased intravascular volume, which peaks in the third trimester, is a potential problem in women with obstructive cardiac lesions, such as mitral or aortic stenosis, or with impaired ventricular function (Roberts & Adamson, 2013).
2. A progressive decrease in systemic vascular resistance (SVR) in pregnancy enables the mean arterial pressure (MAP) to be preserved despite an increase in cardiac output (CO). The MAP and systolic blood pressure (SBP) fall during pregnancy but returns to baseline in the late third trimester (Roberts & Adamson, 2013).
3. Marked fluctuations in CO during labour impose stress on an expectant mother's compromised cardiovascular system. During pregnancy, the overall CO increases by 30% to 50% and can unmask previously asymptomatic cardiac diseases (Roberts & Adamson, 2013). The CO then peaks in the final stage of labour from 10 to 30 min (Hall, George, & Granger, 2011; Harris, 2011; Roberts & Adamson, 2013). This increase is attributed to autotransfusion from the uterus and the venocaval release of volume in the lower extremities; however, the volume returns to the pre-labour level within an hour of delivery. In women who have pre-existent cardiac lesions with a fixed CO (i.e. pulmonary hypertension and mitral stenosis), adapting to these fluctuations may trigger clinical deterioration (Arafeh & Baird, 2006; Kaleschke & Baumgartner, 2011).
4. Hypercoagulability in pregnancy requires anticoagulation in women who have a high risk of arterial thrombosis and embolization or have a prosthetic heart valve. The increase in the coagulation factors VII, VIII, X and XII and fibrinogen accompanied by decreased anticoagulatory and fibrinolytic activity during pregnancy contribute to the prothrombotic state and increased risk of deep vein thrombosis. However, hypercoagulability in the peripartum period acts as a protection mechanism for major blood loss during delivery for the mother (Cox, Gogarten, & Marcus, 2005; Kaleschke & Baumgartner, 2011).

Table 1 provides a clinical reference of physiological changes that occur during pregnancy, highlighting the peak effect and potential risks.

4 | THE ROLE OF THE MIDWIFE

4.1 | Antenatal assessment during pregnancy

The midwives' role includes obtaining pertinent medical and cardiac history in the antepartum period. Specific risk factors such as hypertension, pre-eclampsia, smoking, obesity, diabetes, elevated

TABLE 1 Physiological changes that occur during pregnancy, labour and delivery

Haemodynamic alterations	Time of peak effect	Potential risks
Cardiac output increased 30%–50%	20–24 weeks	Women with limited cardiac function or reserve may develop heart failure
Stroke volume increased 20%–30%	20–24 weeks	Increased preload (central venous pressure or filling pressure) presents a problem for obstructed lesions (e.g. mitral or aortic stenosis) or ventricular dysfunction
Heart rate increased 10%–20%	Third trimester	Tachycardia causes palpitations and impairs ventricular filling
Blood volume increased 40%	20–24 weeks	Physiological "anaemia" of pregnancy due to less increase in erythrocyte mass
Peripheral vasodilation due to circulating oestrogen and direct arteriovenous connection with placenta to decrease SVR	Throughout pregnancy	Decreases in both blood pressure and valvular regurgitation
Minute ventilation increased 50%	Second trimester	Sensation of tachypnoea or dyspnoea

Source: Mendelson (2008); Roberts and Adamson (2013).

saturated fats and cholesterol that require referrals and ongoing self-management need to be identified (Knight et al., 2016; Revell, 2016). For example, a woman with a pre-existent cardiac state may have received preconception counselling and, thus, be well informed; however, this is not always the case. Midwives need to be appraised of the "at-risk" populations such as Indigenous people and immigrants, particularly those who are newly arrived or from African nations.

The potential problems with new or undiagnosed cardiac dysfunction in pregnancy could be mitigated by midwives who are able to distinguish between normal and abnormal cardiovascular symptoms and initiate early referral and investigations (Roberts & Ketchell, 2012). This requires knowledge of pre-existent cardiac conditions or conditions unmasked by the physiological changes in pregnancy (Knight et al., 2016). A recent UK-based report emphasized that women presenting repeatedly with cardiac symptoms and objective signs such as raised respiratory rate, persistent tachycardia and orthopnoea should be fully investigated (Knight et al., 2016). Examples of the cardiovascular symptoms observed in pregnancy are summarized in Table 2. The current track and trigger systems in clinical practice for midwives can improve recognition and response to clinical deterioration during pregnancy.

4.2 | Track and trigger systems

James, Endacott, and Stenhouse (2011) discussed the benefits of the current "track and trigger systems" that have been tailored to identify the altered physiology of pregnancy in the antepartum and intrapartum periods. Also known as the modified early obstetric warning system (MEOWS), this readily available tool empowers midwives to make good clinical judgements and recognize early clinical deterioration to escalate care (James et al., 2011). However, clinical effectiveness depends on accurate documentation of observations conducted at appropriate frequencies. The global trend has shifted "to examine severe maternal morbidity as well as mortality … to include women who may be moving, undetected, along the morbidity–mortality continuum" (James et al., 2011, p. 65)—and midwives are potentially ideal members of the multidisciplinary team to identify these women. However, this presents a challenge for midwives who may not have the clinical knowledge or skills to perform cardiovascular assessment. Table 3 provides a quick reference guide for midwives detailing the cardiovascular assessment findings during pregnancy that warrant further investigation.

TABLE 2 Cardiovascular symptoms observed in pregnancy

Due to pregnancy	Need to flag, as may represent cardiac disease
Fatigue	Palpitations, symptomatic at rest
Dizziness	
Palpitations	Persistent oedema
Lower extremity swelling/ peripheral oedema	Dyspnoea, progressive, nocturnal or at rest
Dyspnoea	Orthopnoea
Nocturia	Chest pain, exertional or at rest
Chest pain	
Syncope, vasovagal	Syncope, exertional

Source: Mendelson (2008, p. 7); Yu-Ling Tan (2010, p. 108).

Knight et al. (2016) mandated ready access to an electrocardiograph (ECG) machine and someone who can interpret ECGs as priority in consultant-led maternity units. Specialist midwives and doctors who are skilled in 12-lead ECG interpretation should know the changes in normal pregnancy. Left-axis deviation is considered normal, while similarly inverted or flattened T waves may be and so do not require further investigation (Canobbio et al., 2017; James et al., 2011). Pertinent findings in normal pregnancy for chest X-ray and 12-lead ECG investigations are outlined in Table 4. The South Australian Perinatal Practice Guidelines recommend the New York Heart Association Functional Classification Criteria tool for prediction of maternal and neonatal outcomes. These guidelines are used when counselling prospective parents to determine the level of hospital care required (SA Health, 2014). Currently, the modified World Health Organization classification is the most accurate system of risk assessment for maternal cardiovascular complications (Regitz-Zagrosek et al., 2018).

4.3 | Labour and delivery

Midwives need to be cognizant that the haemodynamic changes during labour and delivery present potential challenges for women with heart disease; therefore, they need to anticipate and be prepared for sudden clinical deterioration. Repositioning mothers to a left lateral position to avoid compression of the inferior vena cava by the gravid uterus for women who experience supine syndrome is recommended for labour. However, this may be inappropriate for women with some specific cardiac conditions (Canobbio et al., 2017; McGregor, Barron, & Rosene-Montella, 2015).

During each uterine contraction, a bolus of fluid is expelled into the intravascular space. Although it is transient and repetitive, for some at-risk women, these changes may exacerbate underlying cardiac conditions. During labour, the CO increases by 15%–20% and SBP by 10% (Regitz-Zagrosek et al., 2011). Concurrently, anxiety and pain stimulate the systemic nervous system to further elevate the SBP and heart rate (Canobbio et al., 2017; Harris, 2011). Physiological changes during labour affect various cardiac conditions differently, notably aortic diseases, obstructive valve disease and cardiomyopathy. During the second stage of labour when women use the prolonged "Valsalva" manoeuvre, increasing blood pressure and afterload can complicate aortic disease. Judicious management of fluid therapy and epidural anaesthesia may mitigate the risk of marked fluctuations in blood pressure that are detrimental to women with obstructive valve disease or cardiomyopathy (Arafeh & Baird, 2006; Roberts & Adamson, 2013).

Midwives recognize that delivery and management are tailored to a mother's specific cardiac state following a multidisciplinary team review. This team includes an obstetric high-risk physician, a

TABLE 3 Cardiovascular physical assessment findings during pregnancy

Due to pregnancy	May represent cardiac disease; requires investigation
Tachycardia	Bradycardia (Pulse < 50 bpm)
Ectopic beats	
Dilated/distended jugular/neck veins	Tachycardia (Pulse > 150 bpm)
Bounding pulses or collapsing pulse, dynamic precordium	Jugular venous distension
Loud first heart sound	
Third heart sound	Cardiomegaly
Systolic murmur (mid-ejection) at pulmonary area/lower left sternal edge	Right ventricular heave
Basilar rales	Loud pulmonic component of S2
Peripheral oedema	Summation gallop
	Loud systolic murmur (3–6/6)
	Diastolic murmur
	Cyanosis or clubbing
	Persistent rales
	Peripheral oedema

Source: Mendelson (2008, p. 8); Yu-Ling Tan (2010, p. 108)

cardiologist, an anaesthetist, an obstetrician and midwives (Curtis et al., 2009; SA Health, 2014). The proposed birth plan is also clearly documented, with vaginal delivery being the preferred mode and lower (uterine) segment caesarean section remaining limited to obstetric indications (Canobbio et al., 2017; Curtis et al., 2009). In instances of maternal collapse, both resuscitation and obstetric guidelines recommend that a perimortem caesarean delivery should be carried out within four minutes, but only if there is no return of spontaneous circulation with delivery of the foetus within five minutes beyond 20 weeks' gestation (McGregor et al., 2015; Soar et al., 2010; Vanden Hoek et al., 2010). Table 5 summarizes the risks and commonly encountered problems during labour.

TABLE 4 Chest X-ray and ECG findings in normal pregnancy

Chest X-ray	ECG
Straightened left heart border	Leftward shift of QRS axis
Increased cardiothoracic ratio	Small Q wave, inverted wave in lead III
Increased pulmonary vascular markings	ST segment and T wave changes
Small pleural effusions (early postpartum)	Atrial/ventricular ectopic

Source: Yu-Ling Tan (2010, p. 108).

Pregnancy has been regarded as the ultimate cardiac stress test that a woman may experience in her life (Samuels-Kalow & Funai, 2007; Yu-Ling Tan, 2010). The physiological changes increase the likelihood of a complicated pregnancy and birth in women with latent cardiac dysfunction (asymptomatic cardiac dysfunction) or a pre-existent cardiac dysfunctional state. Thus, it is important to highlight the cardiovascular adaptations that exacerbate acquired cardiac conditions.

5 | CONGENITAL CARDIAC CONDITIONS IN PREGNANCY

5.1 | Risks related to pregnancy and birth

The congenital defects that are likely to be problematic in pregnancy are complicated by pulmonary hypertension, cyanosis and severe left ventricular outflow tract obstruction, with cyanotic CHD posing the most significant risk to both mother and foetus (Cantwell et al., 2011; Kaleschke & Baumgartner, 2011). Cyanosis worsens during pregnancy due to the increased cardiac workload, while polycythaemia, hypoxaemia and cyanosis increase the risk of thromboembolic complications to 32% (van Mook & Peeters, 2008). Women with uncorrected cyanotic CHD also have increased cardiovascular maternal complication rates of up to 30% (Elkayam, Goland, Pieper, & Silversides, 2016), which is precisely why midwives need to be aware that pregnancy will be discouraged when mothers have an oxygen saturation of less than 85%, a haematocrit above 60% and recurrent syncope, due to maternal risk and a live birth rate of only 12% (Canobbio et al., 2017; Regitz-Zagrosek et al., 2011). In particular, hypoxaemia is poorly tolerated by the foetus and is associated with a high incidence of foetal loss, stillbirths, preterm delivery and IUGR. In these cases, the risk to mother and unborn child correlates with the former's resting oxygen saturation (Cox et al., 2005; van Mook & Peeters, 2008; Zöllner et al., 2013).

5.2 | Congenital valvular heart disease

Mitral valve stenosis is the most common RHD valvular lesion observed in pregnancy to require invasive intervention such as open mitral valve commissurotomy or balloon valvuloplasty prior to or during gestation (van Mook & Peeters, 2008). Prophylactic antibiotics are administered in labour to women with valve disease or a history of endocarditis or increased risk of sepsis, and the guarded use of oxytocin infusion during the third stage is recommended (Curtis et al., 2009; SA Health, 2014).

5.3 | Pulmonary hypertension or Eisenmenger syndrome

For women with pulmonary hypertension or Eisenmenger syndrome, the increasing cardiac pressure loads in pregnancy lead to right ventricular failure during the peri- and postpartum period and increase the maternal mortality rate to 30%–50% (Cox et al., 2005; Kempny

TABLE 5 Different diagnoses with corresponding risks and commonly encountered problems

Type of heart disease	Most common complications	Important information
Corrected CHD		
Atrial septal defect	Arrhythmias	Uncorrected ASD ↑risk of pre-eclampsia
Ventricular septal defect	Premature delivery (12%)	Uncorrected VSD ↑risk of pre-eclampsia
Atrioventricular septal defect	Arrhythmias (10%), deterioration of atrioventricular valve regurgitation (17%)	Reoccurrence of CHD (10%)
Tetralogy of Fallot	Arrhythmias (6%)	↑Risk of progression to right ventricular dilation secondary to severe pulmonary regurgitation
Coarctation of the aorta	Hypertensive disorders (11%)	Increased risk of aortic dissection
Transposition of the great arteries (Mustard/Senning procedures)	Arrhythmias (22%), heart failure (11%)	Irreversible ventricular dysfunction in 10%
Fontan operation	Arrhythmias (16%), heart failure (4%)	In case of cyanosis risk of miscarriage
Eisenmenger syndrome	Heart failure (21%), maternal mortality (↑50%)	Mainly in postpartum period (first 3 days)
Valvular heart disease		
Mitral stenosis	Heart failure (31%), arrhythmias (11%)	Mainly in patients with mitral valve <1.5 cm^2
Aortic stenosis	Heart failure (3%–44%), arrhythmias (6%–25%)	Mainly in patients with an aortic valve <1.5 cm^2
Pulmonary stenosis	Right-sided heart failure (9%)	Mainly in patients with moderate to severe pulmonary stenosis
Regurgitation lesions	Heart failure (7%), supraventricular tachycardia (9%)	Mainly in patients with decreased cardiac function at baseline
Mechanical valves	Valvular thrombus (↑10%), maternal mortality (↑4%)	Outcome depends on anticoagulation
Cardiomyopathy		
Peripartum cardiomyopathy (current pregnancy)	Severe heart failure at the end of pregnancy (100%), maternal mortality (15%)	Complete recovery of ventricular function in half of the patients
Peripartum cardiomyopathy (previous pregnancy, minus abnormal ventricular function)	Recurrence of heart failure (21%)	Ventricular function further decreases in some patients
Peripartum cardiomyopathy (previous pregnancy, plus abnormal ventricular function)	Recurrence of heart failure (44%), maternal mortality (20%)	Ventricular function further decreases in most patients
Dilated cardiomyopathy	Heart failure (25%), arrhythmias (19%)	Mainly in patients with abnormal ventricular function (LVEF < 45%) at baseline
Hypertrophic obstructive cardiomyopathy	Heart failure (28%)	Mainly in symptomatic patients at baseline; beta-blockers should be considered
Hypertrophic non-obstructive Cardiomyopathy	Low risk of heart failure	Mainly in symptomatic patients at baseline
Aortic disease		
Marfan syndrome	Aortic dissection (1%–10%)	High risk in patients with aortic diameter> 45 mm
Bicuspid aortic valve disease	Aortic dissection (<1%)	High risk in patients with aortic diameter> 50 mm
Turner's syndrome	Hypertensive disorders (67%), aortic dissection (5%)	Women with Turner's syndrome often not fertile
Ehlers–Danlos syndrome	Maternal mortality (11.5%)	↑Risk of spontaneous uterine rupture
Pulmonary arterial hypertension	Maternal mortality (17%–33%)	Mainly in postpartum period (first 3 days)

Note. ASD, Atrial septal defect; LVEF, left ventricular ejection fraction; VSD, ventricular septal defect.Source: Ruys et al. (2013).

et al., 2017). These women require a detailed delivery plan that considers the optimal timing and mode of delivery, postpartum intensive care and mechanical support and individualized support for many months postdelivery (Regitz-Zagrosek et al., 2018). Further, primary pulmonary artery hypertension secondary to CHD is a contraindication for pregnancy due to the poor prognosis for mother and baby, so termination is recommended (Canobbio et al., 2017; Gei & Montufar-Rueda, 2014; Johns, 2013).

6 | ACQUIRED CARDIAC CONDITIONS IN PREGNANCY

Acquired cardiac conditions are undetected or latent conditions where the stress of pregnancy precipitates clinical deterioration of a woman's cardiac state. In the latest UK-based report, these conditions included ACS, aortic dissection and peripartum cardiomyopathy (PPCM; Cantwell et al., 2011; Johns, 2013; Knight et al., 2016; Ruys et al., 2013).

6.1 | Acute coronary syndrome in pregnancy

ACS is an umbrella term that describes the spectrum of conditions resulting from a reduced coronary blood flow to the heart and range from acute myocardial ischaemia (unstable angina) to injury and necrosism, as seen in acute myocardial infarction (AMI) (Knight et al., 2016). ACS associated with the risk factors of smoking, hypertension, hyperlipidaemia, diabetes and family history in pregnancy was reported in the UK (Borna, Neamatipoor, & Radman, 2012; Clegg & Macnab, 2013; Knight et al., 2016; Pepine et al., 2015), with pregnancy-related risk factors such as pre-eclampsia, eclampsia, postpartum infection, thrombophilia and blood transfusion known to increase the risk of AMI between three- and fourfold (Cantwell et al., 2011; Elkayam et al., 2014; Ruys et al., 2013).

The causes of AMI in pregnancy are classified into two broad categories of atherosclerotic (often with cardiovascular risk factors) and non-atherosclerotic, which includes coronary arterial dissection, thrombosis and coronary artery spasm (spontaneous or drug induced) (Wuntakal, Shetty, Ioannou, Sharma, & Kurian, 2013). Merrigan (2009) stressed the need for recommendations to be implemented across multiple nurse settings to educate and guide staff on the care of pregnant women with AMI. Women with pre-existent CAD have an increased risk throughout pregnancy and immediately postpartum. Often, their clinical presentation will be atypical of ischaemia, with dyspnoea, vomiting or dizziness present (Cantwell et al., 2011). Although AMI in pregnancy was once considered a rare occurrence, recent statistics indicate increased incidence, with a maternal death rate ranging between 20%–37% (Knight et al., 2016; Merrigan, 2009; Wuntakal et al., 2013). With a growing number of women delaying childbirth to later reproductive years, ischaemic cardiac disease is expected to become more prevalent (Roth & Elkayam, 2008; Turitz & Friedman, 2014). Thus, women with AMI require complex care by a multidisciplinary team that includes the assistance of capable midwives (Cantwell et al., 2011; Elkayam et al., 2014; Johns, 2013; Knight et al., 2016; Merrigan, 2009).

Management of AMI is primarily interventional cardiac procedures (i.e. percutaneous coronary intervention) with introduction of bare-metal stents and/or coronary artery bypass surgery to improve coronary blood flow (Babic et al., 2011). The aim is to avoid the use of thrombolytics until after delivery because of the increased risk of heavy haemorrhage (Knight et al., 2016; Ruys et al., 2013).

6.2 | Aortic dissection

Aortic dissection, once considered rare in pregnancy, is now comparable to PPCM. In a recent Australian maternal mortality report, there were four deaths due to dissection of the aorta and four due to cardiomyopathy between 2008–2012 (Humphrey et al., 2015). This condition is evident in women who are diagnosed with Marfan or Ehlers–Danlos syndrome (connective tissue disorders), a bicuspid aortic valve, coarctation of the aorta (and a previous repair) or hypertension (Cantwell et al., 2011; Johns, 2013; Yu-Ling Tan, 2010). The exact precipitating cause is uncertain, but there is speculation that pregnancy predisposes women to aortic dissection because of the hormonal changes involved and the increased haemodynamic shear stress results in structural damage to vasculature (Zöllner et al., 2013). Midwives need to be cognizant of the fact that when a pregnant woman presents with severe chest, abdominal or back pain that requires opiate analgesia (excluding labour or postoperative pain), this warrants thorough investigation (Knight et al., 2016).

6.3 | Cardiomyopathies and heart failure

Cardiomyopathies in pregnancy include acquired and inherited diseases such as PPCM and toxic, hypertrophic, dilated, restrictive and idiopathic cardiomyopathies (Knight et al., 2016; van Mook & Peeters, 2008). Takotsubo syndrome, also known as "stress cardiomyopathy," previously reported in postmenopausal women, is a now potential cause for acute heart failure (AHF) in birthing (Kucia, Dekker, & Arstall, 2015; Minatoguchi et al., 2014). In particular, Takotsubo syndrome is a cardiac condition that mimics ACS with no significant CAD seen on angiography, yet the characteristic ballooning of the left ventricle impairs the heart's ability to pump effectively and is evident on early echocardiogram (Brezina & Isler, 2008; Kucia, 2015; Lyon et al., 2016). Published cases describe Takotsubo syndrome as occurring soon after birthing and is associated with multiparity, preterm labour, caesarean delivery and 25% peripartum haemorrhage. It is less commonly associated with pre-eclampsia and haemolysis, elevated liver enzymes and low platelet count syndrome (Kucia, 2015; Kucia et al., 2015). Importantly, early recognition of Takotsubo syndrome for referral to cardiology services helps ensure a full recovery is made and avoids inappropriate use of vasopressors, which have been considered counterproductive (Kucia, 2015).

6.4 | Peripartum cardiomyopathy

Women with AHF symptoms in the last month of pregnancy or up to six months' postpartum, with the diagnosis of PPCM by exclusion, will arrive with breathlessness, orthopnoea and peripheral oedema (Johns, 2013; Knight et al., 2016). The multifactorial risk factors for PPCM are increased haemodynamic stress, advanced maternal age, multiparous pregnancies and/or multiple or teenage pregnancies, African ethnicity, smoking, diabetes, hypertension and pre-eclampsia (Johns, 2013; Yu-Ling Tan, 2010). Women who experience severe AHF and cardiogenic shock may require

urgent delivery, mechanical cardiovascular support (i.e. use of an intra-aortic balloon pump or left ventricular assist device) and progress to heart transplantation (Knight et al., 2016). Midwives should know that subsequent pregnancies are considered high risk, regardless of whether a woman's left ventricular function has returned to normal. Therefore, these women require care in high-risk management facilities to address the increased risk of heart failure reoccurrence (Knight et al., 2016; van Mook & Peeters, 2008).

6.5 | Mitral and aortic valve stenosis

Valvular disease in pregnancy is the result of RHD and the most common lesion mitral stenosis. If severe, the maternal mortality increases up to 5%, with clinical deterioration evident in the third trimester or during labour and delivery (Johns, 2013; Yu-Ling Tan, 2010). Rheumatic mitral stenosis has an asymptomatic phase extending 10 to 20 years, so a woman's initial diagnosis may occur during pregnancy due to the cumulative effect of tachycardia, increased blood volume and cardiac output, leading to cardiac decompensation. This results in tachyarrhythmia (rapid atrial fibrillation) or acute pulmonary oedema (Yu-Ling Tan, 2010). Approximately 10% of women with significant aortic valve stenosis suffer a cardiac event in comparison with those with mild or moderate stenosis, who experience uneventful pregnancies (Canobbio et al., 2017). Aortic valve stenosis contributes to enlargement of the left ventricle, thus restricting the coronary blood supply and causing chest pain (angina pectoris). The key message for midwives is that for women with valvular disease, the presence of a tachyarrhythmia, such as newly acquired atrial fibrillation, affects cardiac function and may cause secondary pulmonary hypertension (Canobbio et al., 2017).

6.6 | Arrhythmias

Benign and problematic arrhythmias are observed increasingly in women with heart disease during pregnancy (Cantwell et al., 2011; Knight et al., 2016). Bradyarrhythmias are well tolerated, but some women will require insertion of a pacemaker (Ruys et al., 2013). The risk of arrhythmias peaks during labour and delivery when tachyarrhythmia (which is the most prevalent) requires prompt treatment using non-teratogenic drug therapy or electrical therapy (Canobbio et al., 2017; van Mook & Peeters, 2008). Midwives will need to monitor closely the maternal heart rate during labour. In cases of women with pre-existing histories of tachyarrhythmia, the risk of exacerbation is 20% to 50%, regardless of whether one has structural heart disease (Regitz-Zagrosek et al., 2011). Sustained tachyarrhythmia is not tolerated in women with structural heart disease or CHD so they require selective drug therapy that is not toxic to the foetus (Canobbio et al., 2017). Catheter ablation therapy of the node or an accessory pathway causing the arrhythmia may be performed prior to or following pregnancy (Regitz-Zagrosek et al., 2011). Digoxin and β-blocking agents are first choice of drug therapy in tachyarrhythmias, and if required, electrical cardioversion can be performed safely in pregnancy (Ruys et al., 2013). The most common antiarrhythmic amiodarone is foetotoxic and, therefore, is administered as a last resort (Regitz-Zagrosek et al., 2011).

6.7 | Sudden arrhythmic death syndrome

According to the latest UK confidential enquiries, sudden arrhythmic death syndrome (SADS) has recently emerged as the most common cause of maternal cardiac death (38%) (Cantwell et al., 2011; Knight et al., 2016). Autopsies have shown no histopathological abnormalities of the heart to account for these women's deaths (Knight et al., 2016). SADS has been defined as "sudden death in an adult for which no cause can be identified" (Zöllner et al., 2013, p. 92) and appears to be related to arrhythmias. Associated factors to consider are cardiac hypertrophy and obesity with a body mass index between 30–45 (Regitz-Zagrosek et al., 2011). Inherited arrhythmic disorders such as long QT syndrome increase the risk of sudden cardiac death, especially in the postpartum months; therefore, β-blocking agents are recommended during and following pregnancy (Canobbio et al., 2017; Regitz-Zagrosek et al., 2011). In view of increased CVD in pregnancy, we need to improve multidisciplinary collaboration, as emphasized in Knight et al. (2016). Alternatively, should we instead explore advanced practice roles such as specialist midwifery tailored to CVD? Indeed, as discussed in Multidisciplinary Management For Both Cardiac Groups7.3, midwives play a key supportive role for pregnant women with a cardiac condition in these multidisciplinary teams.

7 | MULTIDISCIPLINARY MANAGEMENT FOR BOTH CARDIAC GROUPS

Women with cardiac disease and moderate or high risk of complication in pregnancy have better outcomes when managed by a multidisciplinary team—particularly, a pregnancy heart team (Arafeh & Baird, 2006; Regitz-Zagrosek et al., 2018). This depends on good multidisciplinary collaboration between specialties such as congenital cardiac imaging interventional catheterization, congenital cardiac surgery and anaesthesia, heart failure, transplantation, electrophysiology and reproductive and high-risk pregnancy services. Naturally, their individual availability may be limited for women with more complex diseases (Cusimano, Pudwell, Roddy, Cho, & Smith, 2014; Rich-Edwards, 2012).

The teamwork for multidisciplinary management across community-based programmes and tertiary care centres was the focus in Knight et al. (2016). This is a crucial research area, as most adults with CHD are not "cured" and require lifelong comprehensive care from specialists who have expertise in this complex arena (Rich-Edwards, 2012). Women with previously undiagnosed heart disease during pregnancy require immediate referral to cardiologists. However, high-risk obstetric clinics may not necessarily be

supported by grown-up congenital heart (GUCH) teams (Abdin, 2006). Hatchett, McLaren, Corrigan, and Filer (2015) reported on GUCH nursing services and found patients expressed enhanced feelings of safety in coping with the demands of pregnancy and a heart condition, as well as satisfaction with the information provided and continuity of care through important life transitions. Their research findings demonstrated the value and contribution of a specialist nursing service to women's experiences, particularly in terms of effective care coordination, monitoring and support (Hatchett et al., 2015). Given the recent reported deaths as a result of atherosclerosis and ischaemic-related heart conditions, there also needs to be some discussion on the services required and available for women with ACS.

7.1 | Cardiac rehabilitation programmes

Merrigan (2009) stated that women have worse outcomes than men following midlife AMI, and therefore, innovative interventions responsive to women's unique recovery need to be developed. It is recommended a woman traumatized by a cardiac event during pregnancy have a psychologist and a mental health nurse included in the multidisciplinary team involved in follow-up care (Merrigan, 2009). Tailored cardiac rehabilitation programmes that include midwives and lactation consultants who consider the issues of women with a new baby or the appropriateness of attending cardiac rehabilitation with older, post-AMI patients are also recommended for women with AMI during pregnancy.

"Three Ps in a Pod" is an educational initiative that improves the care of women in pregnancy. An informative poster was distributed to all women in acute medicine and emergency departments to assist clinicians in recognizing the key causes of maternal death (Knight et al., 2016). The three Ps represent "pregnancy," "postnatal" and "pick it up" (both the phone and the problem) and help outline the key messages from the maternal mortality report published by MBRRACE-UK (Royal College of Physicians & Surgeons of Glasgow, 2019).

This clinical resource takes the initiative to address some of the factors contributing to maternal deaths from cardiac disease, including:

1. Failure to accurately diagnose cardiac problems.
2. Lack of early involvement of senior clinicians from obstetric and cardiology multidisciplinary teams, particularly when pregnant or postpartum women present to emergency departments.
3. Underestimation of the severity of the condition.
4. Lack of communication between multidisciplinary staff.
5. Absence of clear policies addressing cardiac problems.
6. Lack of pre-pregnancy counselling available both in paediatric cardiology transition services and to women of child-bearing age with known cardiac disease.
7. Lack of co-location of obstetric and cardiac services, which jeopardizes interdisciplinary working and communication (Arafeh & Baird, 2006; Canobbio et al., 2017; Knight et al., 2016).

7.2 | Relevance to clinical practice

The Three Ps in a Pod clinical initiative in the UK highlights working as a team in multidisciplinary programmes to improve mothers' care and save lives (Knight et al., 2016). Evidently, midwives play a key role during pregnancy and need to be appraised of the CVD observed in pregnancy, including its potential risks and anticipated problems and to consider their role within the continuum of care. Midwives are well equipped to assist in the normal birthing process but require additional knowledge to address the changing needs of women with CVD. Alternatively, a specialist midwife could ensure surveillance and management that includes prompt recognition and response to clinical deterioration (James et al., 2011). Future research is needed to explore the current continuum of care for women with CVD during pregnancy to identify gaps in clinical practice.

8 | CONCLUSION

Improving the detection of women with newly acquired cardiac conditions, and improving surveillance and maintaining the continuum of cardiac care for women with CHD will together improve the outcome for both mother and baby. As shown, the role of midwives in childbirth facilitates ongoing surveillance, risk assessment, parental health education, maternal awareness and self-management to optimize outcomes.

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CONFLICT OF INTEREST

The authors of this paper have no conflicts of interest in conducting this study. The authors declare that this study was conducted in the absence of any financial or commercial relationships that could be construed as a potential conflict of interest.

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2.3 Updated literature review

An updated literature review in 2021 identified new research that included quantitative and qualitative analyses with previous search terms and strategies. Search results were managed in the EndNote library (EndNote X9) and duplicates were removed. In the original discursive paper, the PICO (patient/ problem, intervention, comparison and outcome) methodology for selected articles was most relevant to the paper aims. In this updated literature review the PQRS system (preview, question, read and summarise) was more appropriate for the thesis aims and objectives. The search strategy applied to the search from November 2020 to September 2021. Twenty-eight recent studies included in the updated review are outlined in Table 2.

Selection criteria

Articles were selected based on their relevance to the research topic by the title, keywords, abstract or title, but were excluded if there was no available abstract using the PQRS system. The population was restricted to females diagnosed with preexisting cardiac disease or cardiac condition acquired during pregnancy. Studies that described or assessed cardiac-specific CPGs, continuum of care, risk stratification models and management during pregnancy were included. Likewise, papers that reported pregnancy complications and clinical cardiac outcomes were reviewed.

Exclusion criteria

Papers were screened and excluded on the following basis: editorials, letters and opinion pieces, non-English, and not related to the research topic. Although studies from diverse global countries provide innovations and insight into healthcare research findings, substantial contextual differences make the findings irrelevant for translation into practice. Therefore, the review focused on issues in developed countries.

Quality assessment of included literature

The included studies were assessed with the Critical Appraisal Skills Programme (CASP) approach to determine trustworthiness, examine the significance of reported results and assess relevance to the area of practice.[28] Selected papers were critically appraised, summarised and presented as themes, available in the Appendices.

Search results

A total of 746 articles were retrieved, and 28 papers were selected for inclusion. The included studies were prospective/retrospective observational, comparative studies, systematic reviews and meta-analyses, state of the art reviews, and cardiac-specific CPGs. The themes identified encompassed the spectrum of cardiac conditions in pregnancy, risk factors, assessment and management, predictors, and pregnancy outcomes for mother and baby. A limited number of papers addressed clinical practice adherence to CPGs, especially cardiac.

Clinical Practice Guidelines

Of the twenty papers associated with CPGs or clinical practice retrieved, only three articles were specific to cardiac disease in pregnancy and, therefore, included in the Appendices. As discussed in Chapter 1, the initial ESC Guidelines for managing cardiovascular disease in pregnancy published in 2011 were recently revised. An updated version 4.0 of the South Australia perinatal clinical guidelines for cardiac disease in pregnancy was published in 2014.[18] Likewise, contemporary Australian CPGs related to pregnancy but not specific to cardiac disease were published in 2020 apart from the RHD guidelines (see Appendices).[24] The A common theme in the remaining articles was CPGs implementation strategies, which are discussed later in the thesis, and related publications.[28-30] Two Australian research examples are a prospective survey of women's perception of antenatal care, which identified barriers and facilitators, and a study examining the length of time for screening and content of antenatal care.[31,32]

Rheumatic heart disease in Australia

In Australia, Acute Rheumatic fever (ARF) and Rheumatic heart disease (RHD) predominantly occurs in approximately 87%. Aboriginal and Torres Strait islander people but the results are dependent on the dataset used i.e., Australian Institute of Health and Welfare (AIHW) and patient registrations from the RHD Control programs. RHD is a notifiable disease in Western Australia, South Australia, Northern Territory and Queensland. RHD is notifiable for persons aged less than thirty-five years in Queensland. [33]

Females are more likely than males to be diagnosed than males, with highest number of cases reported in the Northern Territory and Queensland through RHD register, whilst in South Australia and New South Wales contain the smallest number of registrants. Also, in the non-indigenous population ARF and RHD are more commonly seen from age of fifty-five which represent the older population affected by ARF and RHD prior to 1960's. [33] Evidence based guidelines specific to RHD were initially created in 2006, updated in 2012 and 2020 and more recently in March 2022. The current RHD guidelines have been substantially revised, with the former chapter on RHD in pregnancy renamed women and girls with RHD, and incorporates a whole-life approach, with an emphasis on the importance of transition to adult care, reproductive health, and preconception care. [33]. Salient practice points identified reduced exercise tolerance or breathlessness in a pregnant woman from a high-risk population should not be attributed to pregnancy or anaemia; but clinicians should consider and investigate for RHD. [33] Also, the need for effective multidisciplinary, community-centred teams, age-appropriate, inclusive of reproductive, cardiac, and other health care and continues through the lifespan. Pre-conception diagnosis of RHD allows optimisation of management including surgical management before pregnancy. [33] The most current SAPPGS (2021) and SA pregnancy record include clinical prompts in the antenatal assessment checklist for clinicians to identify those pregnant or post-partum woman at

higher risk of or diagnosed with RHD who presents with breathlessness, orthopnoea, wheeze or worsening fatigue and will need to be investigated with an echocardiogram. [33]

The American College of Obstetrics and Gynaecology (ACOG) contemporary practice bulletin on pregnancy and heart disease, incorporated the recent ESC CPGs but added contextualised clinical toolkits developed within the USA.[34].The California Maternal Quality Care Collaborative (CMQCC) CVD evaluation toolkits aimed to help clinicians distinguish between signs and symptoms of cardiac disease and those of normal pregnancy and therefore, triage to appropriate cardiac evaluation; see Figures 1 and 2.[34]. Appropriate care allocation and assessment are tabled using traffic light colours. Green indicates clinicians can rely on routine care and reassurance, while yellow flags suggest caution and non-urgent evaluation. Red prompts clinicians stop and promptly assess and contact the pregnancy heart team. The assessment requires clinicians to obtain the woman's CVD history and self-reported symptoms, vital signs and physical evaluation [34]. These toolkits equip clinicians with a concise reference to facilitate the uptake of rapid assessment and triage guidelines. The ACOG CPGS also included who should be in the 'ad hoc' pregnancy heart health team aligned with the mWHO risk classification for women with preexisting CVD [34]. The management of specific cardiac lesions, acute coronary events, and cardiac arrest during pregnancy was also discussed [34]. The SAPPGs has not yet taken up this specific toolkit.

Figure 1 CVD assessment algorithm for pregnant and postpartum women

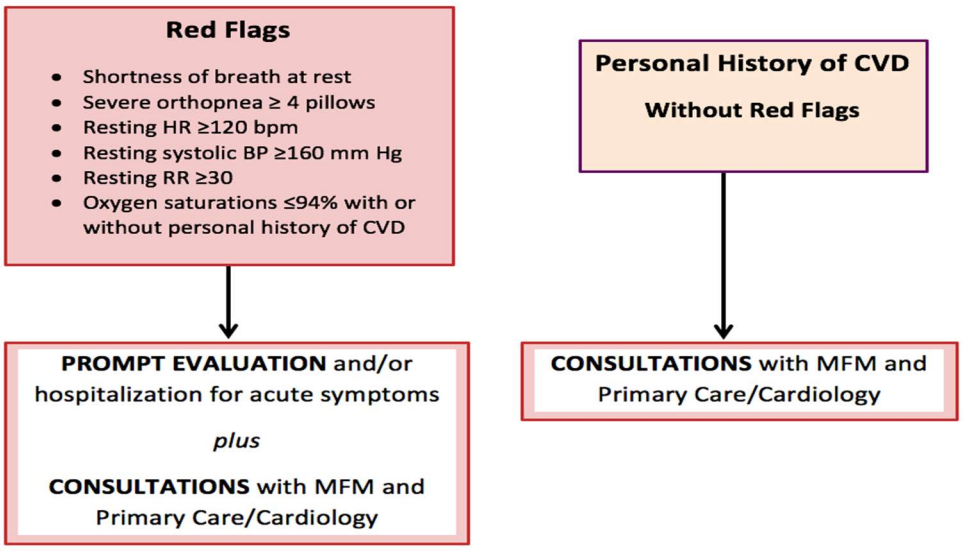
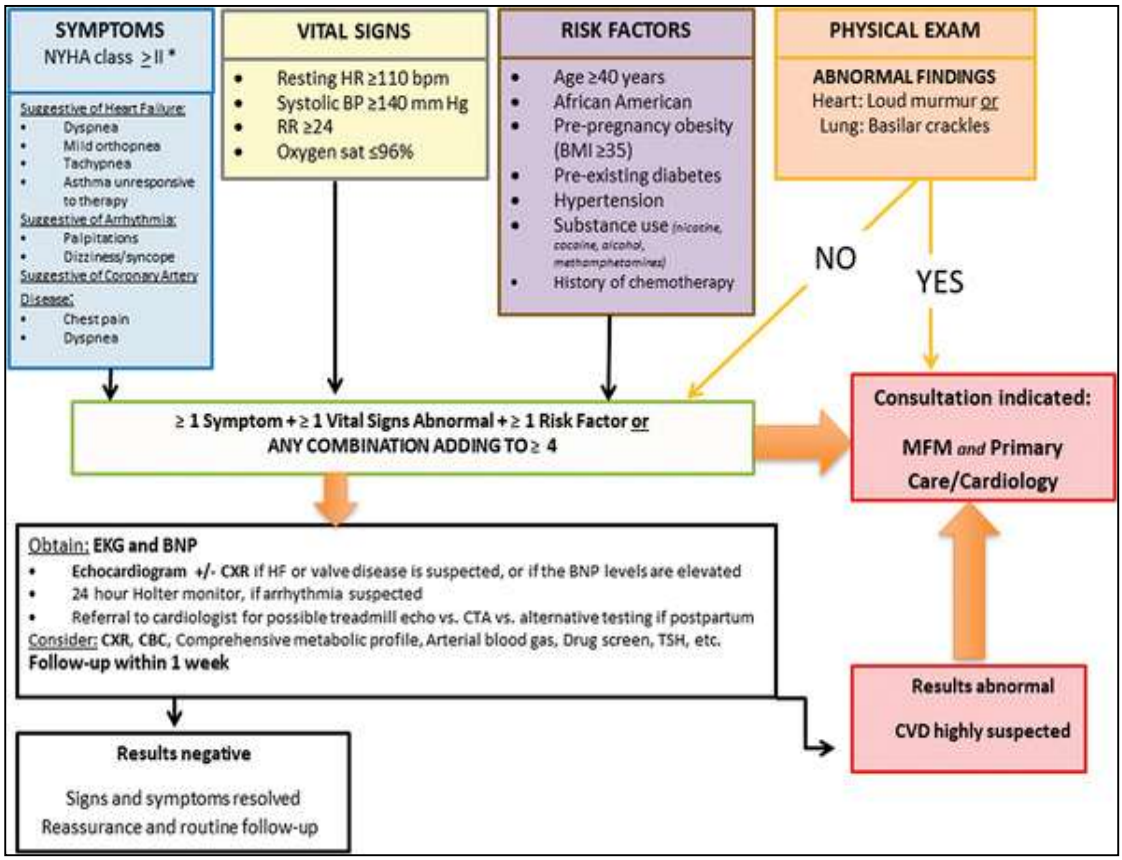


Figure 2 CVD assessment algorithm for pregnant and postpartum women



Legend: *The NYHA Functional Classification accessed via http://www.heart.org/HEARTORG/Conditions/HeartFailure/AboutHeartFailure/Classes-of-Heart-Failure_UCM_306328_Article. jsp. **Abbreviations**: **BMI**, body mass index; **BNP**, brain natriuretic peptide; **BP**, blood pressure; **CBC**, complete blood count; **CVD**, cardiovascular disease; **CXR**, chest x-ray; **EKG**, electrocardiogram; **HR**, heart rate; **MFM**, maternal-fetal medicine; **TSH**, thyroid-stimulating hormone; **NYHA**, New York Heart Association; **RR**, respiratory rate**.** California Department of Public Health, 2017; supported by Title V funds. Developed in partnership with California Maternal Quality Care Collaborative Cardiovascular Disease in Pregnancy and Postpartum Taskforce. Both images were used with permission from CMQCC org. October 2021. Visit www.CMQCC.org for further details

Congenital heart disease and pregnancy outcomes

Twelve publications from the international prospective ROPAC registry reported the results of observational studies describing characteristics and frequencies of specific structural cardiac conditions and their pregnancy outcomes [3,7,9,21,37-42,44, 49]. The prospective registry timeframe extended from 2007 to 2018 and included 53 countries and 138 centres. Primary outcomes were defined as maternal death or heart failure. Reducing maternal mortality was a World Health Organization (WHO) global health goal, which the ROPAC studies aimed to address by defining contemporary disease-specific outcomes in pregnant women with heart disease. Secondary outcomes were other cardiac, obstetric and fetal outcomes. The most prevalent diagnoses were congenital (57%) and valvular heart disease (29%) of the 5,739 enrolled pregnant women with a mean age of 29.5.[3] Overall mortality was 0.6% but highest in the pulmonary hypertension group (9%).[3] The ROPAC registries was the first of its kind in quality, scope and governance. The prepregnancy state of women' cardiac health was shown to strongly correlate with adverse pregnancy outcomes in women with CHD.[7] The implication of

these studies is that CPGs' recommendation that preconception counselling should be followed by an individualised guideline driven care plan in any subsequent pregnancy and include a multidisciplinary pregnancy health team.[7]

Recent ROPAC publications provide a more detailed overview of congenital heart disease. They also examine subgroups of women with aortic coarctation (CoA), repaired Tetralogy of Fallot (TOF), preexisting and pregnancy acquired IHD. In the subset of 303 CoA pregnancies, 9.6% of the women had unrepaired CoA and 27.1% preexisting hypertension. The results showed low maternal adverse outcome events (MACE) and hypertensive disorder rates, implying that pregnancy was safer and better tolerated than previously appreciated. [38] Similarly, TOF, the most common cyanotic congenital heart defect, was examined in a subgroup of 421 women with a mean age of 28.8 years and 53.3% nulliparous to explore pregnancy outcomes and assess right ventricular (RV) dimensions. No maternal deaths occurred, and complication rates were low. [38] Pulmonary regurgitation (PR) was a predictor of RV dilation occurring in 49% of women but was significantly associated with severe PR. There were 48% caesarean sections as the mode of delivery, reported as a suboptimal implementation of guidelines recommendations.[38] Maternal mortality was highest in the women with pulmonary artery hypertension (PAH) group (9%).[3]. Pregnancy outcomes are poor in women with pulmonary hypertension and classified as mWHO class IV. Therefore, CPGs recommend these women avoid pregnancy. [2, 41]

In the ROPAC study, pregnant women in the cohort (n=151) were categorised according to their PH aetiology consisting of idiopathic (iPAH), associated with CHD (CHD-PAH) or other diseases (oPAH), e.g., connective tissue disease or vascular malformations as Group 1. Most women (75%) were diagnosed with PH before pregnancy. Group 2 consisted of 74% of the women with PH and resulted from left heart disease (LHD-PAH, n=112), i.e., left ventricular systolic dysfunction, valvular disease or congenital/acquired left heart inflow or outflow tract obstructions or congenital cardiomyopathies [41]. Seven maternal deaths occurred, five of them in the first week postpartum following a spontaneous or induced delivery and attributed to acute heart failure. [41] One woman reached full-term pregnancy but died of cardiogenic shock postpartum. There was one sudden death caused by maternal heart failure. The highest mortality was in iPAH (3/7, 43%), followed by LHD-PAH (3/112, 2.7%) and, lastly, CHD-PAH (1/28, 3.6%). [41] Caesarean sections were the prevalent mode of delivery in 92 women (63.4%) but were planned in 83 women (90.2%), mainly for cardiac indications. Complications were miscarriage (5.6%) fetal mortality (2%), premature delivery 921.7%), low birth weight (19.0%) and neonatal mortality (0.7%). [41] Lower mortality rates than previously reported reflected the specialised care available for the pregnancy and delivery.

Limitations for the large prospective ROPAC registry, which included all heart disease groups and described the real-life clinical practice, are summarised below.

- Both maternal and neonatal mortality was reported only up to one week postpartum. Therefore, underestimating one component of the primary endpoint was highly likely and needed to be considered upon comparisons with other studies.
- Women with cardiac disease in their cohort were predominantly managed in specialised tertiary centres interested in this field. Outcomes in non-tertiary centres may differ, so caution is required in generalising of the results to whole populations.
- Although the major advantage of a prospective registry was documentation of clinical reality, potential selection bias was present. There was no guarantee (although requested and stressed) that consecutive patients from all centres were included.

The ROPAC registry analyses took into account disparities in health resources in the different countries participating in the registry. This was adjusted for statistically specifically in the primary ROPAC paper the authors state "We considered the patients without PAH and AOP. Trends were analysed for developed and emerging countries and for CONHD, VHD and CMP patients separately. We applied generalized linear mixed effect (LME) models (Logit link function) to accommodate within country and site clustering, both for determinants of the study endpoints and for trends over time." [3] Furthermore, the number and constitution of participating centres changed over the timeframe. [3].

In the ROPAC study the primary endpoint was maternal outcome, defined as all-cause maternal mortality and/or heart failure. Maternal mortality was defined as the death of the mother during pregnancy or within one week post-partum. Heart failure was defined according to the ESC and AHA guidelines and heart failure episodes were only included where hospital admission, new treatment or changes in existing treatment occurred. Secondary endpoints included other cardiovascular outcomes (arrhythmias, thrombotic events (including valve thrombosis) and aortic dissection. Also, Supraventricular or ventricular arrhythmias requiring treatment or hospitalization were included. Obstetric events (post-partum hemorrhage, emergency Caesarean section, pre-eclampsia, eclampsia or pregnancy-induced hypertension) and fetal events (prematurity (<37 weeks), fetal mortality, early neonatal mortality, intra-uterine growth retardation, low birth weight (<2500 gram) or low Apgar score (<7) as well. Post-partum hemorrhage was defined as increased blood loss (>500 mL after vaginal delivery or >1000 mL after caesarean delivery) directly after delivery and within 24 hours postpartum and Haemolysis, Elevated Liver enzymes and Low Platelets (HELLP) syndrome, pre-eclampsia, eclampsia and pregnancy-induced hypertension were defined according to the 2012 the International Society for the Study of Hypertension in Pregnancy (ISSHP) statement.[49] Fetal mortality was defined as the death after 24 weeks of gestation up until before birth, including still birth. Early neonatal mortality was defined as the death of a live-born baby within one week of life. Neonatal mortality was defined as the death of a live-born baby within the first six months of life. Premature birth was defined as birth before 37 weeks of gestation. Low birth weight was defined as a birth weight of below 2500 grams. Low Apgar score was defined as an Apgar score at 5 minutes of below 7. [3]

Acute coronary syndrome and ischaemic heart disease

Ischaemic heart disease in pregnant women is increasing, but there is a paucity of data. This was the impetus to describe the pregnancy outcomes of these women in the ROPAC registry. Both pregnancy-onset and preexisting IHD pregnant women were included (n= 117). Of the 104 women with preexisting IHD, 11 suffered from ACS during pregnancy. ST-segment elevation myocardial (STEMI) was more prevalent than non-ST-segment elevation myocardial infarction (NSTEMI) and the underlying pathology of atherosclerosis. Thirteen women with pregnancy-onset IHD experienced NSTEMI. Smoking in pregnancy correlated with ACS. The primary mode of delivery was a caesarean section in 55.8% of women with preexisting IHD and 84.6% with pregnancy-onset IHD. The rates of preterm births were significant, at 20.2% for preexisting IHD and 38.5% for pregnancy-onset IHD [9]. Given the high rate of ischaemic events, these findings support the SAPPGs recommendations that these women should be considered moderate to high risk and should address the lifestyle risk factors of smoking and ACS during pregnancy [9].

Risk assessments and predictors for pregnancy outcomes

The Cardiac Disease in Pregnancy study (CARPREG II) prospectively enrolled consecutive pregnant women (n=1,938) with heart disease to examine their cardiac outcomes during pregnancy and their temporal trends and incorporate these into a new risk index [17]. Women with congenital and acquired heart disease or arrhythmias who received care at two large Canadian tertiary care hospitals were included. The initial CARPREG multicentre study developed a risk index for predicting maternal cardiac complications utilising general maternal clinical and echocardiographic data obtained during the baseline antepartum visit.[17]. Therefore, CARPREG II used the three available risk index models in all pregnancies to score the women in the cohort to update the CARPREG risk index. The models are CARPREG, ZAHARA (Zwangerschap Bij Aangeboren HARtAwijking (Pregnancy in Women With Congenital Heart Disease), a weighted risk score that includes components of the CARPREG risk index), and the consensus modified World Health Organization (mWHO) classification [2,41,44]. Further descriptions of the risk models are included in Appendices A. This study highlighted the need for further research on the process of practice/care during pregnancy for these women. The 2021 version cardiac-specific SAPPGs have been updated with these international risk assessment models.

Synthesis of review

The updated literature review confirmed emerging interest in cardiac disease in pregnancy, given an increasing trend of pregnant women presenting in the high risk category. Research has been limited to risk stratification, predictors of pregnancy outcomes, and management during pregnancy. However, the core issues that require further investigation are validating the efficacy of available CPGs, identifying

the optimal model of care for women with cardiac conditions during pregnancy, and integrated care of the multidisciplinary pregnancy heart team.

2.4 Summary of Chapter 2

The updated literature review identified the body of work related to women with heart disease in pregnancy and best practice guidelines that inform clinical decision-making in practice. Registry-based studies described the characteristics and frequencies of structural, preexisting and acquired cardiac conditions in pregnancy and pregnancy outcomes. It has also highlighted updated international and statewide cardiac-specific CPGs. These are supported by the consensus of expert panels and evidence limited to prospective, retrospective observational studies, systematic reviews and reviews. Understanding how the care process affects maternal outcomes in pregnant women with heart disease is an important research gap; specific cardiovascular and obstetric care components may improve these women's outcomes. Therefore, the updated literature review strengthens the case for further research that evaluates the care process, namely cardiac-specific CPGs for pregnant women with cardiac conditions.

Table 2. Summary of characteristics of studies identified in the updated literature review

Study	Design	Country / Sample size	Location	Outcomes measured/comments
Ramlakhan et al. 2021[7]	Prospective International Observational ROPAC registry	53 countries/ overall cohort *5,739 pregnancies, and n= 3295 (57.4%) CHD*	*138 centres*	**ROPAC registry report**: A detailed overview of the characteristics and pregnancy outcomes for women with CHD. The prepregnancy cardiac state is strongly related to adverse pregnancy outcomes. Therefore, prepregnancy counselling is important. Follow-up during and after pregnancy must be individualised to the woman's needs and the complexity of her CHD and include a multidisciplinary pregnancy heart team. If the required expertise is unavailable locally, telephone or digital consultations with a specialist tertiary centre should be considered.
Ramlakhan et al. 2021[37]	Prospective International Observational ROPAC registry	53 countries/ overall cohort *5,739 pregnancies*	*138 centres*	**ROPAC registry report:** Pregnancy in women with aortic coarctation (CoA) has an estimated moderately increased risk (mWHO II–III) of adverse cardiovascular, obstetric or fetal events, but prospective data to validate this risk classification are scarce**.** This study examined pregnancy outcomes and identified associations with maternal cardiac adverse outcomes (MACE). There were 303 pregnancies (mean age 30 years, with pregnancy duration 39 weeks), 9.6% involved unrepaired CoA, and 27.1% were in women with preexisting hypertension.
Baris et al. 2021 [38]	Prospective International Observational ROPAC registry	53 countries/ overall cohort *5,739 pregnancies*	*138 centres*	**ROPAC registry report**: Describes the outcomes in 421 women with repaired TOF; 21.4% were from an emerging country. All women had undergone surgical correction for their heart defect before pregnancy **The primary outcome**: occurrence of maternal cardiovascular events. **Secondary outcomes**: obstetric and fetal events, right ventricular (RV) dilatation, and pulmonary valve deterioration.
Parsonage et al. 2021 [11]	State of Art Review	Australia and New Zealand	NA	**State of Art Review paper**: Contemporary review summarises some of the critical issues faced concerning prevention, diagnosis, treatment and health service delivery in this patient group and concludes with suggested priorities for policy and research. • Pregnancy and childbirth present a specific challenge to the maternal cardiovascular system. • Preexisting cardiac diseases, or cardiac diseases that occur during pregnancy, are associated with a significant morbidity and mortality risk for both mother and baby. • In recent decades, cardiac disease has emerged as a leading cause of maternal death in most high-income countries, including Australia and New Zealand. • The burden of cardiac disease in pregnancy is likely to be growing due to an increase in adult survivors with congenital heart disease embarking on pregnancy coupled with

Table 2. Summary of characteristics of studies identified in the updated literature review

Study	Design	Country / Sample size	Location	Outcomes measured/comments
				demographic shifts in the age and cardiovascular risk factors of women giving birth and the persisting high incidence of acute rheumatic fever in First Nations women. • Call for a national strategy for clinical practice and service delivery to improve clinical outcomes for women with cardiac disease in pregnancy.
Baris et al. 2020 [9]	Prospective International Observational ROPAC registry	53 countries/ overall cohort *5,739 pregnancies*	*138 centres*	**ROPAC registry report**: describes the pregnancy outcomes in women with preexisting and pregnancy-onset IHD. **Primary endpoint**s included maternal cardiac events during pregnancy, maternal mortality, heart failure, Atrial Fibrillation/Flutter or ventricular tachyarrhythmias, endocarditis, new acute coronary syndrome (ACS) and thromboembolic event in women with preexisting IHD. **Secondary endpoints** included obstetric and neonatal outcomes as in previous studies There were 117 women with IHD, of which 104 had preexisting IHD. Women revascularised before pregnancy had fewer events compared to those women who had not.
Park et al. 2020 [13 P2]	Contemporary literature review		NA	**Review paper:** Highlighted contemporary evidence in cardiovascular risk assessment and risk modification and the role of potential risk reduction therapies before, during, and after pregnancy • Adverse pregnancy outcomes, including hypertensive disorders of pregnancy and gestational diabetes, are significant causes of maternal mortality. • There is substantial evidence of an association between adverse events during pregnancy and long-term maternal cardiovascular risk. • Therefore, it is essential to understand the role of risk modification before, during, and after pregnancy to reduce adverse outcomes. • These efforts include risk assessment, routine screening for cardiovascular risk factors, and potential pharmacotherapeutic risk reduction. .
Denayer et al. 2020 [45]	A comparative exploratory study of three risk stratification	Leuven, Belgium / Random 100 women from the database of paediatric and CHD	University hospitals	**Research** exploratory study that compared the four models of risk stratification used to predict adverse cardiac outcomes in women with CHD who become pregnant included CARPREG, CARPREG II, ZAHARA risk scores and mWHO risk classification**.** The recent ESC pregnancy guidelines for women with cardiovascular disease preferentially recommended mWHO risk stratification**.** This study evaluated the feasibility of identifying the risk model that most accurately

Table 2. Summary of characteristics of studies identified in the updated literature review

Study	Design	Country / Sample size	Location	Outcomes measured/comments
	models to predict adverse cardiac outcomes in women with CHD in pregnancy			predicts outcomes. *All models overestimated maternal cardiac risk*. The ZAHARA risk model appeared to be a more accurate reflection of maternal risk in the cohort, but a larger study population is needed.
Wang et al. 2020 [46]	Meta-analysis of risk models predicting cardiac complications in pregnant women with CHD	New Zealand / six studies with 3426 pregnancies timeframe 1980 to 2018 for relevant studies	Auckland city hospital	**Research review:** meta-analysis assessed the predictive utility of pregnancy risk scores for women with CHD. The first study to pool performance of risk models for predicting cardiac complications for pregnant women with CHD. The CARPREG, ZAHARA risk scores and mWHO scores of studies were evaluated risk classification
Lameijer et al. 2019 [47]	Systematic review		Included individualised patient data	**Systematic review paper** addresses the gap in research of women with preexisting IHD in pregnancy, the pregnancy risks in these women and their offspring. The **primary outcome endpoints** were a composite of ischaemic complications, including maternal death, acute coronary syndrome and ventricular tachycardia. Pregnancies in women with preexisting IHD are high-risk pregnancies. These women have a high risk of ischaemic cardiovascular complications, including 2% maternal mortality. The risk of ischaemic complications is especially high among women with atherosclerotic coronary artery disease.
Roos-Hesselink et al. 2019 [3]	Prospective International Observational ROPAC registry	53 countries/ overall cohort *5,739 pregnancies*	*138 centres*	**ROPAC registry report:** The study aimed to define contemporary diagnosis-specific outcomes in pregnant women with heart disease**.** Prevalent diagnoses were congenital (57%) and valvular heart disease (29%). Mortality (overall 0.6%) was highest in the pulmonary arterial hypertension (PAH) group (9%). Heart failure occurred in 11%, arrhythmias in 2%. Delivery was by caesarean section in 44%. Obstetric and fetal complications occurred in 17% and 21%, respectively. The number of high-risk pregnancies (mWHO Class IV) increased from 0.7% in 2007–2010 to 10.9% in 2015–2018. The highest complication rates occurred in women with pulmonary arterial hypertension (PAH).

Table 2. Summary of characteristics of studies identified in the updated literature review

Study	Design	Country / Sample size	Location	Outcomes measured/comments
				Recommendations: This study reiterated that all women with heart disease should be cared for in a hospital. Women in mWHO class I and II can be cared for in a local hospital, and women in Class II–III in a referral hospital. In contrast, in Class III and IV, women should be managed in specialised tertiary centres by a specialised, multidisciplinary team. Pre-conceptional counselling is advised for women in all mWHO classes as it is associated with a better outcome.
Grandi et al. 2019 [48]	**Systematic review**			**Systematic review** aimed to determine an association between a broader array of pregnancy complications and the future risk of CVD. CVD risk was highest in women with gestational hypertension (OR 1.7; 95% ICI, 1.3–2.2). Women with broad pregnancy complications are at increased risk of future CVD. Postpartum assessment /risk factor management is recommended.
ACOG Practice Bulletin No. 212: Pregnancy and Heart Disease 2019 [34]				**Clinical practice bulletin**: The purpose of this document is to 1) Describe the prevalence and effect of heart disease among pregnant and postpartum women. 2) Guide early antepartum and postpartum risk factor identification and modification 3) Outline common cardiovascular disorders that cause morbidity and mortality during pregnancy and the puerperium 4) Describe recommendations for care for pregnant and postpartum women with preexisting or new-onset acquired heart disease 5) Present a comprehensive interpregnancy care plan for women with heart disease.
van Hagen et al. 2018 [21]	Prospective International Observational	53 countries/ overall cohort 5,739 pregnancies	*138 centres*	**ROPAC registry report:** aimed to describe pregnancy outcomes in women with rheumatic mitral valve disease and no prepregnancy valve replacement cohort n= 390 women. Cardiac, obstetric, and neonatal outcomes as reported in other ROPAC studies. The researchers were restricted to the guidelines used when the majority of the patients were included. Prepregnancy counselling and

Table 2. Summary of characteristics of studies identified in the updated literature review

Study	Design	Country / Sample size	Location	Outcomes measured/comments
	ROPAC registry			considering mitral valve interventions in selected women are important to prevent these complications.
Regitz-Zagrosek et al. 2018 [2]	ESC Guidelines for the management of cardiovascular diseases during pregnancy.	The task force that reviewed the guidelines and published evidence represented relevant subspecialty groups of specialists from European countries, Canada and South Africa.	N/A	**Clinical Practice Guidelines** are specific to cardiovascular disease in pregnancy. A critical evaluation of diagnostic and therapeutic procedures was performed, including assessing the risk-benefit ratio. The evidence and the strength of the recommendation of management options were weighed and graded according to predefined scales. Update of previously published 2011 ESC Guidelines by the same authors.
Silversides et al. 2018 [17]	Prospective recruitment of women with CHD acquired heart disease or arrhythmias	Toronto and Vancouver, 1,938 pregnancies		**Research Paper** on updated CARPREG (Cardiac Disease in Pregnancy Study) study examined cardiac complications during pregnancy and their temporal trends. Prediction of maternal cardiac complications in women with heart disease is enhanced by integrating general, lesion-specific, and delivery of care variables. Also, derive a risk stratification index, and these predictors helped form the updated risk index (CARPREG II).
Mayer et al. 2018 [50]	Mixed method evaluation of Multidisciplinary care for pregnant women with cardiac disease	The United Kingdom/ n= 42 medical records audit women interviewed n=7 MDT clinics observations one site n=8 women, n=4 clinicians. Small study	2 National Health Service (NHS) maternity units in the south of England	**Nursing Research paper** on CPGs that described the composition and processes of multidisciplinary care between maternity and cardiac services before, during and after pregnancy for women with cardiac disease, and explored clinicians' (cardiologists, obstetricians, nurses, midwives) and women's experiences of delivering/receiving care within these models. Although a small study with a mixed-methods approach of case-note audit, interviews and observation at two National Health Service (NHS) maternity units in the south of England, it examined important aspects of CPGs. Women with significant cardiac disease (either arrhythmic or structural, e.g., Tetralogy of Fallot) who delivered between 2014 and 2015 (audit/interviews) or attended multidisciplinary team clinic (obstetric/cardiac) during 2016 (observation). The limited evidence and guidance to support multidisciplinary teams working for pregnancy in women with cardiac disease, particularly those with acquired conditions, has led to variable models and pathways of care. Evidence-based guidance on implementing integrated care between maternity

Table 2. Summary of characteristics of studies identified in the updated literature review

Study	Design	Country / Sample size	Location	Outcomes measured/comments
				and cardiac services that includes care pathways between local and specialist centres for all women with cardiac disease in pregnancy is urgently required.
Homer et al. 2018 [51]	Report on updated national CPGs on pregnancy care	Australia	NA	**Review paper:** Australian updated generic CPGs on pregnancy care for health professionals providing antenatal care. Eleven topics were updated, with new guidance on substance use in pregnancy added. The recommendation for health professionals to offer advice to pregnant women about weight, diet and physical activity, and the opportunity to be weighed will help women make changes leading to better health outcomes for themselves and their babies. Highlighted the need for additional care for those women with high-risk comorbidities such as CVD. There are no details on the delivery of care throughout pregnancy
Cauldwell et al. 2018 [52]	A single retrospective study	In the United Kingdom, a cohort of pregnant women with Fontan circulation n= 50 women 124 pregnancies	Ten specialist ACHD centres	**A research paper** describes pregnancy and outcomes in a cohort of patients with Fontan circulation in the United Kingdom. A retrospective study with a timeframe of 2005 to 2016 includes ten specialist ACHD centres in the UK. Notably high incidence of miscarriage was reported n=68 (54.8%). Cardiac complications in pregnancies with a live birth included heart failure (n=7, 13.5%), arrhythmia (n=6, 11.3%) and pulmonary embolism (n=1, 1.9%). Obstetric and neonatal complications were common: preterm delivery (n=39, 72.2%), small for gestational age (<10th percentile, n=30, 55.6 %;< 5th centile, n=19, 35.2%) and PPH (n=23, 42.6%). There were no maternal deaths. Women with a Fontan circulation have a high rate of miscarriage and, even if pregnancy progresses to a viable gestational age, a high rate of obstetric and neonatal complications.
Bonnet et al. 2018 [53]	Registry study Neonatal and maternal outcomes of pregnancy with maternal cardiac disease (the NORMANDY	France /small cohort of 147 timeframes 2000-2014	University hospital,	**NORMANDY Research report**. Pregnancies complicated by congenital or acquired heart diseases are at high risk of maternal, obstetrical and neonatal poor outcomes. A maternal cardiac event complicated 13 pregnancies. Obstetrical and neonatal complications occurred respectively in 35.0% (95% CI [28.3–41.7]) and 37.0% (95% CI [30.3–43.7]) of pregnancies. All complications were more frequent among cardiomyopathies or obstructive and conotruncal lesions. While left-to-right shunts are less prone to complications. Timing of complications noted at the end of the second trimester to the middle of the third trimester or postpartum. Caesarean section in 37% (95% CI [30.3–43.7]), and general anaesthesia was performed in 8.6% of cases (95% CI [4.7–12.5]). Despite relatively mild heart diseases, this study illustrates the evolution in managing pregnancies complicated by cardiopathies. Vaginal delivery under loco-regional anaesthesia can be achieved in many

Table 2. Summary of characteristics of studies identified in the updated literature review

Study	Design	Country / Sample size	Location	Outcomes measured/comments
	study): Years 2000–2014			pregnancies, whereas others require strict multidisciplinary follow-up in a specialised centre. Creating a large, multi-centric registry might help improve and personalise the management of these high-risk pregnancies.
van Hagen et al. 2016 [44]	Prospective International Observational ROPAC registry	Worldwide countries/ overall cohort 2742 pregnancies		**The ROPAC registry** reported the frequency of events, validated the modified WHO (mWHO) risk classification, and searched for event-specific predictors. The time frame included 2008 to 2014. The mWHO classification is unsuitable for the prediction of obstetric and fetal events in women with cardiac disease. Maternal complex CHD was independently associated with fetal growth restriction and aortic valve disease with preeclampsia, providing insight into the pathophysiology of these pregnancy complications. High rates of adverse obstetric and fetal outcomes in women with preexisting heart disease highlight the importance of preconception counselling as indicated in CPGs.
Hayward et al. 2017 [55]	A retrospective study Inpatient delivery admissions data	California, USA/ 3,642 041 admission deliveries	Maternal and Fetal Outcomes of Admission for Delivery in Women With Congenital Heart Disease	**A research paper** reports on delivery outcomes for women with and without CHD. A retrospective study of inpatient delivery admissions in the California State Inpatient Database compared maternal and fetal outcomes between women with and without CHD using multivariate logistic regression. Cardiovascular morbidity and mortality were hypothesised to be higher among women with CHD. The timeframe was included 2014 to 2017, inclusive of women with non-complex and complex CHD. Maternal outcomes were in-hospital arrhythmias, eclampsia/ preeclampsia, congestive heart failure (CHF), length of stay, preterm labour, anaemia complicating pregnancy, placental abnormalities, infection during childbirth, maternal readmission at one year, and in-hospital mortality. Fetal outcomes included growth restriction, distress, and death. **A cohort** of 3 ,642, 041 identified delivery admissions. In this study, CHD was associated with incident CHF, atrial arrhythmias, fetal growth restriction and complex CHD was associated with ventricular arrhythmias and in-hospital maternal mortality, although these outcomes were rare, even in women with complex CHD. These findings inform monitoring decisions and risk assessment for pregnant women with CHD at the time of delivery concerning CPGs.
Goland et al. 2017 [39]	Prospective International Observational	Worldwide countries, a cohort of pregnant women with Hypertrophic		**ROPAC registry report** that describes pregnancy outcomes for a cohort of women with hypertrophic cardiomyopathy (HCM). **The primary endpoint** was a major adverse cardiovascular event (MACE), including death, heart failure (HF), thromboembolic event, and arrhythmia. Baseline and outcome data were analysed and

Table 2. Summary of characteristics of studies identified in the updated literature review

Study	Design	Country / Sample size	Location	Outcomes measured/comments
	ROPAC registry	cardiomyopathy (HCM) from ROPAC database n=60		compared for patients with MACE vs without MACE and patients with obstructive HCM vs non-obstructive HCM. MACE occurred most during the 3rd trimester and postpartum period. In total, 3 (5.0%) women experienced fetal loss.
Ertekin et al. 2016 [40]	Prospective International Observational ROPAC registry	World-wide 39 countries 2966 pregnancies	99 hospitals	**ROPAC registry report:** Describes the incidence, onset, predictors and outcome of ventricular tachyarrhythmia (VTA) in pregnant women with heart disease and impact on fetal outcomes. Addresses the fact that insufficient data exist on the incidence and outcome of VTA in pregnancy. Time frame: 2007 to 2013, 2966 pregnancies. VTA occurred in 1.4% of pregnant women with CVD, mainly in the third trimester, and was associated with heart failure during pregnancy. NYHA class before pregnancy was predictive. VTA during pregnancy had a clear impact on fetal outcomes and therefore informed CPGs recommendations.
Sliwa et al. 2016 [41]	Prospective International Observational ROPAC registry	Global registry / Cohort of 151 women with Pulmonary hypertension (PH)		**ROPAC registry report** described the pregnancy outcomes in women with pulmonary hypertension. The cohort n=151of women with pulmonary hypertension (PH) either diagnosed by right heart catheterisation or diagnosed as possible PH by echocardiographic signs, with 26% having pulmonary arterial hypertension (PAH), and three subgroups: idiopathic (iPAH), associated with congenital heart disease (CHD-PAH), or related to another condition (oPAH), and 74% having PH caused by left heart disease (LHD-PH, n=112).75% of women the diagnosis of PH had been made before pregnancy. Mortality in this group of patients with various forms of PH was lower than previously reported as specialised care during pregnancy and delivery was available. However, maternal and fetal mortality remains prohibitively high in women with iPAH, although small numbers restrict this conclusion. Early advice on contraception, pregnancy risk, and the fetal outcome remains paramount as recommended by CPGs
Pillutla et al. 2016 [56]	A single-centre, retrospective study of pregnant women	California, USA / small cohort of 43 women reported 61 pregnancies.	An Adult Congenital Heart Disease Center (ACHDC)	**Research paper**: Previous studies mainly on low-risk women with CHD. The ACHDC protocol for managing pregnant women includes cardiology / maternal-fetal medical specialist consultation every trimester. Timeframe 1994 to 2012. This study examined women with high-risk CHD with analysis of cardiovascular and neonatal outcomes. Maternal cardiac (31%) and neonatal (54%) complications were frequent, but no maternal

Table 2. Summary of characteristics of studies identified in the updated literature review

Study	Design	Country / Sample size	Location	Outcomes measured/comments
	with CHD registry database			or neonatal deaths. Antepartum counselling and assessment of maternal fitness are crucial for the woman with CHD as recommended in CPGs
Kamel et al. 2016 [57]	large cohort crossover analysis administrative data	3 of the four most populated US states and ≈25% of the US population/ Among 6 566 826 pregnancies in 4 933 697 women, a cohort of 36 cases of aortic dissection or rupture	,	**Research paper**: A large cohort crossover analysis that addresses the gap in population-based data exist to support an association between pregnancy and aortic dissection or rupture—timeframe between 2005 and 2013. The outcome was a composite of aortic dissection or rupture. Among 6 566 826 pregnancies in 4 933 697 women, 36 aortic dissection or rupture cases were identified during the pregnancy or postpartum period and nine instances during the control period one year later. The risk of aortic dissection or rupture is elevated during pregnancy and the postpartum period.
Elkayam et al. 2016a [15]	**State of the Art Review**		USA	**State of the Art review Part I** identifies the rising trend of cardiovascular disease in pregnancy and the leading cause of obstetric maternal morbidity and mortality. This paper reviews published reports to provide recommendations for managing women with high-risk cardiovascular conditions during pregnancy gestation.
Elkayam et al. 2016b [16]	**State of the Art Review**		USA	**State of the Art review Part II** This paper reviews contemporary published reports to recommend managing women with high-risk cardiovascular conditions during pregnancy. Focuses on more complex congenital heart disease
Ruys et al. 2014 [42]	Prospective International Observational ROPAC registry	International registry 28 countries / 1321 women between 2007 and 2011	60 hospitals	**ROPAC registry report** identified heart failure as one of the most critical complications in pregnant women with heart disease, causing maternal and fetal mortality and morbidity. HF was the most common complication in this pregnancy registry. Timing of HF was dependant on the underlying cardiac diagnosis and occurring in the second trimester, mainly in patients with shunt lesions or VHD. Yet, women with CMP and IHD developed HF shortly after delivery. In addition to the previously recognised risk factors such as prepregnancy signs of HF, high NYHA class or WHO category ≥3, new predictors for HF were CMP or PH. Preeclampsia during pregnancy was associated with HF, and premature delivery was more frequent.

Chapter 3: Adherence to clinical practice guidelines for South Australian pregnant women with cardiac conditions between 2003 and 2013

3.1 Overview of Chapter 3

The discursive paper and updated literature review in Chapter 2 reported the need for further research on heart disease in pregnancy and the continuum of care, contextualised to Australia's health care system. As reported, there are no national CPGs specific to managing cardiac disease in pregnancy, except two states, South Australia and Western Australia, who independently developed their own local policies– the SAPPGs for cardiac disease in pregnancy and the KEMH policy on cardiac diseases respectively. (see Appendices D)[18,26] Literature yielded no studies on evaluating adherence to best practice CPGs related to cardiac disease in pregnancy. The discursive paper also explored the role of the midwives in the pregnancy heart health team.

Although, the SAPPGS recommend at the initial antenatal visit, routine heart disease screening this was not undertaken on all pregnant women. In South Australia over the last twenty years, midwives' assessment in the public hospital triage booking visits, has worked well for most women and improved the detection of psychosocial issues and domestic violence. However, the midwives' level of knowledge, expertise and interest in cardiac complications in pregnancy may influence their uptake of CVD screening recommended in the SAPPGs. If a preexisting cardiac diagnosis is identified at the midwife triage visit, then referral is made for review by an obstetrician for more detailed assessment of this issue. The clinical audit in this study examined routine cardiovascular disease screening, reported in the overall adherence score, and the healthcare professionals who assessed the women at their first visit.[58]

This chapter addresses three research objectives of this thesis: to evaluate real-life clinical practice for women with heart conditions during pregnancy, benchmarked against the statewide best practice guidelines, which were readily accessible to the public hospitals in the study; to identify the predictors and associated factors for adherence to the guidelines; and to evalaute varainces in guideline adherence across the three SA Health metropolitan university-affiliated public hospitals that provide obstetric services.

3.1.1 Background and context

Cardiac disease in pregnancy is an under-researched area with little available evidence. However, it is emerging as a significant cause of maternal mortalities and morbidities.[11] International and statewide guidelines highlight the importance of cardiac conditions in pregnancy and make recommendations proposed by expert panels but unsubstantiated by high-level evidence. As discussed in Chapter 1, there are ethical complexities associated with RCTs in combined cardiology and obstetric contexts. The ESC advocates surveys and registries that verify real-life practice benchmarked against CPGs recommendations

to complete the loop between clinical research, writing guidelines and implementation into practice.[2] This study helps support the recommendations of statewide cardiac-specific guidelines by examining real-life practice in South Australia.

3.1.2 Research aims

The paper presented in Chapter 3 aimed to evaluate the adherence to the perinatal guidelines for women with preexisting and newly acquired heart conditions during pregnancy, identify the predictors for adherence for these women, and evalaute varainces in guideline adherence across the three hospitals examined.

3.1.3 Methods overview

The study presented in this chapter is a retrospective cross-sectional observational design that analysed data abstracted from medical records. The three hospitals selected for the clinical audit represent the SA Health metropolitan public hospitals that provide inpatient obstetric services outlined in the SAPGGs. The researcher collaborated with SA health coder and the SA Pregnancy Outcome unit to identify those women who met the inclusion criteria of 'pre-existent' or 'newly acquired' heart disease during pregnancy. The exclusion criteria included women who did not have 'pre-existent' or 'newly acquired' heart conditions during pregnancy up to 12 months post-partum and with age limit of less than seventeen years of age.

The SA health coder utilised the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM), specific codes to identify conditions related to or aggravated by pregnancy, childbirth, or the puerperium (maternal or obstetric causes) at the time of data collection. The SA health coder collaborated with the researcher and three hospital site medical records managers with pertinent codes with ICD 085-092:

- Complications predominantly related to the puerperium, ICD 099 other maternal disease classified elsewhere but complicating pregnancy childbirth and puerperium.
- Type 1 excludes preexisting heart disease complicating pregnancy and the puerperium. Cardiomyopathy in the puerperium (ICD 0.90.3);
- Hypertensive disorders (ICD 010-016);
- Obstetric embolism (ICD 088) venous complications and cerebrovenous sinus thrombosis in labour, childbirth, and the puerperium (ICD 087) pregnancy (ICD 022).
- ICD 090 complications of the puerperium not elsewhere classified. Examples of these conditions included cardiac complications such as obstetric pulmonary embolism, amniotic fluid embolism, cardiac arrest of failure.
    - ICD 090. 3 Peripartum cardiomyopathy could be used to specify a diagnosis, and conditions in code 142 i.e., dilated, obstructive or hypertrophic cardiomyopathy.
- ICD O89.1 cardiac complications of anaesthesia during the puerperium, 089.1 and include cardiac arrest or failure due to anaesthesia, ICD 088 Obstetric embolism includes pulmonary emboli in

pregnancy, childbirth or the puerperium, specific obstetric embolism 088.2 obstetric (pulmonary or /and puerperal (pulmonary).

- ICD 099.4 Diseases of the circulatory system complicating pregnancy and the puerperium and including conditions in 100-199., i.e.
    - I00-I02 acute rheumatic fever,
    - 105-109 chronic rheumatic heart diseases,
    - I20-I25 ischaemic heart disease,
    - I30-I52 other forms of heart disease,
    - I11.0-I11.9 hypertensive heart disease,
    - I13-I13.9 Hypertensive heart and kidney disease,
    - I46-I46.9 Cardiac arrest,
    - O10.1 pre-existing hypertensive heart disease complicating pregnancy, childbirth, and the puerperium,
    - O10.3 pre-existing hypertensive heart and kidney disease complicating pregnancy, childbirth and the puerperium,
    - O29.1 cardiac complications of anaesthesia during pregnancy,
    - O74.2 cardiac complications of anaesthesia during labour and delivery,
    - O75.4 other complications of obstetric surgery and procedures.
- ICD 151: Complications and ill-defined descriptions of heart disease, namely
    - 151.6 cardiovascular disease, unspecified, and
    - 151.7 cardiomegaly: cardiac dilation and hypertrophy and ventricular dilation.
- ICD 142 Cardiomyopathy: excluding cardiomyopathy complicating pregnancy 142 (099.4) and Puerperium (090.3) & ischemic cardiomyopathy (125.5). ICD 142.0 arise during pregnancy and the puerperium and includes dilated, or obstructed other hypotrophic cardiomyopathy, Type 1 excludes ischemic cardiomyopathy (125.5) and peripartum cardiomyopathy (0990.3) Type 2 excludes ventricular hypertrophy (151.7) but includes myocardiopathy 089.1 and lastly ICD 120-125 Ischemic heart disease and cardiomyopathy (125.5).

The researcher developed the online data abstraction tool (DAT) by Auditmaker from the cardiac-specific SAPPGs, which collected numerical and string data. An initial meeting with both the Care Track system analyst and president of Australian Patient Safety Foundation with their research on appropriateness of health care delivery in Australia, was informative in the development process of the clinical audit and utilising available guidelines or clinical indicators from clinical expert- consensus. The DAT was revised following feedback from key stakeholders i.e., senior clinical specialists and academics across disciplines who reviewed input from practice guidelines and key clinical indicators. The researcher undertook Auditmaker training to set up the data base, and complete the DAT. Four cases were piloted using DAT with further refinement to include perinatal outcome of baby data. The clinical DAT published in *PLoS One* (2020) is included in the Appendices. Demographics, the cardiac pathology entry point and causes of

cardiac disease data were captured. Documentation of the recommended NYHA Functional Classification on admission to determine the level of hospital care was included. Also, the guideline recommendations were grouped under preconception care and education, antenatal management, clinical assessment and investigations, and planned care, i.e., high-risk management in labour and preterm labour imminent and perinatal outcomes.

The audit tool collected data from the medical record as regards the documented plan of care throughout the pregnancy. (see Appendices D). Evidence of adherence to the SAPPG was obtained from the medical record including any documented care plan.

A novel approach was the scoring system that calculated a score for adherence to the SAPPGs recommendations. These represented forty variables that produced a score for documented evidence of adherence; the maximum potential overall adherence score was 40 (see Appendices B). To determine the minimum acceptable adherence score for women in the two cardiac groups in the study, namely, those women with preexistent cardiac condition (PEC) and those women with newly acquired cardiac condition (AC) the researcher collaborated with senior clinicians within the research team. As there was no precedent for this scoring tool in the literature, the researcher in collaboration with senior clinicians reviewed the guidelines and the score obtained in normal pregnancies in contemporary SA Health records and made a clinical judgement of what would be a reasonable minimum standard for any pregnancy. This was extrapolated to the expected care for women in each group.[58]. Importantly, the expected the variance for women in the AC group that would be contingent upon at what stage of the pregnancy a cardiac event occurred and how complete the care delivered in terms of standard delivery care reiterated in the manuscript.

3.2 Manuscript, Paper Two – Adherence to clinical practice guidelines for South Australian pregnant women with cardiac conditions between 2003 and 2013

The following paper, ‘Adherence to clinical practice guidelines for South Australian pregnant women with cardiac conditions between 2003 and 2013’, was published in March 2020. Original research *PLoS One*.

Statement of authorship for publication 2

Statement of Authorship

Title of Paper	Adherence to clinical practice guidelines for South Australian pregnant women with cardiac conditions between 2003 and 2013
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Principal Author

Name of Principal Author (Candidate)	Sandra Millington
Contribution to the Paper	Conceptualisation of project, data collection and validation of analysis with the statistician, interpreted data, wrote manuscript and acted as the corresponding author.
Overall percentage (%)	85%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	Date 4/8/2021

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate in include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	Margaret Arstall
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Contribution to the Paper	Conceptualisation, interpretation of data and critical revision of the manuscript for pertinent intellectual content
Signature	[redacted] Date 3 8 21
Name of Co-Author	Judith Magarey
Contribution to the Paper	Conceptualisation of original draft manuscript, interrater reliability and validation of Data abstraction tool (DAT)
Signature	[redacted] Date 4/8/21
Name of Co-Author	Robyn Clark
Contribution to the Paper	Conceptualisation, interpretation of data and critical revision of the manuscript for pertinent intellectual content Robyn Clark
Signature	[redacted] Date 19/08/21

PLOS ONE

RESEARCH ARTICLE

Adherence to clinical practice guidelines for South Australian pregnant women with cardiac conditions between 2003 and 2013

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Abstract

Background

For pregnant women with a known cardiac condition or those who develop cardiac disease during pregnancy, there is an increased risk of complications during pregnancy, to both mother and foetus. To reduce this risk, best practice guidelines have been developed and available in South Australia for several years. Measuring clinical practice against the guideline recommendations verifies real-life practice and an essential part of any clinical practice quality improvement project by identifying gaps. This study is the first report on adherence to statewide perinatal guidelines for these women in South Australia.

Objectives

- To evaluate adherence to evidence-based clinical practice perinatal guidelines
- To identify predictors of adherence.
- Make comparisons across three practice settings examined.

Design

A retrospective cross-sectional observational design that analysed data from medical records.

Setting

Three SA Health public metropolitan, university-affiliated teaching hospitals with an obstetric service within a ten-year timeframe (2003–2013).

Funding: The author(s) received no specific funding for this work

Competing interests: The authors have no competing interest

Participants

271 admissions of women who were categorised as 'pre-existent' or 'newly acquired' cardiac condition during their pregnancy.

Outcome measures

Adherence to guidelines was measured using a purposefully designed scoring system across the three sites. The researcher chose a minimum acceptable score of 17 applicable to the 'newly acquired' group and 35 for the 'pre-existent' group.

Results

Overall adherence to the perinatal guidelines for the combined groups (n = 271) reported a mean score of 16.3, SD ± 6.7, with a median score of 17. Women in the 'newly acquired' group scored less compared to women in the 'pre-existent' group (Estimate -2.3, CI -3.9,-0.7). Variance in adherence was observed across the three hospitals (P value <0.0001). The most significant predictor of adherence to guidelines was pre-pregnancy cardiac consultation which increased the likelihood of preconception care by Odds ratio 18.5 (95%, CI 2, 168). Similarly, compliance with mental health screening was associated with improved adherence to antenatal assessments (OR: 11.3(95% CI 4.7, 27.3).

Conclusion

There was overall suboptimal adherence to the statewide guidelines for women with cardiac conditions in pregnancy. The variance in the level of adherence across the three hospitals correlated with the exposure to higher acuity cases, and that appropriate up- referral to a higher acuity hospital was intrinsically linked to better adherence. Recommendations include preconception counselling, and to ensure that all health practitioners have the skills, sufficient training and time to complete a comprehensive initial antenatal assessment

Trial registration

ACTRN12617000417381

Introduction

The epidemiology of cardiac disease in pregnancy varies internationally with 0.2–4% estimates; however, it remains under-researched in Australia as reported by Australian Maternity Outcome Surveillance System (AMOSS) [1, 2]. Cardiac disease in pregnancy encompasses a broad spectrum of conditions that include congenital heart disease (CHD), structural and aortic disease, cardiomyopathies, rhythm disorders and pregnancy acquired conditions such as ischemic heart disease (IHD) [3, 4]. Cardiac disease is associated with increased rates of morbidity and hospitalisation during pregnancy, with one in four women requiring admission, and is now one of the leading causes of maternal mortality [4–6]. These women have an increased likelihood of eclampsia, caesarean birth and postpartum haemorrhage [4]. Importantly, there are reportedly higher rates of unintended pregnancies in women with cardiac disease, which raises questions about health literacy, contraceptive knowledge and access to preconception and pregnancy counselling by appropriately qualified healthcare practitioners [7]. Evidence-

based and best practice guidelines help to define the current known optimum quality of clinical care for maternal and newborn health; therefore, adherence to these best-practice standards is a measurable objective for quality improvement efforts [8].

Background and rationale

Clinical practice guidelines provide clinicians with updated evidence to maintain consistency and accelerate best practice [9]. Where obstetric guidelines were agreed upon and implemented, there has been a significant improvement in the clinical outcomes, as reported in Sweden and the Netherlands [9, 10]. The Registry of Pregnancy and Cardiac disease (ROPAC) established to study pregnant women with structural heart disease reported that adherence to guidelines, such as prepregnancy assessment, counselling, and interventions, was an essential factor in reducing mortality and cardiac deterioration [11].

Australian national guidelines for the care of healthy pregnant women published online in 2018 provide recommendations that support high quality, safe prenatal care in all settings; however, there were no specific guidelines for women with cardiac conditions during pregnancy [12,13]. Recent research which examined women's perception of prenatal care, provider adherence to antenatal care guidelines, the risk of pregnancy complications, and guidelines associated with cardiovascular risk factors reported suboptimal adherence [12, 14–16]. Given the increased risk of cardiovascular complications during pregnancy, with consequences for both mother and foetus, we need to identify the gap between existing evidence and clinical practice.

The South Australian Perinatal Practice Guidelines (SAPPGs), implemented in 2010, represented the Australian practice guidelines at the time and included those specific to cardiac disease in pregnancy [17]. While regular revisions occur, this is the first evaluation on the uptake of the statewide guidelines across the public health sector. Measuring clinical practice against the best practice is a crucial step to address the evidence-practice gaps [18]. This study aimed to evaluate three public hospitals' adherence to the guidelines, with the following three objectives:

1. Evaluate the adherence to the perinatal guidelines for women with pre-existent and newly acquired heart conditions during pregnancy.
2. Identify predictors of adherence for these women.
3. Make comparisons across the three hospitals examined.

Methods

Study design and setting

The study design was a retrospective cross-sectional observational study, using data collected from a comprehensive medical record review. All women who had been admitted for their obstetric care to one or more of the three SA Health public metropolitan, university affiliated teaching hospitals with an obstetric service between 2003 and 2013.

Setting. The three hospitals in this study represent the complete SA Health (Government funded) metropolitan public hospitals inpatient obstetric service, as described in the guidelines [17]. Hospital One provided intermediate care (level five) that encompassed tertiary maternal services, maternal cardiac and intensive care and specialised neonatal care services excluding babies less than 32 weeks. The quaternary centre, hospital Two provided (level six) care that included maternal cardiac, cardiothoracic surgical and intensive care, and neonatal intensive care services. Hospital Three provided a neonatal intensive care unit but no maternal cardiac or intensive care services.

Participants and selection criteria

Inclusion criteria. The participants in the study were women with 'pre-existent' or 'newly acquired' heart disease during pregnancy. The 'pre-existing' group included women with both structural and electrical cardiac conditions before conception. Structural cardiac conditions included cyanotic and acyanotic congenital heart disease, a previous history of hypertensive, valvular and cardiomyopathic heart disease as well as those women with ischemic heart disease. Electrical cardiac conditions included genetically inherited channelopathies as well as the full spectrum of acquired bradyarrhythmias and tachyarrhythmias. Women with symptomatic benign ectopic beats were excluded from this group. Similarly, women in whom undiagnosed congenital cardiac conditions were unmasked during pregnancy were included in the 'newly acquired group'.

The 'newly acquired' group included women with pregnancy-associated cardiac events.

This includes any new symptomatic sustained arrhythmia, the unmaking of underlying prior cardiac conditions previously unrecognised, and new onset cardiac disease such as acute coronary syndrome, cardiomyopathy with or without decompensated heart failure, and infective endocarditis during pregnancy or up to 12 months postpartum. These inclusion criteria were similar to those used in the United Kingdom survey of obstetric deaths [19].

The International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM), identifies conditions related to or aggravated by pregnancy, childbirth or the puerperium (maternal or obstetric causes). The codes for this project were 099, 090.3, 089, 088, and 151, 142 and 125.5.

Exclusion criteria. Women excluded from the study did not have 'pre-existent' or 'newly acquired' heart conditions during pregnancy up to 12 months post-partum and specifically amniotic fluid embolism and non-cardiac related pulmonary embolus were excluded as 'newly acquired' heart conditions.

Guideline adherence variables

All pregnant women had the prescribed standard care in their pregnancy record in addition to specific perinatal guidelines [17]. A scoring system was devised that measured adherence to available protocols and guidelines in this study [20,21]. The forty guidelines adherence variables used in this study [S1 Table] were equally weighted, giving a maximum score of forty to measure adherence. Positive documentation of the guidelines, regardless of the entry point, achieved a score.

Shared minimum guideline adherence variables are the routine antenatal care expected for both cardiac groups that include lifestyle risk assessment factors, such as smoking, weight, height and body mass index (BMI), prescribed and illicit drug use, medical comorbidities and foetal risk assessments [17]. Completion of the centre of perinatal excellence (COPE) national mental health screening tools was a shared guideline adherence variable. These tools include the Antenatal Psychosocial Risk Questionnaire (ANRQ) for depression and the Edinburgh Postnatal Depression Scale (EPSD), with both scores entered in the pregnancy record.

Predictor variables. The predictors for adherence to the guidelines analysed were hospital sites, the two categories of cardiac disease (pre-existent or acquired heart conditions), the risk level of pregnancy, collaboration with multidisciplinary teams, and maternal, perinatal factors.

The Perinatal predictor variables analysed were; gestational age at delivery, mode of delivery, live baby weight, birth weight percentile, length, and head circumference at birth, and Apgar scores. Anthropometric measures of newborn, i.e. length at birth and head circumference correlate with live baby weight as a simple, practical method for detecting 'small for gestational age' (SGA) and therefore were chosen as more reliable surrogate factors for foetal risk assessment where birthweight was less than 10^{th} percentile [17].

Data sources/measurement

The medical record review utilised an online data abstraction tool (DAT) by Auditmaker, developed from the statewide clinical guidelines for cardiac disease in pregnancy, version 2.0 [16]. Clinicians reviewed the feasibility of the DAT [S1 File]. Further validation and testing of inter-rater reliability occurred by comparing the data collected from four medical records by the researcher and research supervisor. There was 100% agreement in the data collected.

The data collection from medical records occurred at the three hospitals over two years from December 2014 to July 2016. The data were extracted from the women's pregnancy record, labour and anaesthetic charts, medical and nursing notes, and clinical pathways documentation. The study included a final number of 271 medical records for the statistical analysis (see Fig 1).

Selection bias. The data collected from the three hospitals excluded private hospitals. Whenever cross-sectional studies occur exclusively in hospital settings, there is the potential for 'admission bias', and so the women studied do not reflect the population of SA [22]. The maternal and neonatal services available at each of the three hospitals may influence the interpretation of results.

Sample size and power calculations.. As this type of study was unique, the sample size and power were calculated using current data from pregnant women who had a documented plan of care. This calculation to determine the required sample size indicated that a sample of 196 patients would have > 99% power to detect a difference of 13% of patients with a care plan. This number would provide a margin of error of 0.02 and α set at 0.05 (Gold standard is 99%, expected was 86%). The final sample size of 271 provided a substantial 'margin for error' to compensate for missing data in some patient's notes.

Sampling. The sample was data abstracted from all the medical records that met the inclusion criteria within the timeframe between 2003 and 2013.

Statistical methods

The analysis was completed using both SPSS statistics Version 26 and Statistical Analysis System (SAS 9.4, SAS Institute Inc., Cary, NC, USA). Descriptive statistics of the overall adherence score and the two cardiac groups included frequency tables of the relevant categorical data and some text variables. Continuous data variables were identified as normally distributed on inspection of the histogram. Initially, the Pearson Chi-Square test was used to determine the relationship between hospitals and various variables and tabulated in a contingency table that reported frequencies, column percentages, and Chi-Square P values. A one-way analysis of variance (ANOVA) calculated a p value for continuous variables normally distributed on inspection of a histogram. The continuous variables not normally distributed on examination of the histogram, the Kruskal-Wallis test calculated a P value. Logistic regression models determined the significant predictors utilising the software, the Statistical Analysis System (SAS 9.4, SAS Institute Inc., Cary, NC, USA). The p value for all analyses was set at < 0.05 or 95% CI to consider statistical significance.

Univariate logistic regressions identified the factors for adherence to the guidelines[S4 Table]. Multivariable logical regression examined the correlation between various predictors and adherence to the guidelines[S5 Table]. Multivariable models constructed by the following method: for each outcome, predictors with p value < 0.05, and the two broad cardiac categories and hospitals were in the initial multivariable model. Where suspected collinearity was evident between several predictors (such as parity and gravida), the most significant were included. Using backward elimination, the predictor with the highest p value was removed, and the model rerun until all predictors had p value <0.05; except the two broad cardiac

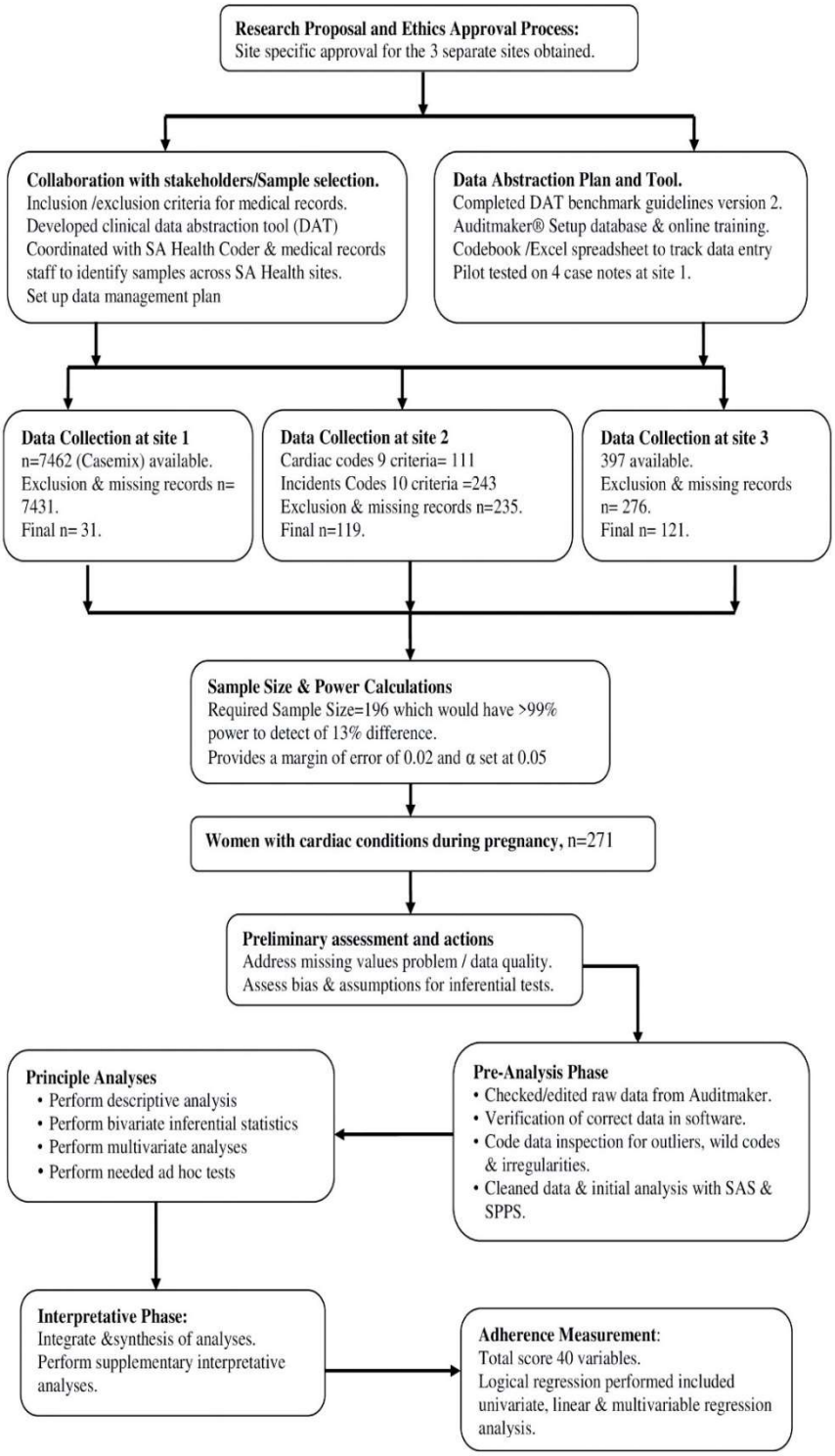


Fig 1. Research flow chart.

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categories and three hospitals, which are included as priori predictors. The analysis yielded odds ratio for greater or lesser adherence score for content of the guidelines such as preconception, antenatal and planned care, anaesthetic and pain management during birth with individual factors that may have influenced the uptake of guidelines. Assumptions underlying these tests, such as the absence of collinearity, confounders and goodness of fit, were assessed [S2 Table].

Ethics approval

South Australian Health Human Research Ethics Committee approved this study (Reference HREC 13 TQEH/LMH 226: Extension to Approval 03/08/2015). Separate site-specific ethics approvals were obtained from the three hospitals. Consent was not required from the participants for medical record review as the application for Low and Negligible Risk (LNR) Research Ethics approval granted the researcher access to medical records to collect data. To ensure anonymity, the participants' identifiable information was coded and stored with a separate password protected file on the university server and labelled for deletion in 15 years.

Results

Maternal characteristics are detailed in Table 1. For the total cohort of women, most were born in Australia (81%), Caucasian (78%), married (61%), and lived in Adelaide metropolitan vicinity (77%) (Table 1). The mean age was 30 ±6years (SD). Multigravida women were predominant with 3 ± 2.1 pregnancies in the entire group. The mean parity of the women was 1.6 (SD ± 2.1) with 36% primiparous and 7% multiparous (parity $\geq$ 5 live or stillborn over 20 weeks gestation).

Over half the women ('pre-existent group', n = 143, 53%) had experienced a cardiac event during previous pregnancies. On examination of the cardiac conditions in pregnancies, arrhythmias (n = 76, 28%) and CHD (n = 62, 23%) were the most frequent causes. Rheumatic heart disease (RHD) (n = 36, 13%), heart failure (n = 29, 11%), pulmonary embolus in cardiac patient (n = 27, 10%), IHD and systemic arterial hypertension with severe cardiac conditions (equally n = 10, 4%) were less frequently reported.

Adherence to the statewide perinatal guidelines

Overall adherence to the guidelines for the combined groups (n = 271) was normally distributed with a mean score of 16 ± 6.7 and a median score of 17. There was a significant association between the total score and the two cardiac groups (p = 0.001). The 'pre-existent' group reported a higher mean score of 17± 6.5 compared to the 'newly acquired group' with a mean score of 15± 6.8. Only eleven women had a documented NYHA classification, noting that the criterion did not apply to women with a new cardiac event. Both cardiac groups showed suboptimal adherence to the COPE screening tools. The ANRQ for depression reporting a mean adherence score of 18 ±13 while the EPSD a mean adherence score of 6±5.

Predictors of adherence and comparisons across practice settings

Table 2 shows the estimates (and 95% CI) for comparison of the mean adherence scores with various medical and demographic predictors of adherence. Those predictors identified as not significant (Global p >0.05) were maternal age, ethnicity, social status, country of birth, gravida, gestational age and specific cardiac conditions such as RHD, arrhythmias, ischaemia, heart failure, and cardiac arrest, and therefore not presented in the table.

Table 1. Maternal characteristics of women with cardiac disease during pregnancy SA hospitals (2003–2013).

Patient Characteristics	Frequency(Percentage)			Mean ± SD		
	Totaln = 271 (100%)			Total Cardiac	Pre-existing cardiac (PEC) (n = 143)	Acquired cardiac (AC) (n = 128)
Anthropometrics						
• Age (years)	271			30.4 ± 6.	29.8±5.7	31.2±6.3
• Weight (kg)	245			76.3 ± 19.6	73.2 ±17.8	79.9±21.0
• Height (cm)	186			165.1±8.0	165.1 ±8.5	165.0±7.3
• BMI (kg/m^2)	201			28.3±7.5	26.9±6.5	30.1±8.4
†Social parameters						
• Born in Australia	221 (82)				116(81)	105 (82)
• Born overseas	50 (18)				27(19)	23 (18)
†Ethnicity						
• Aboriginal	34 (13)				22(16)	12(9)
• Asian	15 (6)				8(6)	7 (6)
• Caucasian	213 (79)				109(77)	104(82)
• African continent	5 (2)				1(1)	3(3)
• Other	1 (0)				1(0)	0(0)
†Location of Home						
• Metropolitan	208 (77)				103 (72)	105 (84)
• Rural	47(17)				31(2)	17(14)
• Remote	12 (4)				9(6)	3(2)
†Marital status						
• Married	167(64)				84(60)	83 (31)
• De facto	53 (20)				34 (24)	19 (7)
• Divorced /Separated	5 (2)				2 (1)	4(3)
• Single	35(13)				19(4)	15(12)
Peri-natal assessment						
• Gestational age at admission	265			36.8 ± 3.7	36.8±3.71	36.8±3.7
• *Gravida	268			3.1 ± 2.1	3.1 ±2.0	3.1 ±2.2
• *Parity	269			1.6 ±1.7	1.5 ±1.6	1.6±1.9
• Blood pressure						
○ Systolic	265			117.4 ± 17.8	117±17.6	117±18
○ Diastolic	265			72.3. ± 12.6	72.2±14.2	72.4±14.6
Mental Health Scores						
○ **ANRQ	110			17.4. ± 12.6	15.7±12.0	19.6 ±13.2
○ ***EPSD	106			6.1 ±5.7	5.7±6.1	6.68 ±5
Cardiac Characteristics	**Total**	**PEC**	**AC**			
○ Cardiac event (prev preg)	144(54)	103(72)	0			
○ Cardiac event (current preg)						
○ Arrhythmia	74(23)	25(21)	49(45)			
○ CHD	55(24)	53(45)	2(2)			
○ RHD	22(10)	22(19)	0			
○ Heart Failure	40(18)	12(10)	28(10)			
○ † Cardiac PE	1(0)	0	1 (1)			
○ IHD	20 (9)	2(2)	18(17)			
○ Hypertension.		29 (10)	29(10)			

*Gravida on admission = number of times a woman is or has been pregnant, regardless of the outcome. Parity = number of pregnancies reaching viable gestation age (includes live births & stillbirths).

**ANRQ = documented score for Antenatal Risk Questionnaire, self-reported psychosocial assessment tool.

***EPDS = documented score for the Edinburgh Postnatal Depression Scale for risk of perinatal depression with high score indicative of depression. †For these categorical variables only frequency and percentage are reported, see S5 Table.

†Cardiac PE = Cardiac pulmonary embolus.

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Increased body mass index (BMI) was the only anthropometric maternal characteristic that resulted in a small but statistically significant increase in the mean adherence to guideline score.

Of the social characteristics where the woman's home location was important with rural and remote home location predicting a significantly higher mean adherence to the guideline score.

Women with a 'newly acquired' heart condition was a predictor of a lower score in comparison to women with 'pre-existent' heart issues with an estimate of -2.3, (95% CI -3.9, -0.7). Furthermore, a cardiac event in a previous pregnancy predicted a significant increase in adherence to the guidelines was reduced with an estimate of -1.7(95% CI -3.3, -0.1). Where the mode of delivery was planned adherence to the guidelines for caesarean options scored higher than vaginal delivery with an estimate of 6, (95%, CI: 5, 8). The baby characteristics in Table 2 did not directly influence adherence to guideline score, but retrospectively reflect the effect of this adherence. The lower mean adherence score was associated with smaller babies with lower Apgar scores

Comparison across the three hospitals. Table 2 highlights a variance in adherence to the guidelines across the three hospitals ($p < 0.0001$). An expected finding of increased adherence observed at hospital Two, which is the high-risk referral centre for other hospitals, including from remote and rural locations. Hospital Two adherence to the guidelines was greater in

Table 2. A comparison of the mean adherence score versus various 'predictors' for all women with cardiac conditions during pregnancy.

Predictor	Comparison	Effect on Total Guideline Adherence score Mean (95% CI)	Comparison P value	Global P value
Anthropometrics				
◦ BMI		0.1 (0.02, 0.3)		0.03
Social parameters				
◦ Location of home	Metropolitan vs Remote	-5.0 (-8.8, -1.2)	<0.01	<0.001
	Metropolitan vs Rural	-3.1 (-5.2, -1.0)	0.003	
	Remote vs Rural	1.9 (-2.2,6.0)	0.36	
Cardiac characteristics				
◦ Onset of cardiac disease recognition.	Acquired vs Pre-existent	-2.3 (-3.9, -0.70)		0.004
◦ Cardiac event in previous pregnancy	No vs Yes	-1.7 (-3.3, -0.1)		0.04
◦ Congenital heart condition.	No vs Yes	-1.9 (-3.9, -0.07)		0.04
◦ Bradycardia event during pregnancy.	No vs Yes	13.4 (0.4, 26.5)		0.04
◦ Pulmonary embolus during pregnancy	No vs Yes	2.7 (0.1, 5.4)		0.05
Hospital site for delivery	1 vs 2	-3.4 (-5.9, -0.9)	0.008	<0.0001
	1 vs 3	0.5 (-2.0, 3.0)	0.68	
	2 vs 3	3.9 (2.3, 5.6)	<0.0001	
Documented planned mode of delivery.	Caesarean vs Vaginal	6.0 (4.6, 7.5)		<0.0001
Baby characteristics				
◦ Live baby weight per 100g increase		-0.2 (-0.3, -0.17)		<0.0001
◦ Baby's length at birth		0.4 (-0.6, -0.2)		<0.001
◦ Baby's Head circ at birth		-0.4 (-0.7, -0.1)		0.030
◦ Apgar 1min		0.7 (-1.1, -0.2)		.003
◦ Apgar 5min		-1.0 (-1.7, -0.3)		0.005

Significant at $p<0.05$. NB: includes only significant predictors. Site 1 = Tertiary hospital, Site 2 = Quaternary hospital, Site 3 = Stand-alone maternity unit

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comparison to hospital Three (estimate 3.9, 95% CI: 2.3, 5.6, p <0.0001). The tertiary hospital One adherence was lower to the quaternary hospital Two with an estimate of -3.4 (95% CI -5.9, 0.9).

Preconception and antenatal care. Table 3 provides the stratification of both the factors (A) and the priori predictors of cardiac groups and the three hospital sites (B) that contribute to the uptake of components of the guidelines. The priori predictors are included in the table for each outcome variable to compare the cardiac groups, and hospital sites examined. The overall significant findings were that a higher adherence guideline score was predicted if a pre-conception cardiac consultation occurred (OR 18.5: 95% CI 2.0, 168) with no difference seen between hospitals. If mental health screening was performed during the antenatal assessment, this predicted a significantly higher guideline adherence with OR: 11.3, (95% CI 4.7, 27.3). There was a small but significant variation between hospitals for utilisation of these mental health tools. Antenatal documentation of maternal anthropometrics showed higher adherence at hospital One with an odds ratio of 4.6, (95% CI 2.2, 9.5, p <0.0001) reflecting this hospital's overall patient profile with a high incidence of obesity.

Women identified as a high risk pregnancy, with a documented plan of care, were more likely to have an echocardiogram assessment of their cardiac status (OR 2.6, 95% CI 1.1, 5.9) and (OR 9.4, 95% CI 3.1, 28) respectively.

Management in labour. Guideline recommendations for thromboembolism prophylaxis are the use of anti-embolic stockings, administration of subcutaneous low molecular weight heparin (LMWH) or intravenous unfractionated heparin [17]. Prophylactic heparin administration was similar between the three hospitals; however, the greatest adherence was associated with the performance of cardiac consultation for management of pregnancy (OR: 65, 95% CI 3.6, 1171). Paediatric neonatal staff likelihood of attending the birth increased when a paediatrician and medical officer were already present (OR: 16.3, (95% CI 5.8, 45.7) and 7.2 (95% CI 2.3, 22.4) and p value <0.001.

Anaesthetic and pain management during labour. The combined use of spinal-epidural anaesthesia recommended during labour has a positive effect on women with cardiac lesions [17]. When the multidisciplinary team were present at delivery and a plan was in place there was an increased likelihood of combined use of spinal–epidural anaesthesia (OR: 9.6, 95% CI 1, 81) (see Table 3).

Discussion

This study to our knowledge is the first to evaluate adherence to the SA perinatal guidelines for women with cardiac conditions during pregnancy. A minimum score of acceptable guideline adherence was determined after a comparison of the two groups mean, and median adherence scores and expert review of selected cases identifying minimum expected care [S1 Table]. From this analysis, a score greater than 35 (for 'pre-existent') and 17 (for 'newly acquired') cardiac conditions were deemed acceptable guideline adherence.

Given the foreknowledge of the women's cardiac state, the minimum guideline adherence variables for the 'pre-existent group' would include preconception education, comprehensive antenatal assessment including a prepregnancy cardiac functional assessment using New York Heart Association (NYHA) classification and multidisciplinary team collaboration [14].

Conversely, in the 'newly acquired' group with a pregnancy-induced cardiac event, adherence to the guidelines will be contingent upon the timing of the cardiac event during the peripartum period. Furthermore, it is reasonable not to expect 100% concordance with the guidelines. The expected minimum guideline adherence variables would include adult

Table 3. Significant factors that influenced the adherence score for the guidelines for cardiac disease in pregnancy across three public hospitals (2003–2013).

Adherence Guidelines Variable[1]	Factors for the uptake of guidelines.		OR for adherence score (95% CI)		Comparison P value	Global P value
	Predictor	Comparison				
Prenatal care: Preconception care included	A. Cardiac consultation completed.	Yes, vs No	18.5	(2.0, 168.8)		0.009
• Education & counselling for the cardiac condition during pregnancy.	• Gravida		1.6	(1.03, 2.5)		0.04
	B. Cardiac Condition	Acquired vs Pre-existent	0.4	(0.1, 1.8)		0.24
	• Hospital Site for delivery	1 vs 2	0.1	(0.01, 2.1)	0.15	0.28
		1 vs 3	0.09	(0.00, 1.8)	0.12	
		2 vs 3	0.8	(0.2, 3.0)	0.70	
Initial Antenatal Assessment i.e.	A. Documented ANRQ.		11.3	(4.7, 27.3)		<0.0001
• Weight, height & BMI.						
	• Gestational age		1.0	(1.0, 1.2)		0.02
	B. Cardiac Condition	Acquired vs Pre-existent	1.0	(0.6, 1.8)		0.99
	• Hospital Site for delivery	1 vs 2	0.2	(0.06, 0.6)	0.003	< .0001
		1 vs 3	0.8	(03, 2.3)	0.69	
		2 vs 3	4.6	(2.2, 9.5)	<0.0001	
• Oral health, respiratory & breast assessment.	A. Documented ANRQ	Yes, vs No	0.9	(0.9,0.97)		0.001
	• Baby's length birth	Yes, vs No	0.9	(0.8, 1.0)		0.03
	• Identified as high risk	Yes, vs No	3.4	(1.2, 10.3)		0.03
	B. Cardiac Condition	Acquired vs Pre-existent	2.0	(0.7,5.5)		0.21
	• Hospital Site for delivery	1 vs 2	1.8	(0.56, 5.8)	0.30	0.10
		1 vs 3	0.5	(0.1, 1.7)	0.24	
		2 vs 3	0.3	(0.07,0.9)	0.03	
• Abdominal, vaginal assessment & urinalysis.	A. - Identified as high risk	Yes, vs No	1.7	(1.0, 2.8)		0.04
	• A documented plan of care	Yes, vs No	2.6	(1.2, 5.8)		0.02
	B. B. Cardiac Condition	Acquired vs Pre-existent	1.2	(0.73, 1.99)		0.52
	• Hospital Site for delivery	1 vs 2	1.4	(0.54, 3.41)	0.63	
		1 vs 3	1.1	(0.43, 2.7)	0.86	
		2 vs 3	0.8	(0.47, 1.34)	0.39	
Mental Health Assessment: Documented Antenatal Risk Questionnaire Self-reported (ANRQ) (for depression).	A. Documented Edinburgh Postnatal Depression Scale score	Yes, vs No	75	(16.9, 333.1)		<0.0001
	• Live baby weight		1.0	(1.00,1.00)		0.01
	• Cardiac Condition	Acquired vs Pre-existent	0.4	(0.2, 0.8)		0.01
	B. Hospital Site for delivery	1vs 2	0.7	(0.1, 3.5)	0.66	0.003
		1 vs 3	2.5	(0.5, 12.4)	0.24	
		2 vs 3	3.7	(1.7, 7.9)	0.001	
Antenatal/Ongoing Foetal Wellbeing assessment: Fortnightly ultrasound or Growth, Doppler, & [†]AFI & CTG in the third trimester	A. Identified as high risk	Yes, vs No	4.3	(1.6, 11.7)		
	• Pre-planned cardiac drugs in labour	Yes, vs No	3.8	(1.4, 10.5)		0.004
	B. Cardiac Condition	Acquired vs Pre-existent	1.0	(0.4, 2.4)		0.01
	• Hospital Site for delivery	1 vs 2	0.6	(0.09, 3.5)	0.52	0.95
		1 vs 3	2.4	(0.5, 12.8)	0.3	0.03
		2 vs 3	4.4	(1.5 12.6)	0.007	

(*Continued*)

Table 3. (Continued)

Adherence Guidelines Variable[1]	Factors for the uptake of guidelines.		OR for adherence score (95% CI)		Comparison P value	Global P value
	Predictor	Comparison				
Cardiac Echocardiogram	A. Identified as high risk	Yes, vs No	2.6	(1.1, 5.9)		0.03
	• A documented plan of care in place	Yes, vs No	9.4	(3.1, 28.2)		<0.0001
	B. Cardiac condition	Acquired vs Pre-existent	0.5	(0.2, 1.2)		0.12
	• Hospital Site for delivery	1 vs 2	Not significant			0.6
		1vs 3	Not significant			
		2 vs3	1.5	(0.6, 3.40	0.33	
Management in Labour: Prophylactic subcutaneous LMWH or IV unfractionated heparin.	A. Cardiac consultation for management of pregnancy & labour.	Yes, vs No	65.3	(3.6, 1171.7)		0.004
	• Parity		0.4	(0.2, 0.8)		0.01
	B. Cardiac Condition	Acquired vs Pre-existent	0.03	(0.00, 0.07)		0.03
	• Hospital Site for delivery	1vs 2	Not significant			0.86
		1vs 3	Not significant			0.86
		2 vs 3	0.6	(0.06, 5.2)	0.60	0.86
Anaesthetic & Pain Management during labour. • Components, i.e. anaesthetist consultation +epidural & spinal or alternative therapies.	A. Live baby weight per 1kg increase.		0.5	(0.3, 0.7)		<0.0001
	• Obstetrician at delivery	Yes, vs No	2.8	(1.4, 5.7)		0.004
	• Anaesthetist at delivery	Yes, vs No	2.8	(1.2, 6.7		0.02
	B. Cardiac Condition		0.4	(0.2, 0.7)		<0.001
	• Hospital Site for delivery	1vs 2	1.1	(0.5, 3.0)	0.76	0.04
		1vs 3	0.6	(0.2, 1.4)	0.20	
		2 vs 3	0.5	(0.3, 0.9)	0.01	
Anaesthetist consultation for pain management in labour.	A. Live baby weight per 1kg increase.		0.5	(0.3, 0.8)		0.004
	• Identified as high risk	Yes, vs No	2.6	(1.3, 5.2)		0.001
	• Anaesthetist at delivery	Yes, vs No	2.8	(1.0, 7.3)		0.03
	B. Cardiac Condition	Acquired vs Pre-existent	0.4	(0.2, 0.8)		0.008
	• Hospital Site for delivery	1vs 2	1.3	(0.4, 3.9)	0.7	0.2
		1vs 3	0.7	(0.2,2.0)	0.47	
		2 vs 3	0.5	(0.3, 1.0)	0.06	
• Epidural considered.	A. Apgar 1min		1.4	(1.2, 1.6)		< 0.001
	• Anaesthetist at delivery	Yes, vs No	6.8	(2.9, 16.2)		<0.0001
	B. Cardiac Condition	Acquired vs Pre-existent	0.5	(0.2, 1.0)		0.05
	• Hospital Site for delivery	1vs 2	1.5	(0.4, 5.9)	0.53	0.68
		1vs 3	1.1	(0.3, 4.3)	0.86	
		2 vs 3	0.7	(0.3, 1.7)	0.45	
• The combined use of epidural & spinal to decrease preload & reduce afterload.	A. Documented plan of care in place	Yes, vs No	9.6	(1.1, 81.0)		0.03
	• No local anaesthetic with adrenaline used	Yes, vs No	3.9	(1.2, 12.8)		0.02
	• Obstetrician at delivery	Yes, vs No	3.6	(1.07, 12.4)		0.04
	• Medical officer at delivery	Yes, vs No	2.2	(1.03, 4.7)		0.04

(*Continued*)

Table 3. (Continued)

Adherence Guidelines Variable[1]	Factors for the uptake of guidelines.		OR for adherence score (95% CI)		Comparison P value	Global P value
	Predictor	Comparison				
	• Anaesthetist at delivery	Yes, vs No	11.6	(1.4, 94.2)		0.02
	B. Cardiac Condition	Acquired vs Pre-existent	1.4	(0.7, 3.0)		0.35
	• Hospital Site for delivery	1vs 2	0.2	(0.04, 1.2)	0.07	0.20
		1vs 3	0.3	(0.05, 1.3)	0.10	
		2 vs 3	1.1	(0.5, 2. 5)	0.84	
• Inhalational gases, a general anaesthetic or alternative therapies.	A. Live baby weight per 1kg increase		0.6	(0.4, 0.9)		0.02
	• Identified as high risk	Yes, vs No	2.0	(1.0, 3.9)		0.03
	B. Cardiac Condition	Acquired vs Pre-existent	0.5	(0.3, 1.0)		0.03
	Hospital Site for delivery	1vs 2	0.9	(0.3, 2.70)	0.87	0.72
		1vs 3	0.7	(0.2, 2.1)	0.55	
		2 vs 3	0.8	(0.4, 1.5)	0.47	
Paediatric neonatal staff Present at delivery.	A. Live baby weight per 1kg increase		0.4	(0.2, 0.9)		0.04
	• Paediatrician at delivery	Yes, vs No	16.3	(5.8, 45.7)		<0.0001
	• Medical officer at delivery	Yes, vs No	7.2	(2.3, 22.4)		<0.001
	B. Cardiac Condition	Acquired vs Pre-existent	0.6	(0.2, 1.7)		0.4
	Hospital Site for delivery	1vs 2	0.8	(0.1, 5.2)	0.82	0.78
		1vs 3	1.2	(0.2, 7.0)	0.82	
		2 vs 3	1.5	(0.5, 4.8)	0.48	

Significant at $P < 0.05$. A = Factors for the uptake of guidelines. B = Priori Predictors that is cardiac group categories (Prexistent and Acquired) and the three hospital sites. Site 1 = Tertiary hospital, Site 2 = Quaternary hospital, Site 3 = Stand-alone maternity unit applies to all outcomes.

*ANRQ: Antenatal Risk Questionnaire Score for depression, self-reported psychosocial assessment.

**EPDS score: documented score for the Edinburgh Postnatal Depression Scale, 10 item questionnaire to identify women at risk of perinatal depression.

†Amniotic Fluid Index (AFI) and Cardiotocograpghy (CTG).

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cardiologist or physician management soon after the cardiac event and the multidisciplinary team involvement for the rest of the peripartum care.

The study showed an overall suboptimal adherence to the guidelines. As expected, adherence was higher in women with 'pre-existent' heart disease. The most likely explanation would be that clinicians' foreknowledge of a woman's heart condition facilitates increased awareness and planning for potential complications during pregnancy [23, 24].

Stokes *et al.* [25], stated that "we need to understand better why guideline implementation strategies work in some contexts and not in others" and therefore, the variance observed across the three hospitals requires further explanation. The results show that hospitals which have increased exposure to higher acuity cases have improved adherence to the guidelines. Hospital Two is the only high-risk referral centre for SA and therefore, has increased exposure to high cardiac risk pregnancies. The patient selection will drive by default adherence to perinatal guidelines. There also appeared to be an increased awareness of the perinatal guidelines. In recognised complex cases, inserted in the women's case notes were the relevant sections of the guidelines, a delivery plan and speed dial numbers of team members. This strategy kept all clinicians informed of the expected care to facilitate an uncomplicated delivery.

Women identified as high-risk pregnancies in rural and remote locations received comprehensive assessment and investigations before transfer to hospital Two. Women transferred from rural and remote regions present a selection bias, as we were unable to determine the management of other obstetric patients from these locations. International and statewide guidelines recommend that women with moderate or high-risk complications during pregnancy require management and delivery coordinated at an expert centre with a multidisciplinary team [1].

There was documented cooperation between the three hospitals for high risk pregnancies, where women who required advanced care were identified for interhospital transfer [17]. Multidisciplinary team meetings did not occur at all three hospitals. However, high-risk physicians were prompt to refer women who experienced a pregnancy-induced cardiac event to a specialist following their thorough assessment. Hospital One had better adherence to the guidelines than hospital Three, which had limited maternal services so that women who required additional cardiac investigations may need to be transferred to a non-obstetric public hospital.

Elkayam *et al.* [24] emphasised that all women with cardiac disease benefit from pre-conception counselling, which provides a detailed discussion of the risk of pregnancy, and includes a comprehensive history and physical assessment. In this study, early cardiology consultation increased the likelihood of preconception care, particularly at hospitals One and Two. Women from regional, remote and interstate locations generally received preconception care before admission.

In previous studies, retrospective investigations of cardiovascular maternal mortality in pregnancy were, due to a missed diagnosis of a cardiovascular condition or new-onset cardiovascular disease as a common theme [26]. Wolfe *et al.* [27] stressed the importance of early cardiovascular screening for symptoms of CVD and improved management of hypertension as imperative to prevent maternal deaths. Barriers to pre-pregnancy assessment missed opportunities to identify cardiac risk factors during prenatal care, gaps in high-risk intrapartum care and delayed recognition of cardiovascular symptoms were contributory factors [27]. A notable incident in this study occurred when a pregnant primigravida woman attended the women's assessment clinic for blood pressure monitoring. Her clinical condition rapidly deteriorated so that she required advanced life support and a perimortem caesarean in the clinic. Post-cardiac arrest investigations revealed that the woman did not disclose to the midwifery staff her history of paediatric cardiac surgery for CHD, nor that she had no cardiology follow-up with the transition to adulthood. Importantly, routine physical examination, which is no longer included in the antenatal assessment, may have raised questions about the visible sternal scar on the woman's chest. Recent research highlighted inconsistencies in adherence to guidelines for the first antenatal care visit, with longer timeframes required to complete recommended prenatal risk factors screening, cited as a potential barrier [28]. Clinical time constraints and a woman's reluctance to disclose can culminate in abbreviated visits that exclude ideal health education [12, 28].

Antenatal assessments encompassing both the physical and psychological aspects of healthcare had better adherence at hospital One. This higher compliance with the COPE screening tools may be the result of the well-established perinatal mental health services in the hospital's family clinic [29]. Previous research described pregnant women attending the hospital One as among the most socio-economic disadvantaged group, with a high level of exposure to domestic violence during pregnancy, with a history of previous physical and emotional abuse during their childhood, placing them at high risk for mental illness in adult life and especially in the peripartum and postpartum period [30]. Ongoing collaborative research projects such as the Health-e Babies App for antenatal education help embed a research culture within the hospital [29]. Hospital One also had improved adherence to pain management (see Table 3). A likely

explanation could be a more holistic approach with established pain management regimen and interdisciplinary (obstetric and anaesthetic departments) collaboration that prioritises pain relief for vulnerable women from the surrounding socio-economic community.

Factors that influence the uptake of guidelines

Although it was not feasible to objectively measure the barriers and facilitators identified in previous research in this retrospective study, three broad categories resonated in this project. The three broad categories of external barriers, patient and health care team factors were considered pertinent and are presented in Fig 2 [9, 23, 31].

Although recent research reported a disparity in maternity services for Australians living in rural and remote areas, interesting results were observed in this study [32]. Health care professionals in these postcode locations may have an increased risk awareness, initiate early multidisciplinary collaboration and retrieval of the women to the appropriate maternal centre. It is important to consider the fact that the study results only reflect those women referred to a metropolitan hospital, while the indigenous women dying in remote locations are typically poorly registered, and by default not captured in this type of hospital-based research. An example in this study of the lack of physical resources was the explanation provided for the omission of a requested 12 lead electrocardiograph (ECG) due to the inability to source a functional ECG machine, a situation not unique to Australia [19].

Nair *et al.* [33] identified patient barriers such as reduced health literacy, lack of opportunities for shared decision making, and confidence in healthcare providers. In this study, women frequently did not take the advice offered by the health care team, failed to arrive for appointments and arrived in labour, having had no prenatal care throughout their pregnancy.

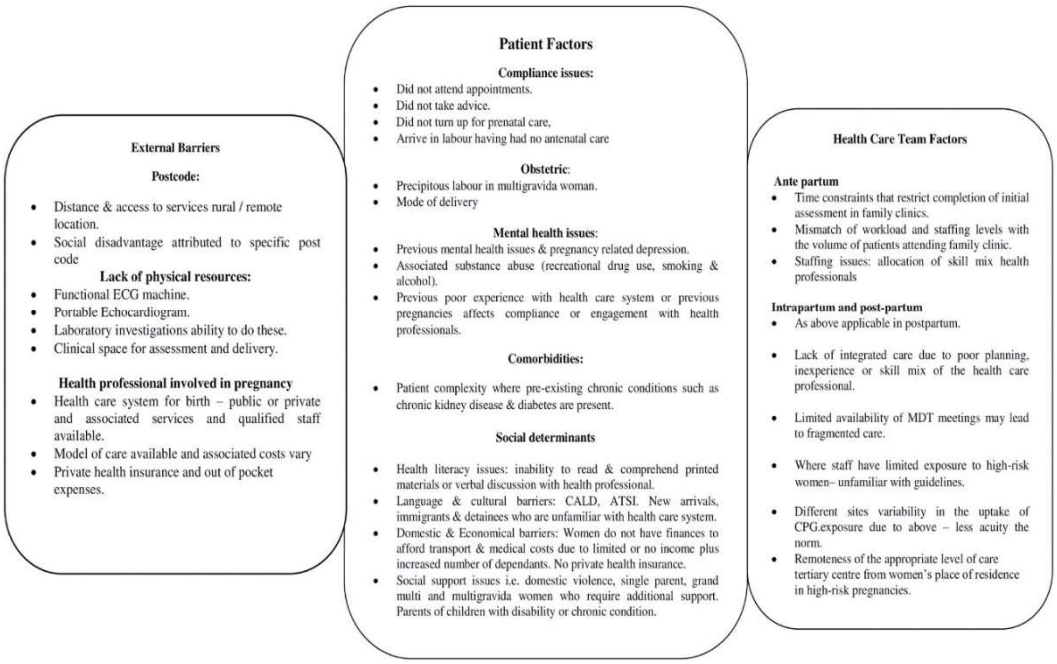


Fig 2. The factors that may influence the uptake of perinatal practice guidelines for women with cardiac conditions during pregnancy.

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Therefore, the resulting low adherence to guideline score could not be attributed to the control of the healthcare team.

Although perinatal staff assist in the development process and revisions of the guidelines, not all health care providers are familiar with the guidelines. Barth *et al.* [34] reported that clinicians lack familiarity with guidelines, agreement with the content, or have a deficit in the necessary skills to deliver care were all barriers to the uptake of guidelines [33]. Staff prioritised documentation of perinatal data for labour and the delivery that is reported to the birth registry. High-quality documentation and extraction of clinical information, as well as dynamic clinical leadership, have been identified as enablers to improve implementation strategies for guidelines [25].

Conclusion

Overall, there was a suboptimal adherence to the SA statewide guidelines for women with cardiac conditions in pregnancy. The actions undertaken comprehensively before or early in the pregnancy resulted in ongoing adherence to the guidelines. The observed variance in the level of adherence across the three hospitals reflected the exposure to higher acuity cases, and that appropriate referral was intrinsically linked to better adherence. The early inclusion of the multidisciplinary team facilitated adherence to the guidelines, mainly with preconception care, and echocardiogram assessment of cardiac status.

The authors propose that perinatal guidelines should contain realistic and clear recommendations, which allow individual clinical judgement orientated for the patient as for efficacy versus safety. Two pivotal recommendations are the completion of preconception counselling and a comprehensive initial antenatal assessment. Therefore, it is vital to ensure that all health practitioners have the skills, training and sufficient time to complete the initial assessment [3].

Generalizability

The data collection was limited to South Australia Health public hospitals due to access and availability of data from the medical records. The sample size and findings are not reflective of the women in South Australia.

Limitations

A limitation of this study is generalizability with the data collected from three South Australian metropolitan public hospitals and private hospitals excluded. This study does not reflect state or national population proportions of women with cardiac conditions in pregnancy. Our study encountered the limitations associated with retrospective medical records reviews, such as missing data and accuracy of documented care delivered. The evidence of adherence to guidelines and the quality of data was contingent upon the quality of documentation. Clinicians may have provided care; yet there was, no documentation in the case notes. The researcher carefully examined individual case notes for other evidence of the care provided in the case notes.

Supporting information

S1 Table. Supplementary information code log for auditmaker and SAS scoring for adherence to the statewide perinatal guidelines.
(PDF)

S2 Table. Assumption testing.
(PDF)

S3 Table. Linear regressions.
(PDF)

S4 Table. Univariate regression.
(PDF)

S5 Table. Descriptive statistics cardiac variables.
(PDF)

S1 File. Perinatal audit DAT.
(PDF)

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Formal analysis: Sandra Millington.

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3.3 Summary of Chapter 3

The study presented in Chapter 3 is the first original report on adherence to the statewide cardiac-specific perinatal guidelines for women with cardiac conditions during pregnancy in South Australia. Although the SAPPGs have been developed and available since 2010, the research showed that overall adherence was not optimal across three SA Health public metropolitan, university-affiliated hospitals, with the level of variance correlating with exposure to higher acuity cases.

Predictors identified for improved uptake of the guideline recommendations included transfers from rural and remote locations; women who experienced previous cardiac events in pregnancy or were identified as high risk, with a known diagnosis of a preexisting cardiac condition, therefore requiring a multidisciplinary team; and women requiring elective surgical delivery.

Although not measurable in the study, factors that were barriers to the uptake of SAPPGs were highlighted – namely, external, patient and health care team factors. Women's heart health literacy during pregnancy is an important area to be considered in future research. The cohort of women included no women diagnosed with cardiac conditions up to 12 months and there was only one woman aged 17 years.

This study highlighted two core guideline recommendations of preconception counselling and comprehensive initial antenatal assessment that must be addressed in clinical practice. Importantly, health practitioners require upskilling or training and adequate time to allow women to disclose their relevant medical history and for staff to complete a thorough initial assessment. This clinical audit and feedback of this study measured the recommended care process for discussion with healthcare practitioners to improve the care processes. [19,20] Therefore, this study supports guideline recommendations, shows future work, and raises awareness of pregnancy-related cardiac conditions for mothers and babies.

Chapter 4: The association between guideline adherence and clinical outcomes during pregnancy in a cohort of women with cardiac comorbidities

4.1 Overview of Chapter 4

Pregnant women with cardiac conditions are at increased risk of maternal, obstetric and neonatal complications. [1,3,17,48] As highlighted in the first study (Chapter 2), the statewide SAPPGs integrate all evidence levels and aspire to reduce maternal and fetal/neonatal mortality and morbidity. Chapter 3's cross-sectional retrospective observational study reported adherence to these guidelines as suboptimal across the three hospital sites but also correlated with the level of exposure to higher acuity cases. However, the clinical outcomes and complications and their association were not reported. This chapter includes the third published paper describing the frequency of clinical morbidities, outcomes and interventions in the preexisting and acquired cardiac groups of women with cardiac conditions during pregnancy and their association with the guideline adherence score.

4.1.1 Background and context

The two broad cardiac categories of conditions seen in pregnancy have been described as preexisting heart disorder and pregnancy-acquired cardiac conditions. The updated literature review in Chapter 2 highlighted international efforts to address the global maternal mortality and morbidity attributable to cardiovascular disease in pregnancy through ROPAC, established to evaluate the outcomes of women with structural heart disease. Multiple published reports describe the CHD spectrum, report on the maternal and neonatal outcomes, and highlight the primary and secondary outcomes. However, there is limited research in Australia and no reported studies that evaluate clinical outcomes associated with adherence to cardiac-specific CPGs.

Literature reports discuss pertinent primary maternal cardiac complications and secondary pregnancy adverse outcomes that clinicians can anticipate for women with cardiac disease in pregnancy, notably CARPREG II research, with risk assessment models.[17] But the continuum of care for women with cardiac conditions and how it may influence their pregnancy outcomes needs to be addressed. In South Australia, there are four main models of maternity care: General practitioner (GP) shared care; Obstetrician-led care or medical model of care; Hospital or Clinic; and Continuity of midwifery care (CoC) or midwifery group practice (MGP).[59] High-risk pregnant women are often triaged to the medical model, pertinent for most women in this study. This may be explicit where the women' clinical deterioration requires a deviation from the planned model of care. Nevertheless, midwives are integral members of the multidisciplinary team for delivering SAPPGs recommended care for these women, as outlined in the Australian framework for maternal and newborn care.[60]

The substudy presented in this chapter focuses on clinical variables, describing the frequency of interventions, maternal cardiac complications, obstetric and neonatal outcomes and determining an association with overall guideline adherence score. The cardiac groups' PEC and AC, identified as prior predictors in the previous study, were included in this substudy analysis. However, given the unequally matched women for each of the three hospitals and reported disparities in the previous study in Chapter 3, they were not included in the analysis presented in this chapter.

4.1.2 Research aims

This study's principal aim was to describe the frequency of clinical morbidities, outcomes and interventions in the preexisting and acquired cardiac groups of women with cardiac conditions during pregnancy and determine the association between the adherence guidelines score and clinical variables.

4.1.3 Overview of method

In the previous study, the researcher made inferences about women with cardiac conditions in pregnancy and the SAPPGs from the data collected through hypothesis testing. Multivariable logic regression modelling compared differences and associations for the uptake of the SAPPGs across the three hospital sites and the two broad cardiac groups of pregnant women and the overall cohort. Logic regression modelling analysed the overall adherence score to SAPPGs that reflected the calculated scores for each perinatal guidelines' recommendations. The results included an odds ratio with a 95% confidence interval and significance value for all analyses set at p value < 0.05.

Moreover, in this substudy the descriptive analysis reported the frequencies of clinical variables. However, before inferential statistical analysis, the researcher modified the clinical data, i.e., coding string data, categorisation as maternal cardiac, obstetric, and neonatal variables, and created dummy variables. This process set up the dataset for linear regression analysis for any correlations between the overall adherence score and clinical variables reported in the paper and Appendices C.

The sample size was an important consideration in managing type 1 and type II errors in this research project. The initial sample size was reduced to 261 cases in this substudy through the data screening and cleaning process. The rationale for exclusion was the inability to retrieve missing clinical outcome data. In some cases, the women returned to the rural community for delivery, or interhospital transfers occurred, and therefore the researcher could not access medical records. Ongoing adjudication occurred with specialist clinicians, who identified cases that did not meet the study's inclusion criteria and were therefore removed. Although the sample size was reduced, the cohort still met the criteria of the initial power calculation for a required sample size of 196 with > 99% power to detect a difference in 13% of patients.

Also, the level of significance set by the researcher was ($p=0.05$) in the initial study in Chapter 3. But, in this substudy, an adjusted p value <0.2 was used in the multivariable linear regression analysis. This enabled the researcher to build a parsimonious model with a selection of clinical variables described in the paper. [61,62] Although variable selection methods appears simple to use and handy to build multivariable

models, selection issues such as uncertainty or bias in reported quantities can be overlooked by clinicians. However, the researcher collaborated with the senior statistician regarding variable section technique for the clinical variables in the multivariable model building because there was insufficient amount of data to justify elimination or inclusion of variables in a model that just 'let the data speak.' Therefore, the researcher informed by Harrell's on Multivariable Modeling Strategies chose the better option with expert knowledge to guide to robust multivariable models. The rationale for using a higher p value cut off in multivariable modelling is because in smaller samples with complexity, a lower cut off will overfit the data. The SPPS program would choose variables and eliminate others based on chance features of the dataset, and so harm the external validity of the model when applied to new datasets. [61] Generally, very strong predictors will be selected with a $p<0.05$ cut off, because the distributions between groups are well separated and so will be 'statistically significant' different in most samples. However, less strong predictors (but still important, as in this substudy e.g., the clinical variables cardiac arrest or cardiac surgery and maternal death) will tend to have larger observed difference in some samples and smaller observed differences in others. Hence, the use of a $p < 0.05$ cut off, may result in

- Including those weaker predictors which *by chance* have larger differences in this sample and thereby overestimating the effect of these predictors,
- Excluding equally important predictors which happened to have a smaller difference in this sample.

Statistical literature generally do not recommend variable selection be performed at all unless it is necessary because it leads to overfitting, but if it is done then a more lenient criterion should be used.[61,62]

As a prerequisite for multiple regression, assumption testing procedures with the SPPS Statistics output were undertaken. Further information on clinical coding of interventions, complications, and outcomes for SPSS variables is tabled in Appendices C. Likewise, the univariate linear regression model results for all three categories, tabled updated baseline characteristics, and the maternal and neonatal cardiac spectrum diagnoses in the cohort.

4.2 Manuscript, Paper Three – The association between guidelines adherence and clinical outcomes during pregnancy in a cohort of women with cardiac co-morbidities

The following paper, 'The association between guidelines adherence and clinical outcomes during pregnancy in a cohort of women with cardiac co-morbidities', was published *PLoS One*, *16*(7), July 2021. doi:https://doi.org/10.1371/journal.pone.0255070

Statement of authorship and publication 3

Statement of Authorship

Title of Paper	The association between guidelines adherence and clinical outcomes during pregnancy in a cohort of women with cardiac co-morbidities.
Publication Status	☑ Published ☐ Accepted for Publication ☐ Submitted for Publication ☐ Unpublished and Unsubmitted work written in manuscript style
Publication Details	Millington, S, Edwards, S, Clark, R. & Dekker, G, Arstall, M (2021). The association between guidelines adherence and clinical outcomes during pregnancy in a cohort of women with cardiac comorbidities. Original research *PLoS One* 16 (7), e0255070.doi.org/101371/ journal. pone.0255070

Principal Author

Name of Principal Author (Candidate)	Sandra Millington
Contribution to the Paper	Conceptualisation and design, data acquisition and curation. Data analysis and interpretation, drafting and revision of the manuscript for important intellectual content. Also, acted as corresponding author.
Overall percentage (%)	90%
Certification:	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper.
Signature	Date: 4/8/2021

Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:

i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate in include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to 100% less the candidate's stated contribution.

Name of Co-Author	Suzanne Edwards
Contribution to the Paper	Supervision of data analysis and interpretation. Revision of manuscript for important intellectual content.
Signature	Date: 5/8/2021
Name of Co-Author	Robyn A Clark
Contribution to the Paper	Supervision of interpretation of data, and revision of manuscript for important intellectual content.

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Contribution to the Paper	Supervision of data interpretation and revision of manuscript for important intellectual content.		
Signature		Date	4/8/2021

Name of Co-Author	Margaret Arstall		
Contribution to the Paper	Supervision of data interpretation, and revision of manuscript for important intellectual content.		
Signature		Date	17/8/2021

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RESEARCH ARTICLE

The association between guidelines adherence and clinical outcomes during pregnancy in a cohort of women with cardiac co-morbidities

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Abstract

Background/Aims

Maternal and infant morbidities associated with pregnant women with cardiac conditions are a global issue contingent upon appropriate care. This study aimed to describe the clinical variables and their association with the adherence scores to perinatal guidelines for pregnant women with cardiac conditions. The clinical variables included cardiac, perinatal, and neonatal outcomes and complications.

Methods

Using a retrospective cross-sectional medical record audit, data were abstracted and categorised as cardiac, obstetric, and neonatal predictors. Linear regression modelling was used to find the mean difference (MD) in adherence scores for each predictor, including a 95% confidence interval (CI) and a significance value for all the three categories' clinical outcomes.

Results

This maternal cohort's (n = 261) cardiac complications were primarily arrhythmias requiring treatment (29.9%), particularly SVT (28%), a new diagnosis of valvular heart disease and congenital heart disease (24%) and decompensated heart failure (HF) (16%). Women with HF had associated increased adherence scores (MD = 3.546, 95% CI: 1.689, 5.403) compared to those without HF. Elective LSCS mode of delivery was associated with a higher adherence score (MD = 5.197, 95% CI: 3.584, 6.811) than non-elective LSCS subgroups. Babies admitted to intensive /special care had greater adherence to the guidelines (MD = 3.581, 95% CI: 1.822, 5.340) than those not requiring the same care.

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Conclusions

Some pregnancy associated complications and morbidities were associated with higher adherence scores, reflecting that a diagnosis, identification of morbidities or risk factors, initiation of appropriate multidisciplinary involvement and adherence to guidelines were associated. Conversely, potentially avoidable major complications such as sepsis were associated with a low adherence score.

Trial registration

ACTRN12617000417381.

Introduction

Cardiovascular disease is a major cause of maternal mortality, accounting for up to 15% of maternal deaths and complicating between 1% and 4% of pregnancies, with the associated morbidities becoming an increasingly recognised issue, warranting our attention [1–4]. However, limited data is available on cardiac disease in pregnancy in Australia, and research is underreported [5, 6]. The national maternal mortality ratio, i.e. the number of deaths per 100, 000 women giving birth, was reportedly below ten from 2008 to 2017 [6, 7]. Yet cardiac-related maternal deaths occurring during pregnancy are classified as indirect maternal deaths due to preexistent medical conditions or disease acquired during pregnancy rather than the consequence of direct obstetric death [5]. Heart disease in pregnancy consists of a heterogeneous group of disorders inclusive of corrected and uncorrected congenital lesions, valvular disease, arrhythmias, aortopathies, cardiomyopathies, acquired atherosclerotic heart disease, genetic conditions, and cardiac complications associated with severe hypertensive disorders [6, 8]. Due to the increased physiological stress of pregnancy on the maternal cardiovascular system, maternal preexisting or cardiac pathological conditions acquired during pregnancy may have different outcomes than those in the non-pregnant state [9].

Background and rationale

The two broad categories of cardiac conditions in pregnancy are preexistent heart disorders and pregnancy-acquired cardiac conditions [10, 11]. Congenital heart disease (CHD) is the predominant diagnosis of all cardiac lesions in developed countries (75% to 82%). Conversely, rheumatic heart disease comprises 56% and 89% of pregnancy-related cardiac conditions reported in developing countries, i.e. middle and low-income, respectively [8]. However, acquired cardiac complications may occur throughout pregnancy, including six months postpartum, when women recover to their prepregnancy haemodynamic status.

Women with a preexistent medical condition or prior adverse pregnancy outcomes are at increased risk of cardiac complications in subsequent pregnancies and later in life [4, 12, 13]. Adverse pregnancy outcomes include complications, such as maternal placental syndromes and gestational diabetes mellitus (GDM). Likewise, pregnant women with cardiac conditions are at increased risk of obstetric and neonatal complications [14–19]. Therefore, high risk cardiac pregnancies present clinicians with significant challenges.

Consequently, a comprehensive antenatal assessment and, ideally, preconception counselling are firmly recommended in best practice [20]. A healthy mother and baby are the aspirations of all pregnant women and the health care team delivering care during their pregnancy.

The clinical outcomes for women with cardiac conditions during pregnancy are influenced by the health care 'providers' expertise and knowledge of best practice perinatal guidelines and the healthcare system's capacity or limitations [20].

During pregnancy, cardiovascular disease (CVD) management guidelines have been informed by knowledge generated through case reports, registries, and expert opinion rather than evidence from randomised clinical trials [2, 5, 21]. In both South Australia and Western Australia, statewide guidelines integrate all levels of evidence to aspire to reduce maternal mortality and morbidity [22, 23]. This present study contributes to the broader research, of established statewide cardiac-specific perinatal guidelines for women with cardiac disease during pregnancy across the three major public hospitals, in Adelaide, South Australia. The aim was to measure clinical practice against guideline recommendations to verify real-life practice and identify gaps for quality improvement measures.

Aim

The study aimed to describe clinical variables, i.e., morbidities, outcomes, interventions, and their association with the adherence score for the cardiac-specific statewide perinatal guidelines for women with cardiac conditions during pregnancy, with the following objectives:

- Describe the frequency of clinical morbidities, outcomes, and interventions in the preexistent and acquired cardiac groups of the cohort of women with cardiac conditions during pregnancy.
- Determine the association between the adherence to guidelines score and clinical variables, i.e., outcomes, complications and required interventions.

Methods

Study design and population

This research is a preplanned sub-study of the retrospective cross-sectional observational audit that evaluated adherence to clinical practice guidelines for South Australian pregnant women with cardiac conditions between 2003 and 2013. Details of the study design, data abstraction tool, settings, selection criteria and the evaluation of adherence to clinical practice guidelines across three hospital sites were published previously. In summary, we showed that variance in adherence correlated with the exposure to the higher acuity cases and appropriate up-referral to the only high risk referral centre for the state, the quartenary hospital two, which provided (level six) care, i.e. maternal cardiac and neonatal intensive care services. Likewise, hospital one offered intermediate care (level five) inclusive of tertiary maternal services, intensive care and specialised neonatal care services but excluded babies less than 32 weeks. Also, hospital three was a stand-alone maternity unit attached to a large neonatal intensive care, yet without a maternity intensive care service onsite [20].

The previous study evaluated the adherence to recommendations within the guidelines. The predictors for adherence were examined, such as the hospital sites, the two broad cardiac groups, underlying cardiac causes, risk level of pregnancy, multidisciplinary team collaboration, maternal and baby demographic factors. The participants included only women with 'preexistent' and 'newly acquired' heart disease during pregnancy, with a more comprehensive discussion on the selection criteria presented in Millington (2020) et al. [20].

The cohort's broad spectrum of maternal cardiac diagnosis and neonatal diagnosis which includes rare syndromes namely Scimitar, Goldenhar and Noonan are available in S1 and S2 Tables [24–26].

Ethics approval

South Australian Health Human Research Ethics Committee approved this study (Reference HREC 13 TQEH/LMH 226: Extension to Approval 03/08/2015). The Research Ethics approval granted the researcher access to medical records to collect data, and consent was not required from the participants. Anonymity was ensured with the 'participants' identifiable information coded and stored with a separate password-protected file on the university server and labelled for deletion in 15 years.

Data sources /measurements

Guideline adherence score. The total adherence score, a numerical value for each participant, reflected the adherence to the contents of the statewide perinatal guidelines. Scoring encompassed preconception counselling, antenatal care (clinical assessment and investigations), foetal wellbeing assessments, planned risk stratification, mode of delivery and labour recommendations as per guidelines [20]. A scoring system was devised that measured adherence variables used in this study were equally weighted, giving a maximum score of forty to measure adherence. Positive documentation of the guidelines, regardless of the entry point, achieved a score. A minimum score of acceptable guideline adherence was determined after comparing the two cardiac groups mean, and median adherence scores with expert review of selected cases identifying the minimum expected care. From this analysis, a score of 35 (for the 'preexistent') and 17 (for the 'newly acquired') cardiac conditions were deemed acceptable guideline adherence.

Clinical outcomes. The data collected from the retrospective clinical audit of medical records identified pregnancy complications for mother and baby, including morbidities, outcomes, the expected clinical investigations and interventions. Therefore, the string data required coding and categorisation. Likewise, variables utilised in the statistical analysis were categorised into three groups, namely: maternal cardiac (n = 17), obstetric (n = 17) and neonatal (n = 20) see S3 Table. Explicitly, the clinical variables for both primary and secondary clinical outcomes, investigations, and interventions during pregnancy could alter the trajectory for mother and baby, thus influencing the uptake of guidelines and acute complications related to poor guideline adherence [19].

Data cleaning and screening process

The study implemented a three-step process to screen and clean data, repetitive screening, diagnosis and editing [27]. The procedures encompassed checking for consistencies in the data flow, exploring construing factors, comparing the analysis dataset and raw database for errors such as double entry, missing values, unreadable data, and writing error. Those cases with data missing for the clinical variables were excluded in the final analysis. Thus, the sample size reduced from 271 to 261 for the final analysis.

Bias

Inherent bias may be apparent when women presented late to prenatal care or delivered prematurely, such that their access to guideline-based healthcare was delayed or curtailed. Furthermore, data collection was by a single reviewer (author one) with selected case adjudication sessions undertaken with authors four and five who are specialists in a tertiary hospital multidisciplinary team for high risk pregnancies.

Sample size and power calculations

A sample size and power calculation were performed and reported on in a previous paper on this topic [20] based on adherence to guidelines. The sample size acquired provides a substantial 'margin for error' to compensate for missing data, but possibly not for rare events such as maternal deaths (n = 1).

Clinical outcome variables

The clinical outcomes have been subdivided into three groups, namely cardiac, obstetric and neonatal.

Cardiac variables. The cardiac data collected were adverse cardiac events in the puerperium, including six months post-partum. Our primary clinical outcomes were maternal cardiac death, cardiac arrest, decompensated heart failure (HF) and acute pulmonary oedema, acute myocardial infarction (AMI), and a new diagnosis of valvular heart disease (VHD) or congenital heart disease (CHD) diagnosis during pregnancy [3, 28–31]. Women in the preexistent cardiac group diagnosed with additional cardiac pathologies such as VHD or CHD to their known heart disease during pregnancy were recorded.

Secondary clinical outcomes were arrhythmias requiring treatment and non-specific chest pain. Likewise, all invasive cardiac interventions appropriate to the statewide guidelines were included. Non-invasive procedures included computed tomography (CT), pulmonary angiography (CTPA), and echocardiography. Invasive procedures included coronary angiography with or without percutaneous coronary intervention (PCI), electrophysiology (EP) studies with or without accessory pathway ablation, placement of a cardiac internal electrical device (CIED), balloon valvoplasty and cardiac surgery [28, 32, 33].

Obstetric variables. Given the known correlation between obstetric complications and pregnant women with cardiac conditions, obstetric data were collected [4, 13]. These included gestational hypertension (GH), preeclampsia (PET), antepartum and post-partum haemorrhage, placental dysfunction, i.e., placenta praevia and accreta, threatened premature onset of labour, preterm birth, failure to progress in labour, intrauterine growth restriction (IUGR) and maternal sepsis [4, 16]. Also, the guidelines recommend vaginal delivery for women with cardiac conditions, with a shortened active phase in the second stage of labour to mitigate cardiovascular stress and potential complications; therefore, data on delivery methods were collected [34].

Data were collected for normal vaginal deliveries (NVD), instrumental vaginal deliveries (forceps and vacuum device), both elective and emergency lower segment caesarean sections (LSCS) and where the surgical approaches proceeded to hysterectomy or laparotomy. Likewise, where the women's planned delivery deviated with potential changes in adherence to the perinatal guidelines was examined. The obstetric variable 'deviation from the planned delivery mode' captured this data.

Neonatal variables. Preexistent maternal heart disease, possibly via a decline in maternal cardiac output during pregnancy (IUGR) and obstetric complications, are associated with an increased risk of neonatal complications [14, 19]. Therefore, this study collected data for neonatal complications. Our primary outcomes of neonatal mortality (death within 30 days of delivery), intrauterine foetal death (IUFD) (> 20 weeks gestation) and medical termination of the pregnancy for a maternal cardiac condition. Secondary neonatal outcomes of prematurity (< 37 weeks), clinical diagnosis of IUGR, congenital heart disease and genetic abnormalities data [35]. Perinatal data had birthweight <10^{th} percentile or birthweight <2500g if the gestational age was unknown, low Apgar scores (< 7 at 1 and 5 minutes), and respiratory distress syndrome (RDS) with and without respiratory support. The data collected for resuscitation

measures at birth ranged from low intensity, i.e., tactile stimuli, suction, oxygen therapy with bag-mask ventilation, invasive intubation, and ventilation. Data for interhospital retrievals with admissions to Neonatal Intensive Care Unit (NICU) or Special Baby Care Unit level 3 (SBCU3) were collected [29, 36, 37].

Statistical analysis

Analyses were performed using SPSS for Windows (version 26.0 IBM Corp, Armonk, NY). Descriptive analyses of the overall adherence score, frequency tables of the relevant categorical data and coded variables for women in the two cardiac groups were carried out. Cross-tabulations of the categorical variables and cardiac group indicated whether these variables were related. The total adherence score was normally distributed on inspection of the histogram and presented as mean +/- standard deviation (SD).

Univariate linear regression analysis of the total adherence score versus the separate cardiac, obstetric, and neonatal categories was performed (see S5–S7 Tables). The following are reported for all clinical variables: mean difference with 95% confidence interval (CI), significance value, adjusted R Squared, change in R Squared, and frequencies. The linear regression assumptions: normality of residuals and homoscedasticity (equal spread of variance) were found to be upheld in all univariate models by inspection of histograms and scatterplots of residual and predicted values.

The authors performed multivariable regression analysis using a p value cut-off criterion of 0.2 on the univariate linear regression results [38, 39]. Specifically, the inclusion of all covariates with p value <0.2 on univariate regression analysis were included in an initial multivariable model, followed by backward elimination until all remaining covariates had a p value < 0.2 [39] refer to S5–S7 Tables. Multivariable regression modelling with backwards elimination was undertaken on three separate regression models for obstetrics, neonatal and cardiac predictors, respectively (refer to Tables 2–4). This is how the final multivariable parsimonious model (presented in Table 5) was built.

Results

Clinical characteristics

The cohort included 261 women of unmatched preexistent cardiac (n = 139) and acquired cardiac groups (n = 122). Updated baseline characteristics are reported in S4 Table. The mean adherence score in the preexistent cardiac group was 17.7 versus 15.2 in the acquired cardiac group. In the preexistent group, more women were from a rural location 30 (21.6%) and aboriginal ethnicity 21 (15%), compared with the acquired group 15 (12%) and 11 (9%). The descriptive frequencies of the categorical clinical variables for the overall cohort of women and the two cardiac groups are reported in Table 1.

Clinical morbidities, outcomes, and interventions. The primary clinical outcome of mortality was low for the cohort (n = 1). The only maternal death occurred in the acquired cardiac group and was associated with a low adherence score of eight. There were no neonatal deaths; however, one intrauterine death late in pregnancy occurred in the acquired cardiac group. One medical termination of pregnancy occurred in the first trimester due to severe mitral valve disease in the preexistent cardiac group.

Within the overall cohort, 11 women experienced a cardiac arrest, predominantly in the acquired cardiac group. Similarly, HF occurred in 42 cases (16%) and was more frequent in the acquired cardiac group (22%) n = 27, compared with the preexistent cardiac group (11%) n = 15. There were 78 (29%) cases of sustained arrhythmias requiring treatment in the overall cohort, with (28%) n = 73 SVT and mainly in the acquired cardiac group (44%) n = 54. Non-

Table 1. The descriptive statistics for clinical variables in the preexistent and acquired cardiac groups of women in South Australia during 2003 and 2013.

Cardiac clinical variables	Combined Cardiac Groups n (%) N = 261	Preexisting cardiac (PEC) n (%) N = 139	Acquired cardiac (AC) n (%) N = 122
Maternal Cardiac Death	1 (0.4)	0	1 (0.8)
Cardiac Arrest	11 (4.2)	3 (2.2)	8 (6.6)
Decompensated Heart Failure	42 (16.1)	15 (10.8)	27 (22.1)
Acute Myocardial Infarction (AMI)	5 (1.9)	0	5 (4.1)
VHD/CHD diagnosis during pregnancy	63 (24.1)	48 (34.5)	15 (12.3)
Sustained Arrhythmias + Tx	78 (29.9)	21 (15.1)	57 (46.7)
Supraventricular Tachycardia (SVT)	73 (28.0)	19 (13.7)	54 (44.3)
Bradyarrhythmias without syncope and HF	12 (4.6)	1 (0.7)	11 (9.0)
Non-specific chest pain	52 (19.9)	18 (12.9)	34 (27.9)
Cardiovascular Implantable Electrical Device (CIED)	6 (2.3)	1 (0.7)	5 (4.1)
Cardiac surgery required	6 (2.3)	5 (3.6)	1 (0.8)
Balloon Valvoplasty required	3 (1.1)	2 (1.4)	1 (0.8)
Cardiogenic shock with Intra-Aortic Balloon Pump (IABP)	1 (0.4)	0	1 (0.8)
Need for invasive cardiac investigations.			
EP studies ±Cardiac ablation	9 (3.4)	1 (0.7)	8 (6.6)
CTPA+ Echocardiogram investigations required	26 (10)	4 (2.9)	22 (18.0)
Coronary angiogram ± PCI	14 (5.4)	1 (0.7)	13 (10.7)
*Other Non-cardiac complications	16 (6.2)	12 (8.6)	4 (3.3)
Obstetric clinical variables	**Combined cardiac Groups** n (%)	**Preexisting cardiac conditions (PEC)** n (%)	**Acquired cardiac conditions (AC)** n (%)
Modes of delivery			
Normal vaginal delivery (NVD)	102 (39.1)	55 (39.6)	47 (38.5)
Assisted vaginal delivery (VD)	27 (10.3)	11 (7.9)	16 (13.1)
Elective Lower Segment Caesarean Section (LSCS)	74 (28.4)	49 (35.3)	25 (20.5)
Emergency LSCS	54 (20.7)	23 (16.5)	31 (25.4)
Emergency LSCS plus Hysterectomy	4 (1.5)	1 (0.7)	3 (2.5)
†Deviated from planned mode of delivery	92 (35.2)	42 (30.2)	50 (41)
Obstetric clinical morbidities/ interventions			
Failure to progress in labour (FTP)	28 (10.7)	13 (9.4)	15 (12.3)
Threatened premature labour (TPL)	30 (11.5)	16 (11.5)	14 (11.5)
Placenta Accreta	3 (1.1)	2 (1.4)	1 (0.8)
Placenta Praevia	8 (3.1)	3 (2.2)	5 (4.1)
Antepartum Haemorrhage (APH)	9 (3.4)	3 (2.2)	6 (4.9)
Postpartum haemorrhage (PPH)	36 (13.8)	20 (14.4)	17 (13.1)
Pregnancy Induced Hypertension (PIH)	39 (14.9)	16 (11.5)	23 (18.9)
Preeclampsia (PET)	25 (9.6)	12 (8.6)	13 (10.7
Suspected Intrauterine Growth Restriction (IUGR)	10 (3.8)	8 (5.8)	2 (1.6)
Sepsis	15 (5.7)	6 (4.3)	9 (7.4)
Neonatal clinical variables	**Combined cardiac groups,** n (%)	**Preexisting cardiac conditions (PEC),** n (%)	**Acquired cardiac conditions (AC),** n (%)
‡Alive and well	189 (72.4)	101 (72.7)	88 (72.1)
IUFD/stillbirth	1 (0.4)	0	1 (0.8)
TOP (Medical)	1 (0.4)	1 (0.7)	0
Prematurity	46 (17.6)	20 (14.4)	26 (21.3))
Prematurity + NICU/SBCU3 transfer	42 (16.1)	18 (12.9)	24 (19.7)

(*Continued*)

Table 1. (Continued)

Active Resus +O_2/BMV/Intubate/IPPV	34 (13)	19 (13.7)	15 (12.3)
Retrieval with CPAP ventilation	9 (3.4)	5 (3.6)	4 (3.3)
Active Resus low invasive	25 (9.6)	9 (6.5)	16 (13.1)
Septic workup/Sepsis	18 (6.9)	6 (4.3)	12 (9.8)
Respiratory Distress syndrome (RDS)	39 (14.9)	23 (16.5)	16 (13.1)
RDS required CPAP	21 (8.0)	13 (9.4)	8 (6.6)
[§]SFD clinical diagnosis	10 (3.8)	8 (5.8)	2 (1.6)
Diagnosis of Congenital Heart Disease (CHD)	6 (2.3)	5 (3.6)	1 (0.8)
Diagnosis of Non-cardiac Congenital Abnormalities	8 (3.1)	6 (4.3)	2 (1.6)
[‖]Apgar Score < 7 at 1 min	35 (13.4)	17 (12.2)	19 (15.4)
[‖]Apgar Score < 7 at 5 min	18 (6.9)	9 (6.5)	10 (8.0)
NICU admission	73 (28)	38 (27.3)	35 (28.7)
SBCU3 admission	29 (11.1)	12 (8.6)	17 (13.9)

VHD/CHD: Valvular Heart Disease or Congenital Heart Disease Diagnosis, HF: Heart failure, CIED: Cardiovascular Implantable Electronic Device, e.g. Pacemaker / implantable cardioverter defibrillator, Arrhythmias + TX: Sustained Arrhythmias requiring treatment, EP studies/Cardiac Ablation: Electrophysiology studies and Catheter Ablation, CTPA+ Echocardiogram: CT computed-tomography pulmonary angiogram, PCI percutaneous coronary intervention. NICU: Neonatal Intensive Care Unit, SBCU3: Special Baby Care Unit level 3, Active Resus+ O_2/BMV/ intubate /IPPV: active resuscitation that required oxygen administration(O_2), bag-mask ventilation (BMV) but also required intubation (intubate) and mechanical ventilation mode of intermittent positive pressure ventilation (IPPV), CPAP: mode of mechanical ventilation Continuous positive pressure ventilation

*Other non-cardiac complications: hepatic encephalopathy and bleeding gastric varices, oesophageal sclerotherapy.

† Deviated from planned delivery mode: planned NVD required alternative (listed) mode of delivery or planned Elective LSCS was precipitous SVD or Emergency LSCS.

[‡] documented as "Alive and Well' by clinicians at birth, IUFD: Intrauterine Foetal Death ≥ 20 weeks gestation, TOP: Medical Termination of pregnancy < 24 weeks.

[§] Clinical Diagnosis of IUGR/SFD small for dates

[‖]Missing data totals = ** 2, ***1(1& 5 min respectively).

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specific chest pain 34 (27%) was prevalent in the acquired group and included only 5 (4%) AMI incidents for the cohort. New diagnosis of CHD and VHD during pregnancy occurred more often in women with a preexistent cardiac condition (34%) in comparison to the acquired group (12%) (See Table 1). These women were diagnosed with different cardiac pathology such as VHD or CHD to their known heart disease during pregnancy. A modest number of cardiac interventions (n = 58, 22%) encompassed cardiac diagnostic investigations, i.e., CTPA with an echocardiogram to the more invasive balloon valvoplasty and cardiac surgery, mainly in the preexistent cardiac group (See Table 1).

Whilst there were 101 (39%) normal vaginal delivery, 92 women (35%) deviated from their planned birthing mode, particularly in the acquired cardiac group (41%) n = 50. The birthing options of elective (28%) n = 74 and emergency LSCS (20%) n = 54 were found to be more frequent than assisted vaginal delivery (10%), n = 27. Additional information on the frequencies of obstetric complications in the cohort is in Table 1.

There were 189 (72%) neonates born with normal Apgar scores (>7 at 1 and 5 minutes), while 34 (13%) babies required active resuscitation at birth, particularly in the preexistent cardiac group. The cohort included six sets of twins, one set of triplets, and all were admitted to NICU for prematurity. Seventy-three (28%) babies were admitted to NICU, and 29 babies (11%) transferred to SBCU3. Nine babies in the cohort required invasive respiratory support

Table 2. Multivariable linear regression model results for the adherence score versus maternal cardiac clinical variables.

Clinical variables	Mean difference Adherence score (95% CI)	Standardized Coefficients Beta	P value	N (%) N = 261
Cardiac clinical outcomes.				
Decompensated Heart failure (HF)	5.062 (2. 976,7.147)	0.286	<0.001	42 (16)
Non- specific chest pain	1.846 (-0.348,4.039)	0.113	0.099	52 (19.9)
Cardiac interventions.				
*CTPA+ Echocardiogram	-3.388 (-6.308, -0.467)	-0.156	0.023	26 (10)
Cardiovascular Implantable Electrical Device (CIED)	4.801 (-0190, 9.792)	0.111	0.059	6 (2.3)
Cardiac Surgery required	5. 962 (0.968, 10.956)	0.137	0.019	6 (2.3)
Balloon Valvoplasty required.	10.027 (3.177,16.876)	0.164	0.004	3 (1.1)
Coronary angiogram with/without †PCI	-2.646 (-6.187, 0.896)	-0.092	0.142	14 (5.4)
Other factors				
Acquired cardiac group	-2.264 (-3.843,-0.686)	-0.174	0.005	122 (46.7)

Significance p value <0.2. All clinical variables were yes vs no.

*CTPA+ Echocardiogram = Computed-tomography pulmonary angiogram and cardiac echocardiogram.

†PCI = percutaneous coronary intervention.

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and retrieval. More neonates (n = 23; 16%) in the preexistent cardiac group experienced RDS, whilst 13 babies with RDS (9%) required respiratory support. A small number of babies (n = 6) were diagnosed with congenital heart disease and abnormalities, particularly in the preexistent cardiac group (See S2 Table).

The association between the guideline adherence score and clinical variables. The initial multivariable regression analysis results for the separate groups of clinical outcomes are presented in Tables 2–4. However, the final multivariable results for the association between guideline adherence score and clinical variables for the cohort are shown in Table 5. The cardiac variable of HF had the statistically most robust association with an improved guideline adherence score ($p < 0.001$). Women with HF had a mean guideline adherence score of 3.546

Table 3. Multivariable linear regression model results for the adherence score versus obstetric clinical variables.

Clinical variables	Mean difference Adherence score (95% CI)	Standardized Coefficients Beta	P value	n (%) N = 261
Obstetric Complications				
Preexistent cardiac group	1.957 (0.552, 3.362)	0.150	0.007	139 (53.2)
Pregnancy Induced Hypertension (PIH)	2.156 (-0.170, 4.482)	0.118	0.069	39 (14)
Preeclampsia (PET)	1.954 (-0.979, 4.887)	0.088	0.191	25 (9.6)
Placenta Previa (PP)	4.802 (-0.489,8.754)	0. 127	0.017	8 (3.1)
Threatened premature onset of Labour	2.015 (-0.131, 4.160)	0.099	0.066	30 (11.5)
Abnormal Intrauterine Growth restriction (IUGR) / Small for dates (SFD)	4.964 (1.366,8.561)	0.147	0.007	10 (3.8)
Modes of Delivery				
Assisted vaginal delivery (VD)	1.946 (-0.427,4.319)	0.091	0.108	27 (10.3)
Lower segment Caesarean Section (LSCS) (Elective)	6.410 (4.733,8.087)	0.445	<0.001	74 (28)
Emergency LSCS	2.983 (0.003,1.025)	0.186	0.003	54 (20.7)
*Deviated from planned delivery mode	1.610 (-0.168, 3.052)	0.118	0.029	92 (35.2)

Significance p value <0.2. All clinical variables were yes vs no.

* Deviated from planned delivery mode; those women with planned NVD who required alternate listed modes or Elective LSCS was precipitous SVD or Emergency LSCS.

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Table 4. Multivariable linear regression model results for the adherence score versus neonatal clinical variables.

Clinical variables	Mean difference Adherence score (95% CI)	Standardised Coefficients Beta	P value	n (%) N = 261
Preexistent cardiac group	2.357 (0.883, 3.832)	0.181	0.002	139 (53.2)
Prematurity +*NICU/SBCU3	2.063 (-0.226, 4.351)	0.115	0.077	42 (16.1)
Retrieval/ †CPAP/ Ventilation	-3.525 (-8.349, 1.299)	-0.099	0.151	9 (3.4)
RDS required CPAP	-3.021 (-6.891, 0.849)	-0.126	0.125	21 (8)
Low Apgar Score<7 at 5 minutes	3.841 (-0.170, 7.852)	0.150	0.060	18 (6.9)
NICU Admission	4.966 (2.990, 6.943)	0.343	<0.001	73 ((28)
Sepsis workup/ sepsis	-2.311 (-5.396, 0.773)	-0.090	0.141	18 (6.9)
Diagnosis of Congenital Abnormalities	4.544 (0.010, 9.098)	0.121	0.050	8 (3.1)

Significance p value <0.2. All clinical variables were yes vs no.

*NICU: Neonatal Intensive Care Unit, SBCU3: Special Baby Care Unit Level 3

†CPAP: mode of ventilation Continuous Positive Pressure ventilation

‡ RDS: Respiratory Distress Syndrome + CPAP continuous positive airway pressure.

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units higher than those who did not have heart failure (mean difference (unstandardised beta coefficient of linear regression equation) = 3.546, 95% CI: (1.689, 5.403). There was a statistically significant association between the adherence score and the following cardiac variables: women in the preexistent cardiac group (p = 0.004), those women who had balloon valvoplasty (p = 0.004), those who required cardiac surgery (p = 0.041), and the investigations of CTPA inclusive of an echocardiogram (p = 0.047), whilst adjusting for all other covariates in the multivariable model. There was no association with adherence score in women who experienced cardiac arrest in the final multivariable analysis.

Elective LSCS mode of delivery had the statistically most robust association with an improved guideline adherence score (p < 0.001). Those women who had an elective LSCS had a mean guideline adherence score 5.197 units more than those who did not (mean difference = 5.197, 95% CI: 3.584, 6.811). The statistically significant associations between the guideline adherence score and other obstetric variables were emergency LSCS (p = 0.0120), diagnosis of preeclampsia (p = 0.034) and placenta praevia complication (p = 0.011), whilst adjusting for all other covariates.

The only neonatal variable reporting a statistically significant association with the guideline adherence score was NICU admission adjusting for all covariates in the model (p <0.001). Those women with babies who went to NICU admission had a mean adherence score 3.581 units greater than those without babies in NICU admission (mean difference = 3.581, 95% CI: 1.822, 5.340). A small number of babies diagnosed with congenital cardiac conditions (n = 6) are included in NICU admission, with some requiring further paediatric care and follow up (refer to S2 Table).

Discussion

The study aimed to compare clinical outcomes against guideline recommendations to verify real-life practice and identify gaps for quality improvement measures. Particularly to describe the frequencies of clinical morbidities, outcomes and interventions in the cohort of women with cardiac conditions during pregnancy and determine their association with the adherence score. We found that the mortality and morbidity findings of this study were consistent with international research. Pregnancy in women with cardiac conditions is associated with significant morbidity, yet maternal cardiac mortality is reportedly rare (our cohort, n = 1) [28]. Our cohort reflected similar findings to the Cardiac Disease in Pregnancy II (CAREPREG II) study

Table 5. Multivariable linear regression model results: Clinical variables versus adherence score of the clinical practice guidelines for South Australian pregnant women with cardiac conditions between 2003 and 2013.

	Clinical variables	Mean Difference in Adherence score (95% CI)	Standardised Coefficients Beta	P value	Frequency N = 261
Obstetric complications.					
	Preeclampsia (PET)	2.573 (0.199, 4.948)	0.117	0.034	25
	Placenta Previa (PP)	4.900 (1.136, 8.663)	0.130	0.011	8
Modes of Delivery					
	Assisted vaginal delivery (VD)	1.631 (-0.593, 3.856)	0.076	0.150	27
	LSCS (Elective)	5.197 (3.584, 6.811)	0.360	<0.001	74
	Emergency LSCS	2.418 (0.529, 4.307)	0.151	0.012	54
	*Deviation from planned delivery	1.104 (0.276, 2.485)	0.81	0.116	92
Neonatal complications.					
	Retrieval/ CPAP/ Ventilation	-3.868 (-8.108, 0.372)	-0.109	0.074	9
	Prematurity +NICU/SBCU3	1.602 (-0.436, 3.641)	0.090	0.123	42
	Respiratory Distress Syndrome required CPAP.	3.077 (-6.543, 0.381)	-0.129	0.081	21
	NICU admission	3.581 (1.822, 5.340)	0.247	<0.001	73
	Low Apgar score <7 at 5minutes	2.939 (-0.628, 6.505)	0.115	0.106	18**
	Covariates/Predictors	**Mean Difference in Adherence score (95% CI)**	**Standardised Coefficients Beta**	**P value**	**Frequency N = 261**
Neonatal complications continued					
	Diagnosis of Congenital abnormalities	3.273 (-0.813, 7.360)	0.087	0.116	8
	Septic workup /Sepsis	-2.613 (-5.355, 0.128)	-0.102	0.062	18
Cardiac complications /interventions.					
	Decompensated Heart failure (HF)	3.546 (1.689, 5.403)	0.199	<0.001	42
	Required Cardiac Surgery	4.642 (0.199, 9.085)	0.107	0.041	6
	Balloon Valvoplasty procedure	5.293 (-0.864, 11.450)	0.087	0.004	3
	CTPA+ Echocardiogram	-2.272 (-4.513, 0.031)	-0.105	0.047	26
	Other factors				
	Pre-existent cardiac group	2.010 (0.643, 3.377)	0.154	0.004	139

Significance $P < 0.2$. All covariates /predictors were yes vs no. LSCS: lower segment

* Deviated from planned delivery mode, i.e., planned normal vaginal delivery but required alternative (listed) modes, or planned Elective but precipitously SVD or Emergency LSCS

** Missing data totals for 2 cases. CTPA+ Echocardiogram: CT pulmonary angiogram and cardiac echocardiogram.

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that cardiac complications in pregnant women with heart disease are more frequently maternal arrhythmias (30%) and heart failure (16%) (Table 1) [28]. This comprehensive retrospective study supports the hypothesis of an association between the adherence score to the guidelines and some clinical variables indicating improved outcomes with greater adherence (Table 2). But the most significant was decompensated heart failure ($p < 0.001$) and elective LSCS ($p < 0.001$), contingent upon the inclusion of multidisciplinary team collaboration in high risk pregnancies [20].

One maternal cardiac death occurred post-partum. The mother presented to the hospital's emergency department in septic shock due to infective endocarditis post-discharge, following the successful term delivery of a live baby six weeks earlier. She died during this admission despite intensive care treatment. On her initial hospital presentation, she arrived in established labour, was diagnosed, and treated for a urinary tract infection. She had not attended antenatal care and was a known current illicit drug user. Therefore, her adherence score was low. One

IUFD occurred during the second trimester. The woman made a telephone enquiry about the absence of foetal movement, but she delayed presentation to the hospital where the diagnosis of IUFD was made. These findings underscore the importance of factors such as nonattendance to antenatal care, non-compliance plus medical error in a known intravenous illicit drug user, late presentation to the hospital resulting in missed care, and low guideline adherence score described elsewhere [20].

Cardiac arrests during pregnancy frequently lead to mortalities and severe maternal morbidities [40, 41]. No reported mortality associated with the cardiac arrests occurred in this cohort, but one woman experienced severe maternal morbidities following a post-partum cardiac arrest (S8 Table). The woman's medical history was multiparity, chronic hypertension, GDM, high BMI, and antepartum diagnosis of Left Bundle Branch Block (LBBB) on ECG. Also, late confirmation of global left ventricular dysfunction consistent with a dilated cardiomyopathy on echocardiogram. This woman repeatedly presented to the emergency departments at different hospitals with chest pain complaints, dysponea and tachycardia. However, the diagnostic echocardiogram occurred following her admission and post-partum cardiac review. Initially, the woman was not on cardiac telemetry and was discovered unresponsive and in cardiac arrest for an unknown period by a medical officer. Following resuscitation, she required prolonged intensive care and hospital admission complicated by a secondary PPH and hypoxic brain injury. She received treatment for her cardiomyopathy, including CIED insertion and tracheostomy for long term respiratory support. Unfortunately, over time neurological recovery was insufficient; therefore, she was discharged to long term residential care [41]. This cardiac arrest may have been prevented if medical staff had promptly adhered to guidelines so that appropriate treatment could be offered for this life-threatening cardiac condition.

The strength of the linear association between the cardiac groups and adherence to the guidelines was more significant in the preexistent cardiac group (global p value = 0.004) compared to the acquired cardiac group reiterating previous findings [20]. Women in the preexistent group had a mean adherence score of 2.010 units greater than those in the acquired cardiac group (mean difference = 2.010, 95% CI: 0.643, 3.374). The guidelines' efficacy and effectiveness were apparent when explanatory clinical variables were more strongly associated with higher adherence score and positive clinical outcomes [20]. Pregnant women with preexistent cardiac conditions, e.g. Tetralogy of Fallot (TOF), where multidisciplinary team management and a documented plan pertinent to the guidelines were in place, despite antepartum cardiac events typically experienced a good clinical course [20].

Women with pregnancy-acquired cardiac complications or congenital heart disease unmasked during pregnancy had a lower adherence score due to the change in their care trajectory during the antepartum period and experienced morbidities (See S1 Table). The lack of routine prenatal health (including cardiac) screening, preterm delivery, and late diagnosis in pregnancy contributed to a lack of awareness and preparedness previously reported [20, 42]. Clinicians were surprised and unprepared for potential cardiac complications in pregnancy if asymptomatic women in the first trimester later experienced sudden clinical deterioration. A study from Turkey demonstrated a 5.2% prevalence of cardiovascular disease (CVD) among asymptomatic first trimester women in a tertiary obstetric centre. This emphasises the importance of opportunistic as well as routine health and CVD screening by general practitioners in all patients whatever their age, and for newly pregnant women at their first antepartum visit [42]. Prenatal screening includes obtaining the pregnant woman's medical history and family members' medical history, cardiac status, and associated risk factors [20]. The authors recommend that skilled medical staff review the cardiovascular status of pregnant women with

associated risk factors, i.e. indigenous and refugee population for RHD, family cardiac history and known illicit drug user.

More women experienced sustained arrhythmias requiring treatment (30%) and decompensated heart failure (16%) in the acquired cardiac group compared to the preexistent cardiac group. Notably, in the final multivariable model, those pregnant women diagnosed with HF were associated with improved adherence to the perinatal guidelines reflected in the increased adherence score (global $p < 0.001$). The clinicians' awareness of previous cardiomyopathies, early symptomatic onset in the antepartum period, and acute post-partum events, prompted adherence to the guidelines [15, 43, 44]. Antepartum HF was more likely to increase the adherence score as clinicians sought specific guideline recommendations to manage the heart failure appropriately during pregnancy [20]. With careful monitoring of volaemic status during pregnancy described in the perinatal guidelines, the heart failure regime ensured clinicians' 'preparedness' [33].

Modes of delivery

The modes of delivery are an essential consideration for women with cardiac conditions to mitigate cardiovascular stress during the active phase of labour and yielded surprising results in this study. Although spontaneous or assisted vaginal delivery is preferred according to perinatal guidelines, the elective LSCS mode of delivery showed a statistically significant association with increased adherence to the guidelines adjusting for all other covariates with p value<0.001. This association demonstrates a consensus on the obstetric rationales for LSCS in women with cardiac conditions, medical conditions, and prior pregnancy complications who are more likely to experience obstetric and neonatal complications [14–19].

Women identified with adverse pregnancy outcomes such as malpresentation, premature onset of labour, multiple births, or clinical deterioration prompted elective LSCS to ensure the best result for mother and baby. As expected, the cardiac scenarios resulting in a decision for emergency or elective LSCS for solely cardiac indications were small (n = 20, 7.6%). Likewise, the rationale for elective LSCS included common obstetrical complications i.e., repeat LSCS (28%) placental dysfunction, i.e., placenta praevia and accreta (6%), pregnancy-induced hypertension, preeclampsia, and eclampsia (18%), delivery related, i.e., fail to progress (10%), malpresentation (2%) and baby-related indications such as compromised foetal wellbeing (4.9%) (S9 Table).

To understand these results, from a clinical perspective, elective LSCS occurred predominantly in the preexistent group (35%); clinicians had a low tolerance for significant obstetric complications. Often multiple adverse pregnancy complications influenced clinicians' decision to proceed with the surgical option of delivery. Women with significant preexistent cardiac conditions such as severe mitral valve disease and pulmonary hypertension, worsening decompensated heart failure and severe heart failure (NYHA classification IV) prompted early admission to hospital for cardiac optimisation. This included advanced life support in cardiac arrest, diuresis in decompensated heart failure, and respiratory support to manage hypoxia. Likewise, women required inotropic support for cardiogenic shock, haemodynamic monitoring during and immediately after delivery and management of cardiac arrhythmias with anti-arrhythmic medication, Direct Current (DC) cardioversion or implantation of an internal cardiac electrical device.

The rationale for elective LSCS included common obstetrical indications like placenta praevia, preeclampsia, or compromised foetal wellbeing. In our cohort, the high rate of elective LSCS (although not considered the first option in the statewide guidelines) increased guideline adherence scores related to other aspects of the guidelines yet improved the overall clinical

outcome for both mother and baby. Early inclusion of multidisciplinary team for surgical delivery options facilitated the uptake of guidelines recommendations such as assessing cardiac status. Therefore the results support the safety of elective LSCS in severe and unstable cardiac conditions. Emergency LSCS was more prevalent in the acquired cardiac group (25%) for obstetric reasons; however, emergency LSCS precipitated by cardiac events mid-trimester had low adherence score and poorer outcomes.

Admission to NICU was the only significant neonatal variable associated with increased adherence to guidelines. $P < 0.001$ indicating an appropriate response for the newborns' care in this cohort.

There were women with cardiac conditions who experienced unexpected non-cardiac complications during pregnancy. Two examples include intracranial bleeding treated with craniotomy and tumour in the distal trachea treated post-delivery with extracorporeal membrane oxygenation (ECMO) support for thoracotomy and debulking of tumour and insertion of a tracheal stent. All 'other' complications were included in the analysis; however, although clinically meaningful, none were significant.

Conclusion

This study reassures clinicians that women in the preexistent cardiac group who had greater adherence to the perinatal guidelines achieved better clinical outcomes for both mother and baby, yet this did not guarantee an uneventful pregnancy journey. This result is encouraging despite the lack of Level 1A recommendations within these guidelines. There is insufficient robust published scientific and clinical evidence in this area of obstetric medicine. However, clinicians' awareness and preparedness of the women's preexisting cardiac conditions and the appropriate care process in the guidelines helped them anticipate potential pregnancy complications and prepare for interventions [20]. Likewise, pregnant women's health literacy has a significant role in guideline adherence; therefore, their cardiac conditions' health education is vital. In women with acquired cardiac conditions during pregnancy, often earlier pre-emptive warning 'signs' are insufficient. Therefore, adherence to cardiac disease guidelines begins at the cardiac event timeframe, resulting in a lower score. However, if the health care team and mother can rapidly readjust the care trajectory according to the guidelines, they may avoid severe complications. Therefore, adherence to the guidelines by both the pregnant women and the healthcare team improves clinical outcomes and provides clinicians with an opportunity for early diagnosis and interventions, mitigating potentially serious complications.

Limitations

This study did not reflect state or national population proportions of women with cardiac conditions in pregnancy and encountered the anticipated limitations with retrospective medical record reviews, such as missing data and inaccurate documentation. The researcher examined individual case notes for additional documented evidence to confirm the care provided.

Generalizability. The data collected was limited to South Australia Health public hospitals due to access and data availability from medical records. Therefore, the sample size and findings do not reflect all women in South Australia.

Supporting information

S1 Table. Cardiac diagnosis.
(PDF)

S2 Table. Neonatal diagnosis of congenital heart disease and abnormalities.
(PDF)

S3 Table. Coding of clinical interventions, complications, and outcomes for SPSS variables for obstetric, neonatal and maternal cardiac.
(PDF)

S4 Table. Baseline characteristics for the cohort.
(PDF)

S5 Table. Univariate linear regression model results for adherence score versus obstetric clinical variables, neonatal clinical variables and maternal cardiac variables.
(PDF)

S6 Table. Univariate linear regression model results for adherence score versus obstetric clinical variables, neonatal clinical variables and maternal cardiac variables.
(PDF)

S7 Table. Univariate linear regression model results for adherence score versus obstetric clinical variables, neonatal clinical variables and maternal cardiac variables.
(PDF)

S8 Table. Cardiac arrests cases, associated pathologies and outcomes.
(PDF)

S9 Table. Cardiac, obstetric and other indications for emergency and elective lower segment caesarean section.
(PDF)

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4.3 Summary of Chapter 4

In Chapter 4, the researcher presented a substudy of the previous original research on adherence to the statewide cardiac-specific perinatal guidelines. This chapter focused on the clinical morbidities, outcomes and interventions in a cohort of women with cardiac disease in pregnancy and their association with the overall adherence score to SAPPGs.

In the maternal cohort (n=261) the updated basic characteristics reported a minimum maternal age of 17yrs. and maximum maternal age of 45yrs, with mean age of 30 yrs. The ethnicity of the cohort was predominantly Caucasian, 78.5% (n=205), ATSI only 12.3 % (n=32) and included rural transfer from Northern Territory and Central Australia.

Primary cardiac outcomes were described as maternal cardiac death, cardiac arrest, decompensated heart failure, APO, AMI and a new diagnosis of VHD or CHD during pregnancy and were more prevalent in the acquired cardiac group, except for the additional cardiac pathologies such as VHD or CHD. In contrast, neonatal morbidities and outcomes were more frequent in the preexisting cardiac group.

More explicit information on the distribution of total adherence score across the cohort of women (n= 261) descriptive analysis reported maximum adherence score of 32 seen in only three women, whilst the minimum total adherence score of 2 reported in one women.

In the multivariable model, the statistically significant association was shown between the adherence score and the following cardiac variables: there was a stronger association with women diagnosed with heart failure than with women in the preexisting cardiac group (p=0.004), those women who underwent balloon valvoplasty (p=0.004), those who required cardiac surgery (p=0.041) and cardiac investigations of CTPA with an echocardiogram (p=0.047), when adjusted for all other covariates. There was no association with cardiac arrests. Among obstetric variables, the elective LSCS delivery mode had the most statistically robust association with an improved guideline adherence score ($p<0.001$). Other associated obstetric variables included emergency LSCS (p=0.0120), preeclampsia (p=0.034) and placenta praevia complication (p=0.011). The only neonatal variable reporting statistically significant association with guideline adherence score was NICU admission ($p < 0.001$).

The main message from this chapter was that greater guideline adherence to the SAPPGs in the preexisting cardiac group was positively correlated with better clinical outcomes for both mother and baby, regardless of complex cardiac conditions. However, this did not always imply an uneventful pregnancy. Additionally, inadequate early pre-emptive warning ‘signs’ resulted in a lower adherence score in the acquired cardiac group of women and needs to be addressed in the future. Given the lack of robust scientific and clinical evidence to support recommendations within the SAPPGs, the study results encourage clinicians who care for women with known cardiac conditions. Moreover, the health practitioners’ awareness of the guidelines meant that they anticipated pregnancy complications and had a contingency plan in place. Poorer clinical outcomes and lower adherence scores observed in the acquired cardiac group provide an opportunity for

improvement so that clinicians can rapidly readjust the care trajectory outlined in SAPPGs and mitigate severe pregnancy complications. The importance of heart health literacy and ongoing education for pregnant women, as highlighted in the previous study, is further strengthened through this study.

Chapter 5: Discussion and conclusion

5.1 Introduction

The final chapter summarises the thesis findings and explores limitations and strengths. Likewise, the implications of the key findings to the SAPPG for women with cardiac conditions in pregnancy are discussed. Based on these findings, recommendations for practice and future research are highlighted. Finally, local implementation strategies that may be applied as a result of this research are described. The overall aim of this exploratory research was to evaluate the current provision of best practices and clinical outcomes for women with cardiovascular disease in pregnancy. The study focused on three metropolitan SA Health university-affiliated public hospitals that provide obstetric services. A novel approach using a purposefully developed scoring system was applied in a retrospective medical record audit for adherence to the cardiac-specific CPGs components. Comparisons were made at the hospital sites and across two broad cardiac groups using logic regression analysis. Subsequently, linear regression analysis of the overall CPGs adherence score determined any association with clinical variables. [11]

Given that cardiac conditions in pregnancy present unique challenges for women and the Australian health care delivery services, yet remain an under-researched and under-resourced area, this is an important study. [11] There are no national CPGs specific to cardiac disease in pregnancy in Australia. Apart from the cardiac-specific SAPPGs, the KEMH Obstetrics and Gynaecology Department in Western Australia updated its online guidelines for cardiac conditions in pregnancy in 2018.[18,26] Although, from a global perspective, only 15% of maternal deaths during pregnancy are attributed to cardiac disease in pregnancy [4], the reported low rates in Australia and New Zealand are due to the lack of valid population-based estimates of prevalence and aetiology of maternal heart disease.[11] However, monitoring severe maternal morbidities (SMM) is recommended to indicate better the quality of care given the declining maternal deaths in high-income countries.[4] Common preventable factors noted were provider-related, such as failure to identify ‘high risk’ status, or delay in diagnosis and treatment. Also, consistent patterns of substandard maternal health care and suboptimal use of evidence-based strategies to prevent and treat morbidities were reported and evident to some degree in this research project. [5]

Therefore, the significance of this research is that it provides new evidence that verifies real-life practices for a cohort of women with cardiac disease during pregnancy in South Australia, identifies disparities and gaps in the recommended guideline care and determines any correlation with clinical outcomes. The outcome of this research is to improve the uptake of established statewide best practice guidelines through audit and feedback, and to promote the adoption of CPGs for women with cardiac disease in pregnancy to enhance mother and baby clinical outcomes. [20,65] Additionally, the findings emphasise the need for continuous quality improvement to prevent SMM and maternal mortalities in these women. Likewise,

revision of the same guidelines considering clinically relevant international evidence that can be contextualised (e.g., embedding succinct clinical risk assessment toolkits) recommended in chapter 2. [34]

The initial scoping of the cardiac-specific CPGs and cardiac disease in pregnancy literature yielded limited high-level evidence, mainly registry-based and observational studies, case studies, and review and opinion papers. An overview in the discursive manuscript in Chapter 2 described the spectrum of cardiac conditions, cardiovascular physiological changes and management during pregnancy yet also raised the important role of midwives within the multidisciplinary team. The findings from the literature informed the aims and methods in the subsequent studies described in the thesis.

5. 2 Summary of key findings

The doctoral research addressed six key objectives.

1. *What is the spectrum of cardiac disease in pregnancy, namely preexisting, congenital and newly acquired cardiovascular conditions?*

The scoping review informed Chapter 2's publication, which provided an overview of the spectrum of heart disease diagnoses with the corresponding risk and commonly encountered problems in Table 5 in the paper.[34] Corrected CHD is reportedly the most prevalent cardiac condition seen in pregnancy, with an estimated 12 million cases in 2017.[6-8] Also, in the updated review, the global ROPAC registry studies – which prospectively enrolled women with structural heart disease – identified 57% of the cohort diagnosed with CHD and 29% with VHD.[3] Further characteristics of the subgroups in the ROPAC studies are tabled and described in the narrative of Chapter 2 and in Appendices A. More recently, the incidence of preexisting and pregnancy-onset IHD and the associated pregnancy outcomes have been reported. [9] The Canadian CARPREG study specifically looked at preexisting and pregnancy-acquired cardiac conditions and included 1,938 pregnancies with cardiac complications of arrhythmias and heart failure. Similar findings attributed to the South Australian women in this research cohort are described in Chapters 3 and 4. Within the preexisting cardiac (PEC) group of 139 women, 48 (34.5%) were diagnosed with new VHD or CHD, 21 (15%) with sustained arrhythmias, 19 (13%) with supraventricular tachyarrhythmia (SVT) and 15 (10.8%) with decompensated heart failure.[65] In the acquired cardiac (AC) group of 122 women, 15 (12.3%) had a new diagnosis of VHD or CHD, 57 (46.7%) experienced sustained arrhythmias, 5 (44%) were diagnosed with SVT, and 27 (22%) with decompensated heart failure.[65] A further description of the maternal and neonatal cardiac diagnosis is available in Appendices C.

2. *What current cardiac-specific evidence-based CPGs informs the continuum of care for women with cardiac disease in pregnancy?*

International clinical practice guidelines relevant to heart disease in pregnancy were highlighted in Chapter 2, which also noted the absence of Australian national guidelines. The three tertiary hospitals in the study were in the same metropolitan city with equal access to statewide best practice cardiac-specific perinatal guidelines for clinical practice. Therefore, these SAPPGs for cardiac disease in pregnancy

provided the benchmark for evaluating real-life practice. Although the SAPPGs were revised in 2014, an earlier version (2.0) was used in keeping with the retrospective medical records audit timeframe. However, the recent modified New York Heart Association (mNYHA) functional classifications for the severity of heart disease for predicting maternal and neonatal outcomes and counselling prospective parents are not included in the guidelines, and the traditional NYHA classification in version 2.0 was underutilised. [2,45]

3. *Do health practitioners adhere to the statewide CPGs for these women across the SA Health metropolitan hospitals with obstetric services?*

In summary, the initial findings reported that overall guideline adherence was not optimal, with a mean score of 16 ± 6.7. As discussed in Chapter 3, the minimum acceptable score for guideline adherence differed between the two cardiac groups, with 35 and 17 for the PEC and AC groups respectively yet was not achieved. [58] Some core components of the guidelines were underutilised by clinicians, particularly preconception counselling and the initial comprehensive clinical assessment that included CVD screening, i.e., previous cardiac events in pregnancy or family cardiac history. However, identifying high-risk women who presented late in pregnancy or were non-attendees to antenatal care were barriers to the uptake of guidelines.

4. *What are the predictors and factors for adherence to the statewide cardiac-specific CPGs?*

The predictors for adherence examined were hospital sites, the two categories of cardiac disease, underlying cardiac causes, risk level of pregnancy, multidisciplinary team collaboration, and maternal and baby demographic factors, as discussed in Chapter 3. Increased body mass index (BMI) was the only anthropometric maternal characteristic that resulted in a small increase in mean adherence guideline score. However, the most significant predictors for greater adherence to the guidelines included pregnant women's history of cardiac events in past pregnancies, known preexisting cardiac conditions, and preplanned delivery mode, with caesarean scoring higher than vaginal delivery.[58] Likewise, there was an overall significant finding of higher guideline adherence score associated with preconception cardiac consultation regardless of the hospital site. Identifying women as high risk and having a documented plan increased the guideline-recommended cardiac status assessment. [58] Factors that influence the uptake of statewide CPGs are presented in Figure 2 in Chapter 3 and reiterate contemporary implementation strategies that consider the social system and communication between stakeholders, attributes of the CPGs and communication process, and, finally, the rate and extent of adoption. [21]

5. *How do the three major obstetric hospitals in SA vary in adherence to the guidelines?*

The findings reported in the first study indicated a significant variance in adherence to the guidelines across the three hospitals ($p < 0.0001$) – this variance correlated with the exposure to higher acuity cases. Increased guideline adherence was associated with greater exposure to more acute pregnancies seen predominantly at the state's only high-risk referral centre, hospital two.[58] Also, the capacity of the hospitals with the available maternal cardiac, obstetric and neonatal intensive care services was important. Appropriate up-referral to the same quaternary hospital, which provided (level six) care, i.e., maternal

cardiac and neonatal intensive care services. Likewise, hospital one offered intermediate care (level five) inclusive of tertiary maternal services, intensive care and specialised neonatal care services but excluded babies less than 32 weeks. But hospital three was a stand-alone maternity unit attached to a large neonatal intensive care without onsite maternity intensive care service. [58] However, there was cooperation between the three sites for interhospital transfer of high-risk pregnant women.[58] The disparities in services across the three hospitals and the unequally matched number of women for each site reduced the analysis's power to examine the association with clinical variables in subsequent analysis. Therefore, it was more feasible to investigate the overall score for adherence to guidelines in linear regression modelling and include the two cardiac groups.

6. *Does the improved adherence (total score) to the CPGs determine the clinical outcomes for mothers and babies?*

Chapter 4 described the clinical outcomes and complications for the overall cohort of 261 women. In this study, the results were consistent with international research that demonstrated the prevalence of cardiac complications, such as arrhythmias with treatment (29.9%), namely SVT (28%), a new diagnosis of VHD and CHD (24%) and lastly, decompensated heart failure (16%). [42,65] The second study aimed to determine an association between guideline adherence score and clinical variables, maternal cardiac, obstetric, and neonatal clinical interventions and outcomes. The maternal mortality rate was notably low. As discussed in Chapter 1, moving beyond maternal mortality, surveillance of severe maternal morbidity is the recommended indicator of maternal health and the quality of care.[4] Therefore, this study reported preventable provider factors of failure to identify 'high risk status, and delayed diagnosis with appropriate interventions in Chapters 3 and 4.[65]

Similarly, poor adherence to evidence-based strategies to prevent and treat morbidities were found in incidences described in Chapter 4. This study supported the hypothesis of an association between guideline adherence score and some clinical variables. Adverse pregnancy events were associated with increased guideline adherence scores, i.e., decompensated heart failure ($p < 0.0001$) and elective LSCS ($p < 0.001$), and mainly indicated for obstetric and neonatal complications. But this was contingent upon early diagnosis of morbidities and risk factors that expedited early multidisciplinary team collaboration. [65]

5.3 Strengths and limitations of the research

The strengths and limitations of each discrete study are discussed within the manuscripts presented in Chapters 3 and 4. Therefore, this section considers the broader strengths and limitations of the research. There are three main strengths of this research. Firstly, the novel approach of a purposefully designed scoring system that measured adherence to the statewide best practice perinatal guideline across the three hospital sites in South Australia. This research is the only type in Australia that verifies real-life practice benchmarked with best practice guideline recommendations in the under-researched research combined obstetrics and cardiology topic. Heart disease in pregnancy is a challenging field of emerging interest but

lacks data and evidence reported in the literature. Furthermore, cardiac pathology is a recognisable cause of maternal mortality and morbidity in developed and developing countries. [11]

Secondly, it is the first comprehensive report on adherence to cardiac-specific SAPPGS for women with cardiac conditions in pregnancy since the implementation of the guidelines in 2010. Finally, the research supports the guidelines recommendations, highlighting the role of the multidisciplinary team, early detection of heart disease in pregnant women and timely direction of high-risk pregnancies to more appropriate higher care facilities, where better follow-up of guideline recommendations occurred. Importantly, the study also highlighted inconsistencies in the standard of care, level of guideline adherence, and specific pathologies that alerted healthcare providers to improve care. But the study presents an overall challenge to bring these levels of adherence for all women even when the diseases may appear to be less complex.

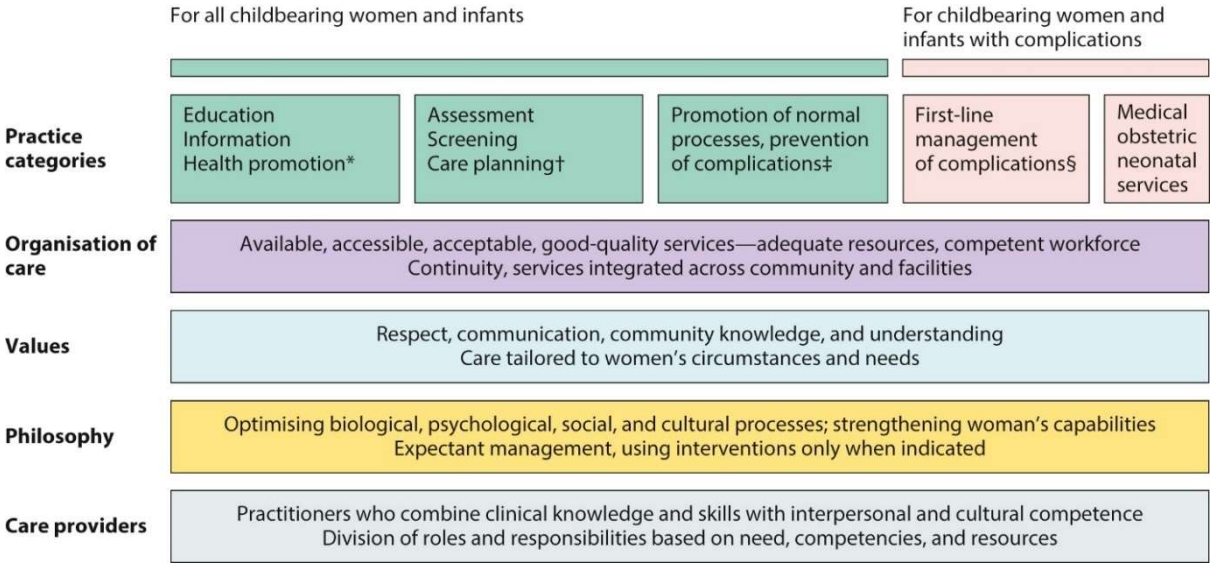
The findings of this study should be interpreted with potential caveats and cautions. The study was conducted in the Australian state of South Australia and limited to public hospitals. The Australian health care system operates with a mixed model comprising both public and private health care services and four main models of maternity care outlined below. [58]

1. General practitioner (GP) shared care is when pregnant women's local GP provides the pregnancy care; however, the labour and birth care are provided by hospital midwives and doctors. Yet, the woman's GP may also oversee labour care and be present for the birth, particularly in rural communities. The GP maintains overall care for the mother and baby after birth and discharges from the hospital.
2. Obstetrical-led care or medical model of care is when the primary care provider is an obstetrician. Labour is monitored by midwives, with the obstetrician typically attending the birth itself. There is limited care following discharge from the hospital, and the length of hospital stay typically is three to five days.
3. Hospital or Clinic care requires pregnant women to attend a hospital or clinic for all care during pregnancy and birth. The women will see a wide variety of doctors and midwives dependant on whoever is on duty that particular day.
4. Continuity of midwifery care (CoC) refers to the care provided by a known midwife and is also referred to as midwifery group practice (MGP). The same midwife provides care throughout pregnancy, labour and birth, and postpartum for up to six weeks if required. The midwives may include other care providers when needed. This model of care is based on a primary health care framework with an emphasis on developing a therapeutic relationship.

Although the focus of the study was on adherence to cardiac-specific SAPPGs, rather than the four maternal models of care, more women encountered the medical model of maternity care, and the midwifery group practices to a lesser degree. Although the researcher has a midwifery background and acknowledges that one of the challenges of quality maternity services in Australia is high medical intervention rates during

pregnancy [19], adverse pregnancy comorbidities expedite the medical model for maternity care.[66] Relationships and role clarity are the keys to improving outcomes in every aspect of maternity care, as illustrated in the evidence-based framework for quality maternal and newborn care (QMNC) and discussed in Chapter 2 in the first published paper. [58] Renfrew et al. report that in keeping with the evidence-based framework for QMNC, every pregnant woman needs a midwife throughout their pregnancy (see Figure 3).[58] Some women will require other services and health providers; however, this approach has yet to be universally applied to the design and delivery of maternity services. For these reasons, the findings may not be generalisable to other countries with different health care systems and models of maternity services.

Figure 3. The framework for quality maternal and newborn care: maternal and newborn health components of a health system



Source: Renfrew, M. J., McFadden, A., Bastos, M. H., Campbell, J., Channon, A. A., Cheung, N. F., . . . Declercq, E. (2014). Midwifery and quality care: findings from a new evidence-informed framework for maternal and newborn care. *The Lancet, 384*(9948), 1129-1145. doi:https://doi.org/10.1016/S0140-6736(14)60789-3. Used with permission. Licence number 5157991029299

5.4 Implications for clinical practice and SAPPGs

Implications for clinical practice have been discussed in the three published papers within the thesis. When completing this PhD, the global COVID-19 pandemic increased the contextual challenges to the Australian health care system in delivering services to these pregnant women with cardiac disease. Therefore, prioritising the uptake of established statewide SAPPGs recommended care already embedded within the healthcare system is feasible and cost-effective.

Promoting the uptake and use of cardiac-specific SAPPGs at the point of care represents the final translation hurdle to move scientific findings into practice. [20] Even though the SAPPGs for cardiac disease in pregnancy are available online through the SA Health website under perinatal guidelines, and have been for some time, timely access may be out of clinicians' reach, explaining the gaps between recommended care and that delivered to pregnant women. One example is the underutilisation of NYHA functional

assessment documentation to predict the risk of maternal and neonatal pregnancy complications reported in Chapter 3. However, the SAPPGs in this study were comparatively less complex than 2018 ESC Guidelines for CVD in pregnancy, with a single flow chart to facilitate clinical decision-making using the NYHA functional classification to align with the appropriate level of hospital care. The more contemporary risk assessment models highlighted in international guidelines may need to be incorporated in the future versions of SAPPGs. Similarly, the lack of recommended preconception counselling for pregnant women with cardiac conditions and poor uptake of early CVD screening for all pregnant women in the study was reported in Chapter 4. Given the maternity models described the lack of awareness of women's heart health issues in pregnancy in primary health care needs to be addressed.

Ongoing quality improvement measures identify gaps in the continuum of care and provide opportunities for improvement. The American Heart Association (AHA) systematic review reported that audit and feedback and educational outreaches were the most effective in improving the care process and clinical outcomes.[29] During the current research project, the researcher raised awareness of available SAPPGs and reported the level of adherence to the statewide guideline-recommended care, associated clinical outcomes for pregnant women with cardiac conditions during pregnancy and their babies in oral presentations, conferences, and through the three publications. Given that this project was retrospective research, and in light of the changes in the healthcare system due to the pandemic, additional barriers and facilitators to uptake of SAPPGs were not measured and thus will need to be considered for this group of women.

Although the SAPPGs are regularly revised and include end-users in the development and revision processes, promoting the adoption of the guidelines through respected clinical leadership or facilitators in the SA Health hospitals is a strategy recommended in the literature [19, 65] The attributes of CPGs of validity, reliability or reproducibility, clarity, clinical flexibility, multidisciplinary process, scheduled review and documentation of the procedures in developing guidelines applied to SAPPGs, despite the lack of level 1A recommendations within the guidelines [20] Valid CPGs are pivotal in delivering quality care, but the recommendations need to be user-friendly and time-efficient for clinicians. Lengthy comprehensive guidelines accompanied by graphical displays and complex algorithms, flow charts or decision trees are difficult for clinical use at the point of delivery. Applying recommendations from CPGs to patient-specific data requires active implementation of CPGs and is more effective in changing behaviours but requires champions or influential leadership [20,29,67-,69]

5.5 Recommendations arising from the research

The recommendations arising from this research encompass both preexisting and acquired cardiac groups

1. **Promotion of the SAPPG and awareness of cardiac complications in pregnancy**

As demonstrated in Chapter 3, the variance in the uptake of the SAPPGs recommendations at the three hospitals reflected the level of exposure to high acuity cases, clinical awareness and preparedness for

cardiac pregnancy comorbidities. Therefore, the increasing trend of pregnant women with cardiac conditions emphasises the need to promote established SAPPGs recommendations across disciplines, i.e., Obstetric, Cardiology and Emergency departments in the SA Health hospitals. Strategies such as digital clinical prompts and reminders can be integrated at the point of care. SMS messaging reminders for women to attend key appointments, used in primary health care settings.

Every effort should be made to increase awareness of cardiac disease in pregnancy for all healthcare professionals and the public. Non-profit organisations like the National Heart Foundation (NHF) already provide access to women's health and CVD resources via their website. The website can include additional resources specific to pregnancy heart health for women and healthcare professionals. Likewise, the Cardiac Society of Australia and New Zealand (CSANZ) and the Australian Cardiovascular Health and Rehabilitation Association (ACRA) provide local and national opportunities to present clinical research and promote best practices at education webinars and annual scientific conferences.

Increasing awareness of the pregnancy cardiac complications for high-risk women with CHD, emphasising early CVD screening in prenatal care, is recommended in the primary health care structure, i.e., GP practices with preventive heart health in pregnancy education. Chapter 2 describes an example of a clinical initiative from the UK – the 'three Ps in a Pod' – that facilitated collaboration across disciplines within NHS hospitals. The three Ps were Pregnancy, Postnatal and Pick up (both the phone and patient), aimed to outline the key messages from the maternal mortality report. An informative poster was distributed in acute medicine and emergency departments to assist clinicians in recognising women at risk of pregnancy-induced cardiac morbidities. A similar initiative could be applied within the local healthcare networks in South Australia to reflect the SAPPGs. The regular lunchtime seminars and grand rounds across disciplines in the SA Health hospitals, and available to all clinicians, provide another opportunity to promote the recommended guideline care.

2. Strategic education at the point of service delivery

Highlighting key guideline recommendations for the clinicians *(end-users*) at the point of service, i.e., the clinical practice sheets and succinct toolkits described in Chapter 2 (see Figure 4).

The initial assessment, CVD screening and risk assessment emphasised in Chapters 3 and 4 underscore how healthcare practitioners' awareness of the normal versus abnormal signs and symptoms in pregnancy can influence pregnancy outcomes. A thorough assessment identifies high-risk categories or potential for pregnancy-induced cardiac complications.

Figure 4 How to differentiate common signs and symptoms of normal pregnancy versus those that are abnormal and indicative of underlying cardiac disease

	ROUTINE CARE Reassurance	CAUTION*† Nonemergent Evaluation	STOP†‡ Prompt Evaluation Pregnancy Heart Team
History of CVD	None	None	Yes
Self-reported symptoms	None or mild	Yes	Yes
Shortness of breath	No interference with activities of daily living; with heavy exertion only	With moderate exertion, new-onset asthma, persistent cough, or moderate or severe OSA§	At rest; paroxysmal nocturnal dyspnea or orthopnea; bilateral chest infiltrates on CXR or refractory pneumonia
Chest pain	Reflux related that resolves with treatment	Atypical	At rest or with minimal exertion
Palpitations	Few seconds, self-limited	Brief, self-limited episodes; no lightheadedness or syncope	Associated with near syncope
Syncope	Dizziness only with prolonged standing or dehydration	Vasovagal	Exertional or unprovoked
Fatigue	Mild	Mild or moderate	Extreme
Vital signs	Normal		
HR (beats per minute)	<90	90–119	≥120
Systolic BP (mm Hg)	120–139	140–159	≥160 (or symptomatic low BP)
RR (per minute)	12–15	16–25	≥25
Oxygen saturation	>97%	95–97%	<95% (unless chronic)
Physical examination	Normal		
JVP	Not visible	Not visible	Visible >2 cm above clavicle
Heart	S3, barely audible soft systolic murmur	S3, systolic murmur	Loud systolic murmur, diastolic murmur, S4
Lungs	Clear	Clear	Wheezing, crackles, effusion
Edema	Mild	Moderate	Marked

Abbreviations: BP, blood pressure; CVD, cardiovascular disease; CXR, chest x-ray; HR, heart rate; JVP, jugular venous pressure; OSA, obstructive sleep apnea; RR, respiratory rate.

*If unclear, any combination of factors in the yellow column that add up to 4 or more should prompt further evaluation.

†Data in this column from Afshan B. Hameed, Christine H. Morton, and Allana Moore. Improving Health Care Response to Cardiovascular Disease in Pregnancy and Postpartum. Developed under contract #11-10006 with the California Department of Public Health, Maternal, Child and Adolescent Health Division. Published by the California Department of Public Health, 2017. Available at https://www.cmqcc.org/resources-toolkits/toolkits/improving-health-care-response-cardiovascular-disease-pregnancy-and.

‡History of CVD or signs and symptoms in the red column should lead to urgent evaluation by the Pregnancy Heart Team.

§Should raise concern about heart failure and should promptly be evaluated.

Source: ACOG Practice Bulletin No. 212: Pregnancy and Heart Disease. Obstetrics and Gynaecology. 2019;133(5) :e320.

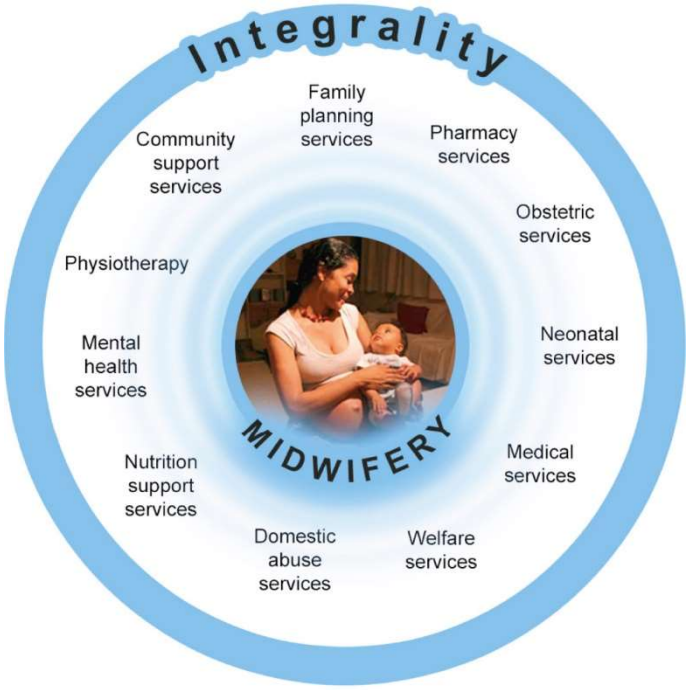
Education outreach utilising respected clinical leadership to promote adherence to guidelines and clinical outcomes has been reported as an effective strategy in cardiology.[29] Therefore, this strategy could be applied in obstetrics and midwifery.[29] Addressing women's health literacy and providing education on heart health during pregnancy during visits to the women's assessment clinic at the three hospitals provides an opportunity for all pregnant women, yet the inadequate timeframes are not conducive for women to disclose the relevant family cardiac history and needs to be addressed.

3. Promotion of woman-centred care in the MDT

The early inclusion of a multidisciplinary team (MDT) has been emphasised in international guidelines for women with high-risk cardiac conditions in pregnancy and is discussed further in Chapters 2, 3 and 4, with improved clinical outcomes associated with the improved adherence to SAPPGs recommendations in this study. Although the planned qualitative phase of the PhD research could not be undertaken, as highlighted in Chapter 2's updated literature review, there is a growing need for patient-reported outcomes. Adopting woman-centred models of care in maternity services incorporates a better understanding of women's

existing knowledge of their cardiac condition (particularly those with preexisting CHD and lived experience of heart disease before pregnancy) and active shared clinical decision-making.[11] Only one hospital in the study held regular interdisciplinary meetings for high-risk women and discussed their pregnancy plan to deliver better-integrated services in line with evidence, as discussed in Chapter 3. A graphical representation of woman-centred care that reflects the diversity and organisations of health providers and services around the woman and baby that need to be woman-centred are seen in the integrality model in Figure 5. [59]

Figure 5 The integrality model



Source: Renfrew, M.J, Homer, C.S.E., Downe, S., McFadden, A. Muir, N., et al. Midwifery: an executive summary for the Lancets series. *Lancet* 388, 1-8. Used with permission: licence number**:** 5157990819002.

5.6 Recommendations for future research

The original doctoral research proposal included a phenomenological study to explore the 'lived experiences' of women with cardiac disease in pregnancy, encompassing the clinical care delivered. However, this was not achieved due to the global pandemic and timeframe restrictions. Therefore, future primary or post-doctoral research on heart disease in pregnancy should incorporate patient-reported outcomes alongside physician-derived clinical outcomes across the continuum of care of maternal cardiac diseases, as discussed in Chapter 2.[11] Limited qualitative studies specific to cardiomyopathy or CHD report women's experiences of living with cardiac disease in pregnancy and provide insight into the quality of engagement with clinicians [70,71], notably, the strong motivation to conceive by women with mild or severe CHD against medical advice. Despite the seriousness of their CHD, the drive for motherhood was reportedly stronger than the drive for self-care reported in Australian qualitative case studies.[71] The 2018 systematic review and metasynthesis explored the experiences of pregnant women with a spectrum of

cardiac disease and highlighted their decision-making experiences and risk awareness with the potential to inform evidence-based guidelines [72] Pregnant women's perspectives and challenges can provide important information for future cardiac-specific guidelines when diagnosed with a new cardiac condition or preexisting cardiac disease.

5.7 Translation into practice

Translation to practice included reporting research findings and increasing awareness of the SAPPGs at local and regional educational seminars as an invited presenter. Additional opportunities to raise awareness on the research topic at conference presentations through my existing association with NHF, ACRA and CSANZ, communicating with members at local and national levels.

5.8 Concluding remarks

The aim of this thesis was to evaluate the continuum of care for women with cardiac conditions during pregnancy benchmarked against the statewide best practice cardiac-specific CPGs across three SA Health metropolitan public hospitals with obstetric services. There are no national clinical practice guidelines specific to cardiac disease in pregnancy, and no nationally coordinated strategies to address cardiac disease in pregnancy. Likewise, there are no comprehensive reports on international or Australian adherence to cardiac-specific CPGs recommendations in pregnancy. Therefore, this thesis fills a gap in research by providing new knowledge contextualised to an Australian state health care network, with a snapshot of pregnant women with cardiac conditions, quantitative measures of the level of adherence to statewide best practice guidelines, identifying local predictors, factors that influence the uptake of guideline-recommended care. The key recommendations arising from this study include updating the established SAPPGs with international recommendations on risk assessment, routine CVD screening for all women, and early inclusion of a pregnancy heart health team (MDT). Likewise, active promotion of the available SAPPGs is a pivotal key recommendation that could influence outcomes for mother and baby in South Australia. The research highlighted the need to address pregnancy heart health literacy for all healthcare professionals and the public. Given the emerging issue of cardiac comorbidities in pregnancy, it prioritises research in an area previously under-researched and under-resourced.

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Appendices

Appendix A – Chapter 2 supplementary material

2. Search strategy
3. PRISMA checklist
4. Search results Clinical Practice guidelines and related research
5. Registry of Pregnancy and Cardiac Disease (ROPAC) related papers: 12 papers
6. The CARPREG registry-based studies
7. CARPREG, CARPREG II, ZAHARA and mWHO Risk models

Appendix B – Chapter 3 supplementary material

1. Perinatal Audit DAT
2. Assumption Testing
3. Linear regression
4. Univariate regression
5. Descriptive statistics cardiac variables

Appendix C Chapter 4 supplementary materials

1. Cardiac diagnosis
2. Neonatal diagnosis of congenital heart disease and abnormalities
3. Coding of clinical interventions, complications and outcomes for SPSS variables for obstetric, neonatal and maternal cardiac
4. Baseline characteristics of cohort
5. Univariate linear regression model results for adherence score versus obstetric clinical variable s, neonatal clinical and maternal cardiac variables
6. Univariate linear regression model results for adherence score versus obstetric clinical variable s, neonatal clinical and maternal cardiac variables
7. Univariate linear regression model results for adherence score versus obstetric clinical variable s, neonatal clinical and maternal cardiac variables
8. Cardiac arrest cases, associated pathologies and outcomes
9. Cardiac, obstetric, and other indications for emergency and elective lower segment caesarean section

Appendix D Additional Supplementary materials

1. SAPPGS Chapter 64 Cardiac Disease in pregnancy 2010.
2. South Australian Pregnancy Record 2004.
3. South Australian Pregnancy Record 2012

Appendix A Chapter 2 supplementary materials

A1. Search strategy

The search included both quantitative and qualitative studies. The search terms were 'Cardiac Pregnancy Nursing' and included the following:

- Heart Diseases/diagnosis*
- Heart Diseases/therapy
- Humans
- Pregnancy
- Pregnancy Complications, Cardiovascular/diagnosis*
- Pregnancy Complications, Cardiovascular/therapy
- Prenatal Care/methods
- Cardiomyopathies/diagnosis
- Cardiomyopathies/aetiology
- Cardiomyopathies/therapy*
- Female
- Humans
- Peripartum Period
- Pregnancy
- Pregnancy Complications, Cardiovascular/diagnosis
- Pregnancy Complications, Cardiovascular/aetiology
- Pregnancy Complications, Cardiovascular/therapy*
- Prognosis
- Puerperal Disorders/diagnosis/Puerperal Disorders/therapy*

Table A1 Search queries used in PubMed, Scopus, CINAHL, and EMBASE search

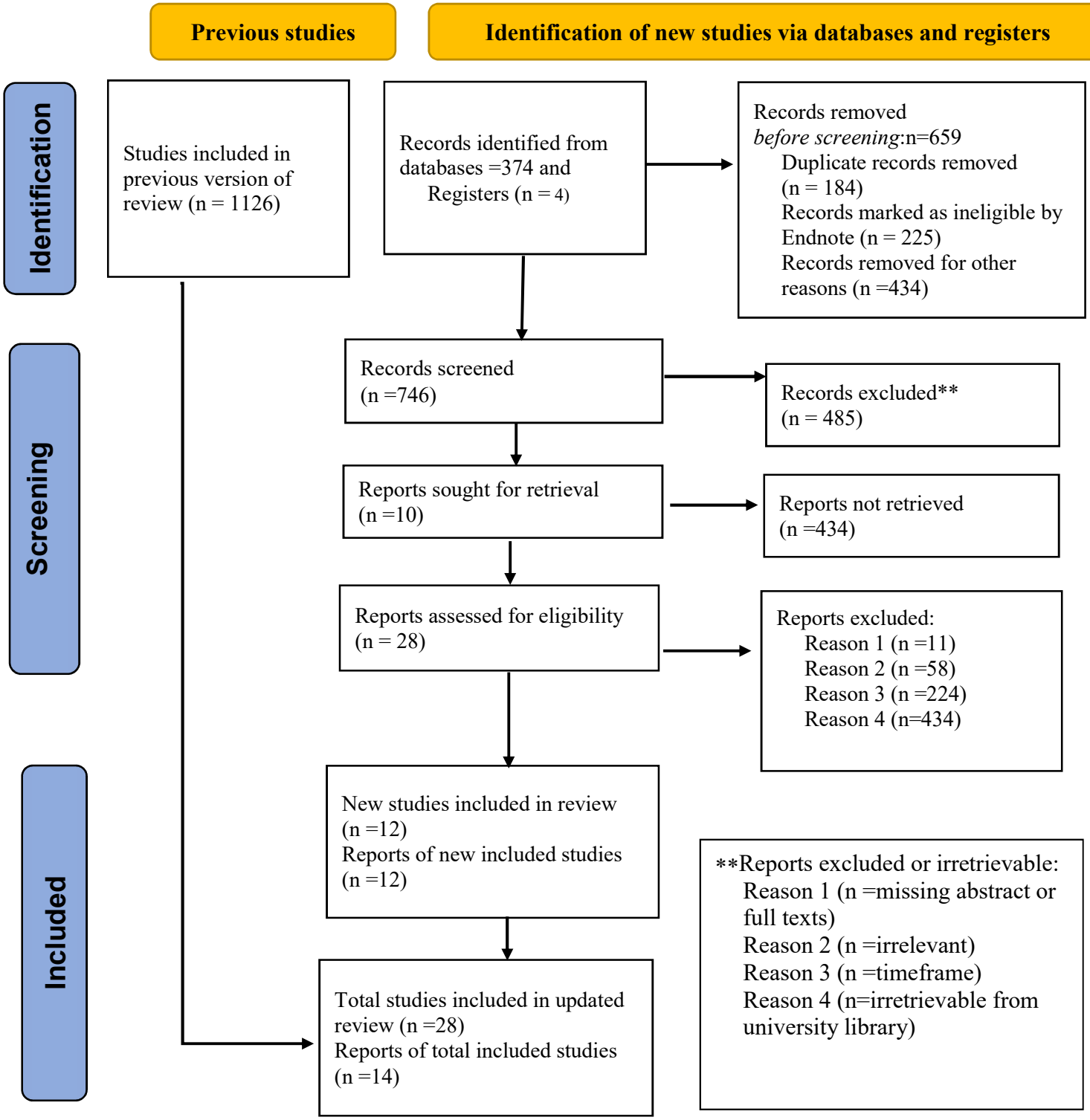
Cardiovascular AND epidemiology/ aetiology/mortality/ pathology	AND Pregnancy or maternal cardiac disease	OR Risk assessment OR Prenatal care	AND/ OR Antepartum care OR Prenatal care AND Maternal mortality, morbidity, AND Nursing assessment	AND Pregnancy Outcomes OR clinical outcomes
Cardiac disease	And pregnancy OR	And /OR risk factors OR pregnancy, high risk OR Risk assessment OR Prenatal care	And Pre-conceptual counselling OR Risk assessment	And Management or clinical outcomes OR Pregnancy Outcomes
Heart disease OR Heart defects, congenital, Heart Disease AND Diagnosis AND therapy	And pregnancy OR (Pregnancy complications, AND cardiovascular, OR diagnosis, OR therapy) OR puerperal disorders epidemiology AND delivery, obstetric methods	OR pregnancy, high risk OR Risk assessment OR Prenatal care AND risk management OR predictors AND clinical outcomes	AND/ OR Antepartum care OR Prenatal care AND Maternal mortality, morbidity, AND Nursing assessment OR Preconception OR Prenatal Care /methods	AND Patient Care Planning /organisation & administration OR Critically ill ACHD pregnant patient

Critical Appraisal Skills Programme (CASP) program used for quality assessment of research https://casp-uk=net

Developed in (CASP) response to clinicians using interventions that were either contradicted or not supported by evidence and therefore aimed to raise awareness of the need for evidence in practice. The key theme participants walk away with is that systematic reviews are the decision-maker's best resource for

- Are the results of the study Valid?
- What are the results?
- Will the results help locally?

A2. PRISMA flow diagram for updated literature review for cardiac pregnancy project



Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi:10.1136/bmj.n71.

visit: http://www.prisma-statement.org/

A3. Search results: clinical practice guidelines and related research

1. Department of Health. (2020). *Clinical Practice Guidelines Pregnancy Care* Canberra, Australian Government https://www.health.gov.au/resources/collections/pregnancy-care-guidelines-and-related-documents accessed 5th July 2021. CPGs documents generic
2. Department of Health. (2020). *Core Practices in Pregnancy Care* Canberra, Australian Government outlined the following guideline updates, providing antenatal care services (Guideline seven), antenatal visits (guideline 8), and preparing for pregnancy, childbirth and parenthood (guideline 9). CPGs documents generic
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4. Regitz-Zagrosek, V., Roos-Hesselink, J. W., Bauersachs, J., Blomström-Lundqvist, C., Cífková, R., De Bonis, M., . . . Group, E. S. C. S. D. (2018). 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. *European Heart Journal, 39*(34), 3165-3241. doi:10.1093/eurheartj/ehy340 ESC publication *Germany Updated CPGs∗ Specific cardiac disease in pregnancy*
5. Regitz-Zagrosek, V. (2018). 'Ten Commandments of the 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. *European Heart Journal, 39*(35), 3269. doi:10.1093/eurheartj/ehy478 ESC publication *succinct CPGs∗ Specific cardiac disease in pregnancy*
6. Homer, C. S., Oats, J., Middleton, P., Ramson, J., & Diplock, S. (2018). Updated clinical practice guidelines on pregnancy care. *MJA, 209*(9), 409-412. doi:10.5694/mja18.00286 Australian publication.
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8. Imamura, M., Kanguru, L., Penfold, S., Stokes, T., Camosso-Stefinovic, J., Shaw, B., & Hussein, J. (2017). A systematic review of implementation strategies to deliver guidelines on obstetric care practice in low- and middle-income countries. *International Journal of Gynecology & Obstetrics, 136*(1), 19-28. doi:10.1002/ijgo.12005 United Kingdom (UK) publication *review paper*
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13. Waller, A., Bryant, J., Cameron, E., Galal, M., Quay, J., & Sanson-Fisher, R. (2016). Women's perceptions of antenatal care: are we following Guideline-recommended care? *BMC Pregnancy Childbirth, 16*(1), 191. doi:10.1186/s12884-016-0984-y Australia publication. *Research paper prospective survey*
14. Yeoh, P. L., Hornetz, K., & Dahlui, M. (2016). Antenatal care utilisation and content between Low-risk and high-risk pregnant women. *PLoS One, 11*. doi:10.1371/journal.pone.0152167 Malaysian publication. *Research paper retrospective cohort study*
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17. Guidelines, E. B. C. (2018). *Clinical Practice Guideline Cardiac Disease* Obstetrics Gynaecology & Imaging Directorate Retrieved from https://www.kemh.health.wa.gov.au/~/media/Files/Hospitals/WNHS/For%20health%20professionals/Clinical%20guidelines/OG/WNHS.OG.CardiacDisease.pdf
18. McDonald, S. D., Machold, C. A., Marshall, L., & Kingston, D. (2014). Documentation of guideline adherence in antenatal records across maternal weight categories: a chart review. *BMC Pregnancy Childbirth, 14*(1), 205. doi:10.1186/1471-2393-14-205 Canadian publication. *Research chart review*
19. Bollini, P., & Quack-Lötscher, K. (2013). Guidelines-based indicators to measure the quality of antenatal care. *Journal of Evaluation in Clinical Practice, 19*(6), 1060-1066. doi:10.1111/jep.12027 Switzerland publication *prospective research*

20. Regitz-Zagrosek, V., Lundqvist, C. B., Borghi, C., Cifkova, R., Ferreira, R., Foidart, J. M. . . . CPG, E. S. C. C. P. G. (2011). ESC Guidelines on management of cardiovascular diseases during pregnancy The Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). *European Heart Journal, 32*(24), 3147-3197. doi:10.1093/eurheartj/ehr218 ESC publication CPGs∗ *Specific cardiac disease in pregnancy*
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A4. Registry of Pregnancy and Cardiac Disease (ROPAC) related papers: 12 papers

Study	Design	Country	Sample size	Aim	Outcome measures	Comments
Registry Of Pregnancy And Cardiac Disease (ROPAC).						
Ramlakhan et al 2021 Congenital Heart Disease in the ESC EORP [1]	*Prospective, observational worldwide registry,*	*138 centres in 53 countries*	*Of 5739 pregnancies* *3295 (57.4%) were women with CHD*	*Overview ROPAC data characteristics/pregnancy outcomes for women with CHD not previously published.*	*Primary cardiac diagnosis / concomitant cardiac disease, prior to interventions, CVS risk factors, NYHA functional /mWHO classification scales. Cardiac medication/ echocardiogram report. Stillbirth defined as fetal death >20 weeks of gestation, low Apgar score as <7 at 5 min, and small for gestational age (SGA) as birthweight <10th percentile.*	*The strength of this study was the inclusion of the most known CHD lesions with relatively large numbers of rare and complex diseases through international cooperation. But diversity of CHD lesions limits data on disease-specific parameters; so that cannot be generalised for all women with the same diagnosis.* ***Recommendations**:* *The prepregnancy cardiac state strongly related to adverse pregnancy outcomes, therefore prepregnancy counselling important. Follow-up during and after pregnancy required to be individualised to the woman's needs and the complexity of her CHD, and include multidisciplinary pregnancy heart team. If the required expertise is unavailable locally, telephone or digital consultations with a specialist tertiary centre should be considered.*
Ramlakhan, 2021 Pregnancy outcomes in women with aortic coarctation.[2]	*Prospective, observational worldwide registry,*	*138 centres in 53 countries y*	*Cohort of 303 pregnancies*	*Pregnancy in women with aortic coarctation (CoA) has an estimated moderately increased risk (mWHO II–III) of adverse cardiovascular, obstetric or fetal events, but prospective data to validate risk classification are scarce.*	*The frequency of and associations with major adverse cardiac events (MACE) and hypertensive disorders (pregnancy-induced hypertension, (pre-) eclampsia or haemolysis, elevated liver enzymes and low platelets syndrome) were analysed.*	*The ROPAC data show low MACE and hypertensive disorder rates during pregnancy in women with CoA, suggesting pregnancy to be safer and better tolerated than previously appreciated.* ***Recommendation:** Women with aortic coarctation without risk factors can safely embark on pregnancy and be counselled accordingly.*
Baris et al. 2021 Pregnancy in Tetralogy of Fallot	*Prospective, observational*	*138 centres in 53 countries*	*Cohort of 421 women with repaired*	*Describe the outcomes in cohort of women with repaired TOF*	*The primary outcome: occurrence of maternal cardiac events. Secondary outcomes: obstetric*	***Recommendations**:* *A closer examination of the physiological changes to the right ventricle in women with*

Study	Design	Country	Sample size	Aim	Outcome measures	Comments
Registry Of Pregnancy And Cardiac Disease (ROPAC).						
data from the ESC EORP ROPAC registry[3]	*worldwide registry,*		*Tetralogy of Fallot (TOF*)		*and fetal events, right ventricular (RV) dilatation, and pulmonary valve deterioration.*	*TOF during pregnancy, particularly pulmonary regurgitation (PR) and the association with adverse pregnancy outcomes for mother and baby. Given the high rates of RV deterioration in pregnant women with the combination of TOF and moderate/severe PR and the lower rates when the PR is accompanied by PS in this study, it suggests that in the patients with asymptomatic isolated PR, a PVR should be considered before pregnancy. However, our sub analysis is of insufficient size to support such a claim.*
Baris et al. 2020 Acute Coronary Syndrome and Ischemic Heart Disease in Pregnancy: Data From the EURObservational Research Programme-European Society of Cardiology Registry of Pregnancy and Cardiac Disease[4]	*Prospective, observational worldwide registry,*	*Global 138 centres in 53 countries*	*Cohort of 117 women with IHD*	*Describe the pregnancy outcomes in women with heart disease.*	**The primary endpoint***: maternal cardiac events during pregnancy & up to 6 months postpartum. Maternal mortality, heart failure, atrial fibrillation or flutter, ventricular tachyarrhythmias, endocarditis, thromboembolic events in the women with preexisting IHD, new acute coronary syndrome (ACS).* **Secondary endpoints:** *obstetric complications (significant PPH, caesarean section(C/S) or emergency C/S, pre-eclampsia/eclampsia.* **Fetal outcomes***: prematurity, fetal mortality, neonatal mortality, IUGR, low birth weight and low Apgar scores, and pregnancy-induced hypertension.*	*Women revascularised before pregnancy had fewer events compared those women who had not Only 13 women with pregnancy-onset IHD, in whom non–STEMI was the most common.* *In comparison to the non –IHD women in the ROPAC study, women with IHD were significantly older, with risk factors such as high BMI, smokers, hypertensive, diabetic and multiparity. Age (>40years) and multiparity were contributing factors to adverse pregnancy outcomes.* **Recommendations**: *This study underscores the importance of prepregnancy counselling and smoking cessation therapy for these women to improve maternal and fetal outcomes Cigarette smoking was associated with ischaemic events during pregnancy. Pregnancy in women with IHD should be considered a moderate to high risk (moderate World Health Organization II–III). All women with known IHD require thorough prepregnancy investigations/ counselling and strict follow-up in a referral centre.*

Study	Design	Country	Sample size	Aim	Outcome measures	Comments
Registry Of Pregnancy And Cardiac Disease (ROPAC).						
Roos-Hesselink J et al. 2019 Pregnancy outcomes in women with cardiovascular disease: evolving trends over ten years in the ESC Registry of Pregnancy and Cardiac Disease.[5]	*International, prospective observational ROPAC registry.*	International registries *Sixty per cent of women were from developed countries*	*5739 pregnancies*	*Define contemporary diagnosis-specific outcomes in pregnant women with heart disease.* *Namely pregnant women with CHD, VHD, CMP or IHD. From 2007 to 2018. However, from 2013, women with pulmonary arterial hypertension (PAH) or aorta pathology (AOP) were also enrolled (PREG 2)*	*Baseline characteristics that included demographics, prepregnancy status, current smoking, hypertension, history of diabetes and atrial fibrillation, signs of heart failure, prior intervention, NYHA classification, prior medication and mWHO classification.* **Cardiovascular outcomes** *Maternal mortality and heart failure, maternal mortality, heart failure event, supraventricular arrhythmia, ventricular arrhythmia, thrombolic event and aortic dissection.* **Obstetric outcomes** *included pregnancy-induced hypertensive disorders, (Pre-) Eclampsia, Postpartum haemorrhage, caesarean section, emergency caesarean section.* **Fetal outcomes** *captured data for fetal mortality, Neonatal mortality, premature birth and low Apgar scores*	*Prevalent diagnoses were congenital (57%) and valvular heart disease (29%). Mortality (overall 0.6%) was highest in the pulmonary arterial hypertension (PAH) group (9%). Heart failure occurred in 11%, arrhythmias in 2%. Delivery was by caesarean section in 44%. Obstetric and fetal complications occurred in 17% and 21%, respectively. The number of high-risk pregnancies (mWHO Class IV) increased from 0.7% in 2007–2010 to 10.9% in 2015–2018.* **Recommendations:** *This study reiterated that all women with heart disease should be cared for in a hospital. Women in mWHO class I and II can be cared for in a local hospital, and women in Class II–III in a referral hospital. In contrast, in Class III and IV, women should be managed in specialised tertiary centres by a specialised, multidisciplinary team. Pre-conceptional counselling is advised for women in all mWHO classes as it is associated with a better outcome.*
van Hagen et al. 2018 *Pregnancy Outcomes in Women With Rheumatic Mitral Valve Disease: Results From the Registry of Pregnancy and Cardiac Disease.* [6]	*prospective observational ROPAC registry of global pregnant women*	*138 centres in 53 countries*	*390 pregnancies*	*Describe the pregnancy outcomes in all women with rheumatic mitral valve disease and no prepregnancy valve replacement.*	*Cardiac, obstetric and neonatal outcomes were collected.* ***Heart failure*** *(HF) as a clinical syndrome characterised by specific symptoms (dysponea and fatigue) and signs of fluid retention (oedema and rales) on physical examination determined by the provider.* ***Maternal cardiac events*** *cardiac arrest, cardiac death, a new*	**Recommendations:** *Although mortality was only 1.9% during pregnancy, ≈50% of women with severe rheumatic MS and 23% of those with significant MR developed heart failure during pregnancy. Prepregnancy counselling and considering mitral valve interventions in selected patients are important to mitigate these complications. . In this study, most patients (75%) were diagnosed with RHD before pregnancy with access to cardiac care. Patients in very low-income areas presenting late in pregnancy with severe disease probably*

Study	Design	Country	Sample size	Aim	Outcome measures	Comments
Registry Of Pregnancy And Cardiac Disease (ROPAC).						
					arrhythmia requiring treatment, heart failure, thromboembolic event, endocarditis, hospitalisation for other cardiac reasons or cardiac intervention. ***Fetal adverse outcomes*** *fetal death>14 weeks, neonatal death < 1-week, low Apgar score, preterm birth, and SGA.*	*have an even worse outcome. More work is needed to understand the impact of RHD in pregnancy in these areas. The researchers were restricted to the guidelines used when most of the patients were included. However, having symptoms of VHD has direct consequences concerning intervention in current guidelines, therefore a sub analysis in patients with and without symptoms done.*
van Hagen, I. M et. al 2017 Incidence and predictors of obstetric and fetal complications in women with structural heart disease.[7]	*prospective observational global ROPAC registry of pregnant women*	*138 centres in 53 countries*	*2742 pregnancies from January 2008 to April 2014*	*Pregnant women with cardiac disease have an increased risk of obstetric and fetal events. This study aimed to report the incidence of events and validate the modified WHO (mWHO) risk classification and search for event-specific predictors*	***Endpoints:*** Obstetric events: *maternal non-cardiac death up to 1 week postpartum, pregnancy-induced hypertension (new-onset >140/90 mm Hg at two occasions), pre-eclampsia (including pre-eclampsia, eclampsia or HELLP syndrome) plus APH /PPH complication, (defined as increased blood loss, >500 mL after vaginal delivery or >1000 mL after caesarean delivery, up until 24 hours postpartum) or other major bleeding resulting in at least 1 g/dL decrease in haemoglobin, the need for blood transfusion or end-organ damage such as a haemorrhagic CVA or retinal bleeding).* Fetal events: *premature birth <37 weeks, small for gestational age (<10th centile), poor Apgar score (<7 at 1 min), fetal death ≥14 weeks of gestation or neonatal death up to 1 week after delivery. Induced and spontaneous preterm*	**Recommendations:** *the mWHO classification is unsuitable for predicting obstetric and fetal events in women with cardiac disease. Most events in this cohort were associated with general predictors such as twin pregnancy, nulliparity and prepregnancy hypertension. Other associations were complex CHD leading to small-for-gestational-age babies, aortic valve disease predisposing to pre-eclampsia and the use of anticoagulants leading to fetal demise. The increased rates of adverse obstetric and fetal outcomes in women with preexisting heart disease should be highlighted during counselling.*

Study	Design	Country	Sample size	Aim	Outcome measures	Comments
Registry Of Pregnancy And Cardiac Disease (ROPAC).						
					births analysed separately. Cardiac event: *a **combined endpoint**: cardiac arrest, cardiac death, new episode of arrhythmia requiring treatment, heart failure, thromboembolic event, aortic dissection, endocarditis, acute coronary syndrome, and hospitalisation for a cardiac reason or a cardiac intervention*	
Goland et al. 2017 Pregnancy in women with hypertrophic cardiomyopathy: data from the Registry Of Pregnancy and Cardiac Disease (ROPAC) of the European Society of Cardiology.[8]	*Prospective observational global registry of pregnant women*	*19 countries from 28 centres*	*60 pregnancies*	*Provide information on the outcome of pregnancy in a cohort of pregnant women with HCM to inform pre-pregnancy counselling and identify women at high-risk of an adverse outcome*	***Primary endpoint**: major CVS event (MACE) maternal death, heart failure, thromboembolic events and SVT arrhythmias i.e., ventricular tachycardia arrhythmia (VTA). **Other endpoints of interest** hospitalisation for cardiac event, caesarean section cardiac indication, birth weight, SGA (<10th percentile) neonatal death, TOP and prematurity.*	*Small number of pregnancies, with no maternal mortalities. 14 patients at least one MACE occurred (23.3%), 9 (15%) women developed heart failure, and 6 (10%) experienced ventricular tachycardia and one (1.7%) atrial fibrillation. Only two women experienced two major adverse cardiac events, during first trimester and third trimester. Fetal outcomes included a miscarriage and two fetal deaths during second trimester – associated with maternal HF and arrhythmias at the time. All women were managed according to the ESC CPGs.* ***Recommendations**: assessing the functional status and signs of heart failure prior to pregnancy are important risk factors to prevent cardiac complications in these pregnant women. Underscores that pre-pregnancy counselling, close monitoring, and optimal care are mandatory.*
Silwa et al. 2016 Pulmonary hypertension and pregnancy outcomes: data from the Registry Of Pregnancy and	*Prospective observational global registry of pregnant women*	*Global 138 centres in 53 countries ROPAC registry*	*Cohort of 151*	*Describe the pregnancy outcomes of women with pulmonary hypertension*	*Pregnant women were categorised on their PH aetiology.* Women *with PAH in case of iPAH, CHD-PAH or oPAH caused by diseases such as connective tissue disease or vascular malformations were*	*The subgroup of the cohort included 151 women with pulmonary hypertension (PH) diagnosed with right heart catheterisation or echocardiogram evidence, with 26% diagnosed with pulmonary arterial hypertension (PAH) in three subgroups:*

Study	Design	Country	Sample size	Aim	Outcome measures	Comments
Registry Of Pregnancy And Cardiac Disease (ROPAC).						
Cardiac Disease (ROPAC) of the European Society of Cardiology.[9]					*classified as group 1. Patients with PH caused by left heart disease (LHD-PH) with left ventricular systolic dysfunction, valvular disease, or congenital/acquired left heart inflow or outflow tract obstructions or congenital cardiomyopathies were classified as group 2. Patients were stratified by RVSP level in three groups: 30–50 mmHg, 50–70 mmHg, and >70 mmHg. Pregnancy outcomes as described in previous ROPAC studies*	*idiopathic (iPAH), associated with CHD (CHD-PAH), or associated with other diseases (oPAH), and 74% having PH caused by left heart disease (LHD-PH), n=112). Right ventricular systolic pressure was <50mmHg in 59.6% of patients, 50–70mmHg in 28.5% and >70mmHg in 11.9%. In more than 75% of patients, the diagnosis of PH had been made before pregnancy.* *Maternal death (postpartum) in five patients (3.3%), with another two out of 78 patients presented for follow-up (2.6%) dying within six months after delivery. The highest mortality was found in iPAH (3/7, 43%).* *Heart failure occurred in 27%. Caesarean section occurred in 63.4% (23.9% as an emergency) and therapeutic abortion in 4.0%. Complications were miscarriage (5.6%), fetal mortality (2%), premature delivery (21.7%), low birth weight (19.0%) and neonatal mortality (0.7%).* **Recommendations**: *Women should be kept in hospital for at least a week post-delivery and possibly longer and be monitored for arrhythmia, heart failure, and uterine bleeding as most deaths occurred postpartum. Preconception counselling on short and long-term risks to women with PH health overall and poor outcomes for their children. If pregnancy occurs, close follow-up with a minimum of monthly visits and echocardiograms to screen for and treat right heart failure are essential. Future research should include larger prospective carefully conducted multicentre studies in patients with PH to determine pregnancy-related risk*

Study	Design	Country	Sample size	Aim	Outcome measures	Comments
Registry Of Pregnancy And Cardiac Disease (ROPAC).						
						accurately, the role of supportive care and advanced PH therapy, as well as predictors of outcome in each subgroup.
Ertekin et al. 2016 Ventricular tachyarrhythmia during pregnancy in women with heart disease: Data from the ROPAC, a registry from the European Society of Cardiology.[10]	*Prospective observational global registry of pregnant women*	Global registry of 39 countries	*2966 pregnancies*	*Describes the incidence, onset, predictors and outcome of ventricular tachyarrhythmia (VTA) in pregnant women with heart disease, and clinical outcomes. VTA during pregnancy will cause maternal morbidity and even mortality and impact the fetal outcome. Insufficient data exist on the incidence and outcome of VTA in pregnancy.*	*Only clinically relevant VTA (when the patient was symptomatic and required treatment for VTA or when the patient had more than 100 consecutive beats) was included*	*VTA occurred in1.4% of pregnant women with cardiovascular disease, mainly in the third trimester, and was associated with heart failure during pregnancy. NYHA class before pregnancy was predictive. VTA during pregnancy had a clear impact on fetal outcomes.* **Recommendations** *pregnant women with cardiac condition in NYHA class >1 and CMP are at particular risk and require preconception counselling on risks before pregnancy and close monitoring during pregnancy*
Ruys, T. P. E et.al 2014 Heart failure in pregnant women with cardiac disease: data from the ROPAC.[11]	*Prospective observational global registry of pregnant women*	Global registry of *28 countries enrolled 1321 women between 2007 and 2011.*	*1321pregnancies*	*Identify heart failure (HF) as one of the most critical complications in pregnant women with heart disease, causing maternal and fetal mortality and morbidity*	*The main outcome measures were onset and predictors of HF, maternal and fetal death.* **The primary endpoint** *was HF.* **The secondary endpoints** *included: birth weight, fetal death (defined as fetal death after 22 weeks of pregnancy or birth weight 500 g), neonatal death, low birth weight (<2500 g), premature birth (<37 weeks of gestation) or Apgar score <7.*	**Recommendations**: *HF was the most common complication in this pregnancy registry. Timing of HF was dependant on the underlying cardiac diagnosis, with HF in the second trimester occurring mainly in patients with shunt lesions or VHD. Yet women with CMP and IHD developed HF shortly after delivery. In addition to the previously recognised risk factors such as prepregnancy signs of HF, high NYHA class or WHO category ≥3, new predictors for HF were CMP or PH. Pre-eclampsia during pregnancy was associated with HF, and premature delivery were more frequent.*

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Detailed information from some of the above studies linked to ROPAC registry are described below:

Ramlakhan, K. P., Johnson, M. R., Lelonek, M., Saad, A., Gasimov, Z., Sharashkina, N. V. . . . Roos-Hesselink, J. W. (2021). Congenital Heart Disease in the ESC EORP Registry of Pregnancy and Cardiac disease (ROPAC). *International Journal of Cardiology Congenital Heart Disease*, 100107-. doi:10.1016/j.ijcchd.2021.100107.

Purpose of study: to provide a detailed overview of the ROPAC data on characteristics and pregnancy outcomes for women with CHD not previously published.

Type of study: *prospective, observational worldwide registry, was initiated in 2007.*

Setting: *Between 2007 and 2018, 5739 pregnancies from 138 centres in 53 countries were included in the ROPAC. The International Monetary Fund classification defined participating countries as low or middle-income (LMIC).*

Data collected included *baseline characteristics, i.e., age***,** *parity, primary cardiac diagnosis and concomitant cardiac disease, prior interventions, cardiovascular risk factors, NYHA functional classification, cardiac medication and if available echocardiographic parameters. Likewise, maternal mWHO classification scale. Stillbirth was defined as fetal death >20 weeks of gestation, low Apgar score as <7 at 5 min, and small for gestational age (SGA) as birthweight <10th percentile.*

Major findings:

- *Of 5739 pregnancies included in the ROPAC, 3295 (57.4%) were women with CHD (mean age 29 years). Compared to the 2444 non-CHD women in the ROPAC, the women with CHD were younger, more often nulliparous and living in a high-income country (all p < 0.001, Table 1).*
- *The CHD group had less prepregnancy hypertension, atrial fibrillation, signs of heart failure, reduced LVEF and cardiac medication use than the non-CHD group (all p < 0.001), but more prior cardiac interventions (68.9% vs36.9%, p < 0.001). Correspondingly, the CHD pregnancies were in lower mWHO risk categories. ASD (n=495) most common diagnosis, followed by VSD (n=463) and TOF (n=426. Maternal mortality was only 0.3%, and heart failure was 6.6%, the latter the most common complication. A composite endpoint of mortality and HF was 6.7%.*
- *Other complications were ventricular tachyarrhythmia in 1.2%, thromboembolic events in 1.2%, atrial fibrillation or flutter in 1.1% and endocarditis in 0.6%. One pregnancy (0.03%) was complicated by aortic dissection in a woman with congenital mitral valve regurgitation and Marfan syndrome.*
- *Hypertensive disorders of pregnancy occurred in 4.1%, and 46.3% were delivered by caesarean section, of which the majority (30.2%) were planned: 9.6% for cardiac reasons and 20.6% for obstetric reasons.*
- *fetal outcomes were stillbirth in 0.5%, preterm delivery in 16%, SGA in 10.3% and a low Apgar score in 5.9%. Fetal congenital heart disease occurred in 3.5%, and non-cardiac congenital disease in an additional 2.2%.*
- *The composite endpoint of maternal mortality and heart failure occurred most in women with Eisenmenger syndrome (58.1%), followed by women with a congenitally corrected transposition of the great arteries (ccTGA, 12.8%), Fontan circulation (11.2%) and double-outlet right ventricle (11.1%,). For all the other CHD diagnoses, the composite endpoint occurred in less than 10% of pregnancies.*
- *Prepregnancy signs of heart failure (OR 10.7, 95% CI 7.1–16), multiple gestations (4.6, 2–10.8), pulmonary hypertension (2.5, 1.5–4), estimated LVEF <40% (2.4, 1.1–5.1), cardiac medication use (2, 1.4–2.7) and low- or middle-income country (1.6, 1.1–2.4) were independently associated with the composite endpoint.*

Recommendations: *The prepregnancy cardiac state strongly relates to adverse pregnancy outcomes, therefore emphasising the importance of prepregnancy counselling. Follow-up during and after pregnancy should be individualised to the woman's needs and the complexity of her CHD, undertaken*

a multidisciplinary pregnancy heart team. When the required expertise is unavailable locally, telephone or digital consultations with a specialist tertiary centre should be considered.

Keywords: *Congenital heart disease, Pregnancy, Maternal health, Observational registry.*

Key thoughts and comments: *The strength of this study is its inclusion of the most known CHD lesions and that the ROPAC has collected relatively large numbers of even rare and complex diseases through international cooperation. However, the diversity of CHD lesions limit data on disease-specific parameters; thus, the reporting cannot be generalised for all women with the same diagnosis. In addition, the women's cardiac function, comorbidities and previous cardiac and obstetric events were taken into consideration in this study yet may contribute to the actual risk of pregnancy.*

Roos-Hesselink, J., Baris, L., Johnson, M., De Backer, J., Otto, C., Marelli, A. . . . Hall, R. (2019). Pregnancy outcomes in women with cardiovascular disease: evolving trends over ten years in the ESC Registry Of Pregnancy And Cardiac Disease (ROPAC). *European Heart Journal, 00*, 1-8. doi:10.1093/eurheartj/ehz136

Purpose of study: *Reducing maternal mortality is a World Health Organization (WHO) global health goal. Although maternal deaths due to bleeding and infection are declining, those related to heart disease are increasing and are now the most crucial cause in western countries. ROPAC study aimed to define contemporary diagnosis-specific outcomes in pregnant women with heart disease***.**

Type of study: *ROPAC is an international, prospective observational registry of pregnant women with CHD, VHD, CMP or IHD. From 2007 to 2018, pregnant women with heart disease were prospectively enrolled in Pregnancy and Cardiac disease (ROPAC).* In addition, from 2013, women with pulmonary arterial hypertension (PAH) or aorta pathology (AOP) were also enrolled. *This vital data source assembles granular clinical data on large numbers of pregnant patients with heart disease from real-life daily practice, informing our understanding of the outcomes in this population with the ultimate goal of improving patient outcomes.*

Setting: international registries *Sixty per cent of women were from developed countries***.**

Data collected: *data was collected from all pregnancies up to 1 week postpartum. The baseline characteristics included***:** *demographics, prepregnancy clinical status, current smoking, hypertension, history of diabetes and atrial fibrillation, signs of heart failure, prior intervention, NYHA classification, prior medication and mWHO classification. Cardiovascular outcomes were abstracted for mortality and heart failure, maternal mortality, heart failure event, supraventricular arrhythmia, ventricular arrhythmia, thrombolic event and aortic dissection. Obstetric outcomes included pregnancy-induced hypertensive disorders, (Pre-) Eclampsia, Postpartum haemorrhage, caesarean section, emergency caesarean section. Fetal outcomes captured data for fetal mortality, Neonatal mortality, premature birth and low Apgar scores.*

Major findings: *5739 pregnancies were enrolled; the mean age was 29.5. Prevalent diagnoses were congenital (57%) and valvular heart disease (29%). Mortality (overall 0.6%) was highest in the pulmonary arterial hypertension (PAH) group (9%). Heart failure occurred in 11%, arrhythmias in 2%. Delivery*

was by caesarean section in 44%. Obstetric and fetal complications occurred in 17% and 21%, respectively. The number of high-risk pregnancies (mWHO Class IV) increased from 0.7% in 2007–2010 to 10.9% in 2015–2018. The determinants for maternal complications were prepregnancy heart failure or New York Heart Association >II, systemic ejection fraction <40%, mWHO Class 4, and anticoagulants use. After an increase from 2007 to 2009, complication rates fell from 13.2% in 2010 to 9.3% in 2017. Maternal mortality and/or heart failure occurred in 629 pregnancies (11%), with maternal death in 34 women (0.6%). In four cases, the cause of death was unknown, and five patients died from non-cardiac causes, four of these being septic shock. Refractory heart failure was the cause of death in 15 patients,5 of which were related to severe PAH. Four patients died from complications of mechanical valve thrombosis, two from endocarditis, two patients from primary cardiac arrest with ventricular fibrillation, and two other patients from haemodynamic complications following abortion and pulmonary embolism, respectively.

Recommendations: *The results from this study reiterate recommendations from the ` Indeed all women with heart disease should be cared for in a hospital. Women in mWHO class I and II can be cared for in a local hospital, and women in Class II–III in a referral hospital. In contrast, in Class III and IV, women should be managed in specialised tertiary centres by a specialised, multidisciplinary team. Pre-conceptional counselling is advised for women in all mWHO classes as it is associated with a better outcome.*

Key thoughts and comments: *An interim analysis of the first 1321 pregnancies (PREG1) was published in 2013. Comparisons were made between the PREG1 and the data collected from 2011 onwards (PREG2***).** *Women with a primary diagnosis of PAH or AOP were excluded from the analysis of trends over time. These women were not enrolled in ROPAC from the start of the registry***.** *The incidence of death/heart failure changed over time.*

Limitations outlined for this prospective and large registry which included all groups of heart disease and describes the real-life clinical practice, are summarised below:
Mortality reported only up to one week; therefore, estimates were highly likely to have underestimated this component of the primary endpoint compared with other studies and considered when making a comparison.
• Many pregnant women with heart disease in their cohort were managed in specialised tertiary centres interested in this field. The outcomes of other non-tertiary centres may be different, and caution is required for the generalisation of results to the whole population.
• Although the major advantage of a prospective registry is how it can document clinical reality, there is potential selection bias present. There was no guarantee (although requested and stressed) that consecutive patients from all centres were included. Furthermore, the number and constitution of participating centres varied over time, creating a heterogeneous cohort in which interpreting results is difficult. • Some countries and centres included more patients than others. However, this was adjusted for this in the analyses.

A5. The CARPREG registry-based studies 4

Study	Design	Site	Sample size	Aim	Outcome measures	Comments
Studies linked to Data from *prospective Canadian studies* **CARPREG**						
Silversides, C. K. et al. 2018 Pregnancy Outcomes in Women With Heart Disease: The CARPREG II Study[1]	*Prospective recruitment of women with CHD, acquired heart disease or arrhythmias*	*Toronto and Vancouver. Canada*	*1,938*	Examine cardiac complications Derive a risk stratification index	**Primary cardiac outcomes** *maternal cardiac death; cardiac arrest; sustained arrhythmia requiring treatment; left-sided heart failure (HF); right-sided HF; stroke or transient ischaemic attack; cardiac thromboembolism; myocardial infarction; and vascular dissection.* **Secondary outcomes** *A decline in NYHA functional class by ≥ two classes during the antepartum period* *or urgent invasive treatment procedure/ surgery during pregnancy and up to the sixth postpartum week.*	*In the CARPREG II risk index, clinical predictors such as the history of previous cardiac events and maternal functional class or cyanosis were associated with a higher odds ratio and therefore scored higher point values than the other predictors.* The study reinforces the foundational role of careful cardiovascular clinical assessment in risk stratifying pregnant women with heart disease. *Risk assessment for the individual women needs to integrate risk score estimates, known lesion-specific information, and clinical judgement by an experienced physician.* *Late pregnancy assessment is associated with more frequent adverse cardiac outcomes, attributed to delayed access to appropriate risk stratification, follow-up, and management plan.* ***Translational outlook**: Additional research is needed to identify specific cardiovascular and obstetrical care components that improve outcomes for pregnant women with heart disease*
Grewal et al. (2014) Pregnancy in Women with Heart Disease *Heart failure Clinics*[2]	Review of Zahara risk assessment and CARPREG study	*Toronto, Canada.*	*Total 851 Canadian women* *(252 retrospective study; 599 in* CARPREG STUDY	***Maternal Global Risk Assessment** Follow-up from the initial CARPREG study in a CHD population suggested the inclusion of subpulmonary ventricular systolic dysfunction or severe pulmonary*	*What precipitates AHF?* *What are the causes of HF in pregnancy, i.e.:* ***Cardiac causes** include all the cardiomyopathies DCMP, PCCM, HCOM, tachycardia-induced CMP, Hypertensive CMP, Ischaemic CMP, Chemotherapy-induced CMP, other rare causes: Congenital CTGA switch operation, congenitally*	*Heart disease, present in 0.5% to 3% of pregnant women, is an important cause of morbidity and the leading cause of death among pregnant women in the developed world. Certain heart conditions are associated with an increased risk of heart failure during pregnancy or the postpartum period; for these conditions, management during pregnancy benefits from multidisciplinary care at a centre with expertise in pregnancy and heart disease.*

Study	Design	Site	Sample size	Aim	Outcome measures	Comments
				regurgitation to the CARPREG risk scores improves maternal cardiac risk s assessment. An adverse maternal cardiac event complicated 25% of pregnancies; 67% were HF. ZAHARA investigators proposed a weighted scoring system for women with CHD and incorporated several additional variables into their risk prediction model	*corrected TGA, TOF, pulmonary atresia, single –ventricle hearts including those with Fontan operation, LVOT, Eisenmenger syndrome: valvular HD aortic and mitral stenosis and regurgitant lesions;* ***Non-cardiac causes*** *include preeclampsia hyperthyroidism, anaemia and pulmonary hypertension.*	*Risk stratification important aspect of care to allow a safe pregnancy plan: lesion-specific risks. Based on lesion complexity, residual disease, functional class, pregnancy risk, and logistical considerations, a woman should be stratified into one of the following three care pathways: 1. Exclusive care by a multidisciplinary expert team at a centre with expertise in pregnancy and HD; 2. Shared care, including regular review by a cardiologist with expertise in pregnancy and HD and 3. Local obstetric care. Management for heart failure was outlined for both chronic and acute during antepartum, delivery and postpartum discussed.*
Drenthen et al. (2010). Predictors of pregnancy complications in women with congenital heart disease[3]	*Retrospective medical records data abstraction plus supplemental data retrieved by telephone questionnaire to verify demographics*	*Belgian tertiary medical centre's ADCHD data base*	*In 1802 women with CHD, 1302 completed pregnancies were observed*	*Follow-up from CARPREG study Risk prediction model and score. To identify patient characteristics associated with adverse pregnancy outcomes in a patient cohort consisting of patients with CHD and propose a modified risk score particularly for complex CHD underrepresented in previous study*	*The following complications were recorded for each completed (>20 weeks of gestation) pregnancy between 1980 and 2007.* ***Cardiac:*** *arrhythmia or heart failure, cardiovascular complications (e.g. thromboembolic complications, AMI and CVA), and endocarditis (including first six months post-partum).* ***Obstetric****: pregnancy-induced hypertension (PIH, new-onset hypertension: blood pressure >140 mmHg systolic or >90 mmHg diastolic without proteinuria after 20 weeks of gestation); preeclampsia (PIH with>0.3 g protein in 24h urine sample); eclampsia (preeclampsia*	*Logic regression used to calculate independent predictors of of cardiac, obstetric, and neonatal complications.* *The most prevalent cardiac complications during pregnancy were arrhythmias (4.7%) and heart failure (1.6%). Factors independently associated with maternal cardiac complications were the presence of cyanotic heart disease (corrected/uncorrected) (P<0.0001), the use of cardiac medication before pregnancy (P< 0.0001), and left heart obstruction (P < 0.0001). New characteristics were mechanical valve replacement (P = 0.0014) and systemic (P=0.04) or pulmonary atrioventricular valve regurgitation related to the underlying (moderately) complex CHD (P=0.03). A new risk score for cardiac complications is proposed.*

Study	Design	Site	Sample size	Aim	Outcome measures	Comments
					with grand mal seizures); haemolysis elevated liver enzymes low platelets (HELLP) syndrome according to the ESC Guidelines premature labour (<37 weeks of gestation);post-partum haemorrhage (vaginal delivery >500 mL, caesarean section >1000 mL). ***Neonatal**: premature delivery (delivery>37 weeks); small-for-gestational-age birth weight (<10th percentile); offspring mortality [demise: in utero (>20 weeks of gestation)—the first-year post-partum].*	*The most prevalent obstetric complications were hypertensive complications (12.2%). No correlation of maternal characteristics with adverse obstetric outcomes was found. The most prevalent neonatal complications were premature birth (12%), small for gestational age (14%), and mortality (4%). Cyanotic heart disease (corrected/uncorrected) (P = 0.0003), mechanical valve replacement (P= 0.03), maternal smoking (P= 0.007), multiple gestation (P=0.0014), and the use of cardiac medication (P=0.0009) correlated with adverse neonatal outcome.* ***Recommendations:** A new risk score for adverse cardiac complications is proposed.* *The authors advocated pre-pregnancy evaluation in an outpatient setting, including physical examination, laboratory evaluation, and echocardiography according to a predefined protocol by an expert in the field.* *In addition to weighing predictors found in ZAHARA and CARPREG and calculating risk scores, disease-specific information should always be used when estimating pregnancy risk to avoid over-simplification implied by risk calculation. Also, existing guidelines and expert articles should be consulted. External validation of the modified risk score in a large prospective study remains necessary before everyday practice is possible.*

Study	Design	Site	Sample size	Aim	Outcome measures	Comments
Siu, S C et al. 2001 Prospective multicentre study of pregnancy outcomes in women with heart disease (CARPREG)[4]	*Prospective ongoing study.*	*Toronto, Canada.*	*562*	*Describe the frequency and predictors of pregnancy-related complications in Canadian women with heart disease to assess outcomes comprehensively in a contemporary cohort.*	*All pregnant women with congenital or acquired cardiac lesions or cardiac arrhythmias referred to a participating centre from October 1994 to November 1999 were eligible for enrolment.* **Primary cardiac events**: *pulmonary oedema (on chest radiograph or clinical symptoms s), sustained symptomatic tachyarrhythmia/ bradyarrhythmia requiring treatment, stroke, cardiac arrest, or cardiac death.* **Secondary cardiac events:** *Decline in NYHA class (≥ 2 classes) compared to baseline or emergency invasive cardiac procedures during pregnancy or within six months after delivery.* **Neonatal events:** *Premature birth (<37 weeks gestation), small-for-gestational-age birthweight (<10th percentile), respiratory distress syndrome (RDS), intraventricular haemorrhage, fetal death (≥20 weeks), or neonatal death (within 28 days after birth).* **Obstetric events:** *Noncardiac death, pregnancy-induced hypertension (PIH), postpartum haemorrhage (PPH). PIH defined as ↑ systolic (≥30 mm Hg) and diastolic (≥15 mm Hg) blood pressure. PPH defined as blood loss >500 mL (vaginal delivery) or >1000 mL (caesarean section), required transfusion or accompanied by ↓ haemoglobin ≥20 g/L.*	*Included 13 Canadian cardiac and obstetric teaching hospitals (55 000 deliveries per year) during 617 pregnancies* *To enhance the risk stratification of pregnant women with heart disease, they developed and validated a risk index to predict cardiac complications during pregnancy.* **Recommendations***: In women at high risk for cardiac events, cardiac interventions should be considered before conception if the risk-benefit ratio is favourable. Women should be referred to a regional centre for ongoing care with intermediate or high cardiac risk (risk score ≥one or lesion-specific risk factors). Women with a low cardiac risk (risk score of 0 and without lesion-specific risk factors) can safely deliver in a community hospital. Women with risk factors for maternal cardiac or neonatal complications may require increased frequency of follow-up.*

[1] Silversides, C. K., Grewal, J., Mason, J., Sermer, M., Kiess, M., Rychel, V. . . . Siu, S. C. (2018). Pregnancy Outcomes in Women With Heart Disease: The CARPREG II Study. *Journal of the American College of Cardiology, 71*(21), 2419-2430. Doi: https://doi.org/10.1016/j.jacc.2018.02.076

[2] Grewal, J, Silversides, CK, Colman JM (2014). Pregnancy in Women with Heart Disease *Heart Failure Clinics, 10*(1), 117-129.

[3] Drenthen, W., Yap, S. C., van Veldhuisen, D. J., Pieper, P. G., Boersma, E., Balci, A., . . . Investigators, Z. (2010). Predictors of pregnancy complications in women with congenital heart disease. *European Heart Journal, 31*(17), 2124-2132. doi:10.1093/eurheartj/ehq200

4 Siu, S. C., Marcotte, F., Taylor, D. A., Gordon, E. P., Spears, J. C., Tam, J. W., . . . Investigators, C. (2001). Prospective multicentre study of pregnancy outcomes in women with heart disease. *CIRCULATION, 104*(5), 515-521. doi:10.1161/hc3001.093437.

Further information from some of the above studies linked to **CARPREG** Data are described below:

Silversides, C. K., Grewal, J., Mason, J., Sermer, M., Kiess, M., Rychel, V. . . . Siu, S. C. (2018). Pregnancy Outcomes in Women With Heart Disease: The CARPREG II Study. *Journal of the American College of Cardiology, 71*(21), 2419-2430. Doi: https://doi.org/10.1016/j.jacc.2018.02.076

Purpose of the study: *A prospective study that sought to examine cardiac complications during pregnancy and their temporal trends; and derive a risk stratification index*

Type of study: *Prospective recruitment of women with CHD, acquired heart disease or arrhythmias receiving ongoing care or referred for consultation in Toronto and Vancouver***.**

Setting: *This* **s***tudy cohort consisted of consecutive pregnancies in women with heart disease receiving care at two large Canadian tertiary hospitals.*

Data collection method: *All women underwent cardiac assessment at baseline and then followed serially throughout pregnancy until six months postpartum. Those women who experienced TOP or miscarriage (<20 weeks) were excluded. Baseline clinical, electrocardiographic and echocardiographic variables were collected at the time of the first antenatal visit. Likewise, maternal age, parity, cardiac lesion, prior cardiac intervention, NYHA functional class, maternal cyanosis confirmed by oximetry, cardiac rhythm, ventricular systolic function, valvular function and right ventricular systolic pressure were obtained. Systemic ventricular ejection fraction (EF) was calculated using validated methods. While systemic right ventricles, EF was visually estimated. Right ventricular systolic function was visually evaluated as normal or impaired. Valvular area and gradients and severity of valvular regurgitation were measured using standardised criteria. Adverse maternal cardiac outcomes during antepartum, peripartum, and postpartum periods were recorded until the sixth postpartum month and verified by a health record review.*

Primary cardiac outcomes *were defined as maternal cardiac death; cardiac arrest; sustained arrhythmia requiring treatment; left-sided heart failure (HF) defined as pulmonary oedema; right-sided HF; stroke or transient ischaemic attack; cardiac thromboembolism; myocardial infarction; and vascular dissection.*

Secondary outcomes *were classified as a decline in NYHA functional class by ≥ two classes during the antepartum period or the need for urgent invasive treatment procedure/ surgery during pregnancy and up to the sixth postpartum week; this cutoff of 6 weeks postpartum was set to exclude elective procedures that were deferred due to pregnancy.*

Major findings: *In total, 1,938 pregnancies were included.* ***Cardiac complications*** *occurred in 16% of pregnancies and were primarily related to arrhythmias and heart failure. Although the overall rates of cardiac complications during pregnancy did not change over the years, pulmonary oedema frequency decreased (8% from 1994 to 2001 vs 4% from 2001 to 2014; p value = 0.012). Structural heart disease was common (86.6%), of which congenital heart disease was the most common cardiac diagnosis (63.7% of pregnancies).*

Ten predictors of maternal cardiac complications *were identified:* ***5 general predictors*** *(prior cardiac events or arrhythmias, poor functional class or cyanosis, high-risk valve disease/left ventricular outflow tract obstruction, systemic ventricular dysfunction, no previous cardiac interventions);* ***4 lesion-specific predictors*** *(mechanical valves, high-risk aortopathies, pulmonary hypertension, coronary artery disease); and one delivery of care predictor (late pregnancy assessment). These ten predictors were incorporated into a new risk index (CARPREG II [Cardiac Disease in Pregnancy Study]). The CARPREG risk score was 0 in 1,135 pregnancies (59%), 1 in 703 pregnancies (36%), and >1 in 100 pregnancies (5%).*

Recommendations: *Pregnancy in women with heart disease continues to be associated with significant morbidity, although mortality is rare. Prediction of maternal cardiac complications in women with heart disease is enhanced by integrating general, lesion-specific, and delivery of care variables. Importantly, in the CARPREG II risk index, clinical predictors such as the history of previous cardiac events and maternal functional class or cyanosis were associated with a higher odds ratio and thereby assigned higher point values than the other predictors. These finding reinforce the foundational role of careful cardiovascular clinical assessment in risk stratifying pregnant women with heart disease. In addition to the variables identified in our risk score, other factors affect outcomes. Risk assessment for the individual patient will need to integrate risk score estimates, known lesion-specific information, and clinical judgement by an experienced physician. Finally, women who receive late pregnancy assessment had more frequent adverse cardiac outcomes during pregnancy, which may be attributed to delayed access to appropriate risk stratification, follow-up, and management plan.*

Key thoughts and comments: *Key paper used in PhD research. Despite the large sample size, patients with uncommon and complex lesions may be underrepresented, e.g., Eisenmenger syndrome associated with high maternal morbidity and mortality was not addressed. Further studies are required to determine the patient and provider factors responsible for delays in referral. Nevertheless, this novel observation supports early referral to a specialised centre for assessment during pregnancy. This recommendation for specialty assessment of all pregnant women with heart disease is reinforced by the 5% risk of cardiac complications in the lowest risk group, concordant with prior studies. TRANSLATIONAL OUTLOOK: Additional studies are needed to identify specific cardiovascular and obstetrical care components that improve outcomes for pregnant women with heart disease.*

Grewal, J, Silversides, CK, Colman JM (2014). Pregnancy in Women with Heart Disease *Heart Failure Clinics, 10*(1), 117-129.

Purpose of the study. *A review paper focuses on cardiac risks and management strategies for women with acquired and congenital heart disease at risk of heart failure.*

Type of study: *Narrative review*

Setting: *851 Canadian women with heart disease (252 retrospective study and 599 in multicentre prospective observational study)* CARPREG STUDY

Data collection method: a review of ZAHARA risk assessment and CARPREG study

Major findings: *Heart disease, present in 0.5% to 3% of pregnant women, is an important cause of morbidity and the leading cause of death among pregnant women in the developed world. Certain heart conditions are associated with an increased risk of heart failure during pregnancy or the postpartum period, for these conditions, management during pregnancy benefits from multidisciplinary care at a centre with expertise in pregnancy and heart disease*

Recommendations: *Comprehensive discussion on specific causes of heart failure with lesion-specific strategies for management provided***.**

Key thoughts and comments: *Discussion on the challenges of diagnosing heart failure in pregnancy presenting the investigations that help diagnose and manage HF in pregnancy, differentiating between normal findings and specific considerations.*

Maternal Global Risk assessment: *HF and arrhythmias are the most common adverse maternal cardiac events during pregnancy in women with heart disease. Risk stratification important aspect of care to allow a safe pregnancy plan: lesion-specific risks. Follow-up study from the initial CARPREG study in a CHD population suggested the inclusion of subpulmonary ventricular systolic dysfunction or severe pulmonary regurgitation to the CARPREG risk scores improves maternal cardiac risk s assessment. An adverse maternal cardiac event complicated 25% of pregnancies; 67% were HF. ZAHARA investigators proposed a weighted scoring system for women with CHD and incorporated several additional variables into their risk prediction model Table 1.*

Management strategies *multidisciplinary team. A woman of childbearing age with HD contemplating pregnancy or already pregnant should be referred to a cardiologist with expertise in pregnancy and HD for at least one visit, review risks, and counsel the patient and health care providers on the approach management. Based on lesion complexity, residual disease, functional class, pregnancy risk, and logistical considerations, a woman should be stratified into one of the following three care pathways: 1. Exclusive care by a multidisciplinary expert team at a centre with expertise in pregnancy and HD; 2. Shared care, including regular review by a cardiologist with expertise in pregnancy and HD and 3. Local obstetric care. Management for heart failure was outlined for both chronic and acute during antepartum, delivery and postpartum discussed.*

What precipitates AHF? What are the causes of HF in pregnancy?

Cardiac causes *include all the cardiomyopathies DCMP, PCCM, HCOM, tachycardia-induced CMP, Hypertensive CMP, Ischaemic CMP, Chemotherapy-induced CMP,* ***other rare causes****: Congenital CTGA switch operation, congenitally corrected TGA, TOF, pulmonary atresia, single –ventricle hearts including those with Fontan operation, LVOT, Eisenmenger syndrome: valvular HD aortic and mitral stenosis and regurgitant lesions;* ***Non-cardiac causes*** *that include preeclampsia hyperthyroidism, anaemia and pulmonary hypertension.*

Keywords: *Pregnancy, heart failure, CHD, Cardiomyopathy. 3. Local obstetric care, with regular cardiology follow-up not required during pregnancy after an initial review by a cardiologist with expertise in pregnancy and HD.*

Drenthen, W., Yap, S. C., van Veldhuisen, D. J., Pieper, P. G., Boersma, E., Balci, A., . . . Investigators, Z. (2010). Predictors of pregnancy complications in women with congenital heart disease. *European Heart Journal, 31*(17), 2124-2132. doi:10.1093/eurheartj/ehq200

Purpose of the study. *Data regarding pregnancy outcomes in women with congenital heart disease (CHD) are limited. However, 'CARdiac disease in PREGnancy' (CARPREG) investigators were the first to identify predictors of adverse pregnancy outcomes in women with established heart disease. The investigators also were the*

first to design a risk score, which is now commonly used to 'predict' cardiac complications during pregnancy in the context of maternal CHD. Limitations of the score for patients with CHD are developed based on a cohort that included patients with the primary electrical disease and acquired heart disease.
Moreover, several types of (mainly complex) CHD were underrepresented. Therefore, it is suggested that the CARPREG cardiac risk score needs to be modified to assess the risk of pregnancy in women with CHD. Thus, the primary objective of the present study is to identify patient characteristics associated with adverse pregnancy outcomes in a patient cohort consisting of patients with CHD and propose a modified risk score.

Type of study: *Retrospective medical records data abstraction plus supplemental data retrieved by telephone questionnaire to verify demographics.*

Setting: *For the present ZAHARA study, female patients with CHD aged 18– 58 years enrolled in the nation-wide CONgenital CORvitia (CONCOR) registry and a Belgian tertiary medical centre's adult CHD database were identified. The databases include patients with CHD .18 years receiving tertiary medical care.*

Data collection method: *Baseline data including maternal date of birth, parity, age at pregnancy when applicable, basic anatomy, prior surgical procedures, co-morbidity, and medical history (using the European Paediatric Cardiac Coding) were recorded all women who gave informed consent. Miscarriages and elective abortions were excluded as data concerning these pregnancies are often disputable and unreliable. The following complications were recorded for each completed (>20 weeks of gestation) pregnancy between 1980 and 2007.*

a. ***Cardiac complications*** *(as diagnosed by a tertiary care cardiologist specialist): clinically significant ('requiring treatment at least including drug prescription') episodes of arrhythmia or heart failure, cardiovascular complications (e.g. thromboembolic complications, myocardial infarction, and cerebrovascular accidents), and endocarditis (including first six months post-partum).*
b. ***Obstetric complications****: pregnancy-induced hypertension (PIH, new-onset hypertension: blood pressure >140 mmHg systolic or >90 mmHg diastolic without proteinuria after 20 weeks of gestation); preeclampsia (PIH with>0.3 g protein in 24h urine sample); eclampsia (preeclampsia with grand mal seizures); haemolysis elevated liver enzymes low platelets (HELLP) syndrome according to the guidelines of the European Society of Gynaecology and Obstetrics; premature labour (<37 weeks of gestation); post-partum haemorrhage (vaginal delivery >500 mL, caesarean section >1000 mL).*
c. ***Neonatal outcome****: premature delivery (delivery>37 weeks); small-for-gestational-age birth weight (<10th percentile); offspring mortality [demise: in utero (>20 weeks of gestation)—the first-year post-partum].*

Major findings: *In 1802 women with CHD, 1302 completed pregnancies were observed. Independent predictors of cardiac, obstetric, and neonatal complications were calculated using logistic regression. The most prevalent cardiac complications during pregnancy were arrhythmias (4.7%) and heart failure (1.6%). Factors independently associated with maternal cardiac complications were the presence of cyanotic heart disease (corrected/uncorrected) (P<0.0001), the use of cardiac medication before pregnancy (P< 0.0001), and left heart obstruction (P < 0.0001). New characteristics were mechanical valve replacement (P = 0.0014) and systemic (P=0.04) or pulmonary atrioventricular valve regurgitation related to the underlying (moderately) complex CHD (P=0.03). A new risk score for cardiac complications is proposed. The most prevalent obstetric complications were hypertensive complications (12.2%). No correlation of maternal characteristics with adverse obstetric outcomes was found. The most prevalent neonatal complications were premature birth (12%), small for gestational age (14%), and mortality (4%). Cyanotic heart disease (corrected/uncorrected) (P = 0.0003), mechanical valve replacement (P= 0.03), maternal smoking (P= 0.007), multiple gestation (P=0.0014), and the use of cardiac medication (P=0.0009) correlated with adverse neonatal outcome.*

Recommendations: *A new risk score for adverse cardiac complications is proposed, although prospective validation remains necessary. The representation of risk factors in the population determines which risk factors emerge. Important risk factors such as pulmonary arterial hypertension are likely to be underrepresented in contemporaneous cohorts, preventing such risk factors to be identified. Therefore, it is important to underline that the calculation of risk scores should be only a part of pre-pregnancy risk assessment. The authors advocate a pre-pregnancy evaluation in an outpatient setting, including physical examination, laboratory evaluation, and*

echocardiography according to a predefined protocol by an expert in the field. In addition to weighing predictors found in ZAHARA and CARPREG and calculating risk scores, disease-specific information should always be used when estimating pregnancy risk to avoid over-simplification implied by risk calculation. Also, existing guidelines and expert articles should be consulted. External validation of our modified risk score in a large prospective study remains necessary before everyday practice is possible.

Key thoughts and comments: *The CARPREG risk score performed inadequately in the study population and largely overestimated risk, in line with other reports. The differences between the populations the authors may explain the poor performance of the CARPREG cardiac risk score in the study population. In addition, the incidence of cardiac complications appears relatively low (7.6%) in comparison to 13 and 19.4% reported by Siu et al. and Khairy et al. However, the cardiac complication rate in the CARPREG study in patients with CHD is 7.1% (32 in 445 pregnancies). Acquired or arrhythmic heart disease patients are at higher risk***.**

Limitations: *First and most importantly, the present study lacks a historical 'matching' control population. This is, however, not as straightforward exercise as the vast majority of healthy women in the Netherlands and Belgium deliver at home with the help of a midwife. Therefore, the women consulting gynaecological hospital care are selected with (mainly obstetric or neonatal) complications or higher risk for these complications.*

*Moreover, the concept of a control population is, only sustainable when both cohorts are followed identically according to a predefined protocol. Therefore, a prospective study would be the best option, on the other hand, to collect the number of pregnancies provided in the present study; data collection would take at least ten years and interfere with the contemporary applicability. A second limitation is the possibility of underreporting. Because data-retrieval was retrospective, only documented complications (by medically educated personnel) were included. Third, the authors considered that for the present study; a survivor cohort was selected, therefore not allowing the investigation of maternal mortality. Finally, the current cohort represents a CHD population receiving tertiary medical care, including patients with complex heart disease; caution, however, is needed when extrapolating the results to populations with another CHD distribution. In summary, the results should be interpreted with caution***.**

Keywords: *Congenital heart disease, Pregnancy, Complications.*

Siu, S. C., Marcotte, F., Taylor, D. A., Gordon, E. P., Spears, J. C., Tam, J. W., . . . Investigators, C. (2001). Prospective multicentre study of pregnancy outcomes in women with heart disease. *CIRCULATION, 104*(5), 515-521. doi:10.1161/hc3001.093437.

Purpose of study: *In the presence of maternal heart disease, the cardiovascular changes of pregnancy may precipitate decompensation or death of the mother or fetus. The risk estimates were primarily based on retrospective studies, focused on a particular cardiac lesion, or examined populations managed at a single institution or earlier. The researchers prospectively examined the frequency and predictors of pregnancy-related complications in Canadian women with heart disease to assess outcomes comprehensively in a contemporary cohort. To enhance the risk stratification of pregnant women with heart disease, they developed and validated a risk index to predict cardiac complications during pregnancy.*

Type of study: *Prospective ongoing study. The study coordinating centre (Toronto General Hospital) validated the accuracy of data entry using supporting documentation from participating centres. In addition, primary cardiac and neonatal events were verified by two physicians unrelated to the study who were blinded to patient baseline characteristics.*

Setting: *This study prospectively enrolled 562 pregnant women with heart disease (aged 28±6 years) receiving care in 13 Canadian cardiac and obstetric teaching hospitals (55 000 deliveries per year) during 617 pregnancies. All pregnant women with congenital or acquired cardiac lesions or cardiac arrhythmias referred to a*

participating centre from October 1994 to November 1999 were eligible for enrolment. To be eligible for inclusion, women in whom cardiac arrhythmia was the primary diagnosis must have had symptomatic sustained tachyarrhythmias or bradyarrhythmias requiring treatment before pregnancy. Women with isolated mitral valve prolapse (moderate or mild mitral regurgitation) or those referred for termination of pregnancy were excluded. All centres received research ethics approval for this study, and subjects gave informed consent.

Data collected: *Baseline data collected at the first prenatal visit included age, gestational age, New York Heart Association (NYHA) functional class, parity status, comorbid conditions, prior cardiac events (for those who underwent cardiac intervention, only events after intervention were considered), cardiac lesions, previous surgery/interventions, cyanosis (oxygen saturation <90%), medications, use of cigarettes and alcohol, educational status (a surrogate for socioeconomic status), 12-lead ECG, transthoracic echocardiographic assessment of systemic (left) and venous (right) ventricular systolic function, Doppler quantitation of inflow or outflow obstruction, Doppler quantitation of valvular regurgitation, and systolic pulmonary artery pressure. Prepartum, peripartum, and postpartum complications were grouped into primary cardiac, secondary cardiac, neonatal, or obstetric events.*

Primary cardiac events *defined as pulmonary oedema (documented on chest radiograph or by crackles heard over more than one-third of posterior lung fields), sustained symptomatic tachyarrhythmia, or bradyarrhythmia requiring treatment, stroke, cardiac arrest, or cardiac death. Likewise,* **secondary cardiac events** *defined as a* decline *in NYHA class (≥ 2 classes) compared to baseline or emergency invasive cardiac procedures during pregnancy or within six months after delivery.* **Neonatal events** *defined as premature birth (<37 weeks gestation), small-for-gestational-age birthweight (<10th percentile), respiratory distress syndrome, intraventricular haemorrhage, fetal death (≥20 weeks gestation), or neonatal death (within 28 days after birth).* **Obstetric events** i*ncluded noncardiac death, pregnancy-induced hypertension (PIH), and postpartum haemorrhage (PPH). PIH was defined as increasing systolic (≥30 mm Hg) and diastolic (≥15 mm Hg) blood pressure. PPH was defined as blood loss >500 mL (vaginal delivery) or >1000 mL (caesarean section), which required transfusion or was accompanied by a drop in haemoglobin ≥20 g/*L.

The data set was randomly divided into derivation (60% of total pregnancies) and validation (40% of total pregnancies) to determine predictors of cardiac events. A retrospectively derived point score (original risk index) related cardiac risks during pregnancy to the number of prenatal characteristics from the following list: heart failure or stroke/transient ischaemic attack before pregnancy, cardiac arrhythmia before pregnancy, baseline NYHA class III or IV or cyanosis, left heart obstruction (mitral valve area <2 cm^2, aortic valve area <1.5 cm^2, or peak left ventricular outflow tract gradient >30 mm Hg), and myocardial dysfunction (systemic ventricular ejection fraction <40% or hypertrophic or restrictive cardiomyopathy). Different combinations of these and other potential predictors most strongly correlated with cardiac outcomes were tested in the derivation set. The coefficients from the logistic regression model were converted into a revised risk index. Additional analyses were performed to identify predictors of (1) the composite outcome of primary and secondary cardiac events and (2) primary cardiac events in the entire data set.

Major findings: *A total of 546 women underwent 599 completed (>20 weeks gestation) pregnancies. The principal cardiac lesion was congenital in 445 pregnancies (74%), acquired in 127 pregnancies (22%), and arrhythmic in 27 pregnancies (4%). Multiple congenital lesions were present in 121 pregnancies. In 30 pregnancies, both congenital and acquired cardiac lesions were present. The cardiac lesion was known before pregnancy in all but 20 pregnancies in which the diagnosis was made prenatally (shunts [n=6], dilated cardiomyopathy [n=6], valvular obstruction [n=6], hypertrophic cardiomyopathy [n=1], and pulmonary hypertension from systemic lupus erythematosus [n=1]).*

In 277 pregnancies (46%), the mother had undergone ≥1 surgical intervention before conception; these interventions included closure of shunts (n=121), coarctation repair (n=44), Tetralogy of Fallot or double-outlet right ventricle repair (n=53), Mustard repair (n=21), arterial switch (n=1), Rastelli repair (n=4), Fontan repair (n=5), valve repair (n=67) or replacement (mechanical, n=11; tissue, n=33; and pulmonary autograft, n=5), reimplantation of left coronary artery (n=2), resection of subaortic stenosis (n=3), heart-lung transplantation (n=1), and aortocoronary bypass (n=1).

The live birth rate was 98%; 164 deliveries (27%) were by Caesarean section. Most Caesarean deliveries (96%) were for obstetric indications; maternal cardiac status indicated 4%.

Predictors of primary cardiac events were incorporated into a revised risk index in which each pregnancy was assigned 1 point for each predictor when present. No pregnancy received >3 points.

- *The estimated risk of a cardiac event in pregnancies with 0, 1, and >1 points was 5%, 27%, and 75%, respectively. Importantly, all three cardiac deaths (1%) occurred in pregnancies with a risk score ≥ 1.*
- *For the revised risk index, there was excellent agreement between the expected and observed rate of events.*
- *The four predictors of primary cardiac events also predicted the combined likelihood of either a primary or secondary cardiac event.*
- *The five predictors of neonatal events were as follows: NYHA class >II or cyanosis during the baseline prenatal visit, maternal left heart obstruction, smoking during pregnancy, multiple gestations, and use of anticoagulants throughout pregnancy.*
- *A primary cardiac or neonatal event complicated 170 pregnancies (28%).*
- *The frequency of a primary cardiac or neonatal event corresponding to the absence and presence of any cardiac or neonatal risk factors was 14% and 45%, respectively. Maternal, fetal, or neonatal death occurred in 18 pregnancies (3%).*
- *The maternal, fetal, or neonatal mortality rate corresponding to the absence and presence of any cardiac or neonatal risk factors was 2% and 5%, respectively.*

Recommendations*: In women at high risk for cardiac events, cardiac interventions should be considered before conception if the risk-benefit ratio is favourable. At intermediate or high cardiac risk (risk score ≥one or with lesion-specific risk factors), women should be referred to a regional centre for ongoing care. Those at low cardiac risk (risk score of 0 and without lesion-specific risk factors) can safely deliver in a community hospital. Women with risk factors for maternal cardiac or neonatal complications may require increased frequency of follow-up.*

Key thoughts and comments: *The strategy of combining cardiac lesions and deriving a common risk index is similar to that used in the risk stratification of patients undergoing noncardiac surgery. The cohort was defined by its exposure to cardiovascular changes in pregnancy, thus analysing multiple cardiac lesions within the same woman.*

Limitations and biases worth noting: *The risk associated with cardiac lesions, which were not well represented in this study (such as Fontan procedure or hypertrophic cardiomyopathy), may have been underestimated. Until additional data are available, clinical management of patients with such conditions should be based on an assumption of intermediate risk. The selection bias associated with patient recruitment from regional centres was minimised because these centres received referrals from wide catchment areas.*

Given that the Canadian health care system provides universal access, the authors expected that only patients at negligible risk would not be referred to a regional centre. Although treatment strategies were not standardised in this study, regional variation was minimised because the participating centres (part of the Canadian Adult Congenital Heart Network) used common practice guidelines∗. Multivariate analyses of complications and predictors with OR 95% CI and p value and accuracy of risk index. The tables and figures included baseline characteristics, Principal Cardiac Lesions, Prenatal Characteristics, and Complications in Completed Pregnancies.

A6. CARPREG, CARPREG II, ZAHARA, and mWHO Risk Models

Table 1. The CARPREG risk model.	
Predictor	Points Allocated
Prior cardiac event (heart failure, transient ischaemic attack, stroke before pregnancy or arrhythmia)	1
Baseline NYHA functional class < II of cyanosis	1
Left heart obstruction (mitral valve area < 2 cm^2, aortic valve area < 1.5 cm^2, peak LV outflow tract gradient > 30 mmHg by echocardiography)	1
Reduced systemic ventricular systolic function (ejection fraction < 40%)	1

Risk estimation**:** For each present CARPREG predictor, one point is assigned. The estimated risk of cardiac complication is 5% when no predictor is present, 27% in case of one predictor and 75% in case of more than one predictor.

Definition of adverse maternal cardiac outcome:

Primary cardiac events were defined as: pulmonary oedema (documented on chest radiograph or by crackles heard over more than one-third of posterior lung fields), sustained symptomatic tachyarrhythmia or bradyarrhythmia requiring treatment, stroke, cardiac arrest, or cardiac death.

Secondary cardiac events were defined as a decline in NYHA class (≥2 classes) compared with baseline or need for urgent invasive cardiac procedures during pregnancy or within 6 months after delivery.

Table 2. The CARPREG II risk model.	
Predictor	Points Allocated
Prior cardiac event or arrhythmia	3
Baseline NYHA III-IV or cyanosis	3
Mechanical valve	3
Ventricular dysfunction	2
High-risk left-sided valve disease/left ventricular outflow tract obstruction	2
Pulmonary hypertension	2
Coronary artery disease	2
High-risk aortopathy	2
No prior cardiac intervention	1
Late pregnancy assessment	1

Risk estimation: The sum of points reflects the risk score, with a total of 0-21 points. The predicted risks for primary cardiac events are 5% for a score of 0 to 1 points, 10% for 2 points, 15% for 3 points, 22% for 4 points and 41% for more than 4 points.

Definition of adverse maternal cardiac outcome:

Primary cardiac outcomes: any of the following: maternal cardiac death; cardiac arrest; sustained arrhythmia requiring treatment; left-sided heart failure (HF) defined as pulmonary oedema; right-sided HF; stroke or transient ischaemic attack; cardiac thromboembolism; myocardial infarction; and vascular dissection.

Secondary outcomes: a decline in NYHA functional class by ≥2 classes during the antepartum period or the need for urgent invasive treatment procedure/surgery during pregnancy and up to the sixth postpartum week.

Table 3. The ZAHARA risk model.

Predictor	Points Allocated
History of arrhythmia	1.50
Cardiac medication before pregnancy	1.50
NYHA class prior to pregnancy > II	0.75
Left heart obstruction (peak gradient > 50 mmHg or aortic valve area < 1.0 cm^2)	2.50
Systemic atrioventricular valve regurgitation (moderate/severe)	0.75
Pulmonary atrioventricular valve regurgitation (moderate/severe)	0.75
Mechanical valve prosthesis	4.25
Cyanotic heart disease (corrected/uncorrected)	1.00

Risk estimation: Eight predictors were defined, with a weighted risk score from 0-13 points. The estimated risk of maternal cardiac complications is 2.9% for a score of 0-0.5 points, 7.5% for 0.51-1.50 points, 17.5% for 1.51-2.50 points, 43.1% for 2.51-3.50 points and 70,/0% for scores > 3.51 points.

Definition of adverse maternal cardiac outcome:

Cardiac complications: clinically significant ('requiring treatment at least including drug prescription') episodes of arrhythmia or heart failure, **cardiovascular complications** (e.g. thromboembolic complications, myocardial infarction, and/or cerebrovascular accidents), and endocarditis (including first 6 months post-partum).

Table 4: Modified WHO Classification
Conditions in which maternal risk is WHO class I
Uncomplicated, small or mild pulmonary stenosis
Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage)
Conditions in which maternal risk is WHO Class II or III
WHO Class II (if otherwise well and uncomplicated)
Unoperated atrial or ventricular septal defect, repaired Tetralogy of Fallot
WHO Class II–III (depending on individual)
Native or tissue valvular heart disease not considered WHO I or IV; repaired coarctation; Marfan syndrome without aortic dilatation, bicuspid valve with aorta <45 mm; mild ventricular impairment
WHO class III
Mechanical valve; systemic RV; Fontan circulation; unrepaired cyanotic heart disease; other complex congenital heart disease; Marfan syndrome with aorta 40–45 mm; bicuspid aortic valve with aorta 45–50 mm
Conditions in which pregnancy risk is WHO class IV (contra-indicated)

Risk estimation: Predictors of maternal cardiac complications according to the mWHO classification. The estimated risk of maternal cardiac complications is 2.5-5% for mWHO class I; 5.6-10.5% for mWHO Class II; 10-19% for mWHO Class II–III and 40-100% for mWHO Class III.

Definition of adverse maternal cardiac outcome:

Primary cardiovascular events were: cardiovascular mortality, clinically significant (needing treatment) arrhythmia, clinically significant (needing treatment) heart failure, thromboembolic events (e.g. pulmonary embolism, valve thrombosis or deep venous thrombosis), vascular events (e.g. stroke, myocardial infarction or dissection), need for urgent or invasive cardiovascular intervention up to 6 months postpartum, and endocarditis.

Secondary cardiac events were: NYHA class deterioration ≥2 points compared to baseline.

Source: Denayer, N., Troost, E., Santens, B., De Meester, P., Roggen, L., Moons, P. . . . Van De Bruaene, A. (2021). Comparison of risk stratification models for pregnancy in congenital heart disease. *International Journal of Cardiology, 323*, 54-60. doi:https://doi.org/10.1016/j.ijcard.2020.09.033 supplemental information.

Appendix B Chapter 3 supplementary materials

B1. Perinatal audit

Demographics

1. Study code
2. Site (Choose one answer)
    a. Tertiary hospital
    b. Quaternary hospital
    c. Stand-alone Maternity Unit)
3. Age
4. Country of birth
5. Geographical postcode (Choose one answer)
    a. Rural
    b. Remote
    c. Metropolitan
    d. Unknown
6. Maternal race classification (Choose one answer)
    a. Caucasian
    b. Aboriginal/Torres Strait Islander
    c. Asian
    d. Other:
7. Previous pregnancies with cardiac history? (Choose one answer)
    a. Yes
    b. No previous pregnancies
    c. Has had previous pregnancies but not with cardiac history
8. Details of previous pregnancy with cardiac history (insert text):
    Follow-up for response of 'Yes'...
9. Weight
10. Height in cm
11. Body mass index
12. Current social status (Choose one answer)
    a. Married
    b. De facto/ living with partner
    c. Divorced/Separated
    d. Widowed
    e. Never married/Single

Cardiac pathology identified

13. Entry point. Group A: Pre-existing cardiac condition, Group B: Newly acquired cardiac condition during course of pregnancy and so care may not be reflective of perinatal guidelines. Congenital (A) (Choose one or more answers)
    a. Acquired A (acute event first trimester) (B)
    b. Acquired B (at delivery) (B)
    c. Acquired C (post-partum) (B)
    d. Cyanotic (A)
    e. Acyanotic (A)
    f. Other:
14. Cause of cardiac disease (Choose one or more answers)
    a. Rheumatic heart disease (A)
    b. Congenital heart disease (A)
    c. Arrhythmias (B) (A)
    d. Ischaemic Heart Disease (IHD) (B) (A)
    e. Heart Failure (B) (A)
    f. Cardiac arrest (B)
    g. Conduction disorders (B)

h. PE (B)
i. Hypertension with severe cardiac condition (B)
j. Interventional coronary procedure (B)
k. Other (B) (A)

15. New York Heart Association (NYHA) Functional Classification on admission or documented. Applicable to category A conditions only (Choose one or more answers)
    a. I
    b. II
    c. III
    d. IV
    e. Not applicable
    f. Unknown

Pre-conception care

16. Documented discussion before conception, which is applicable to group A only. For all others leave as not applicable (Choose one answer)
    a. Yes
    b. No
    c. Not applicable
    d. Unknown.
17. General physical assessment (Tick all which apply, Choose one or more answers)
    a. Weight
    b. Height
    c. BMI
    d. Oral health
    e. Respiratory examination (auscultation)
    f. Breast Examination
    g. Abdominal Examination
    h. Vaginal examination (speculum/vaginal exam + swabs if clinically indicated)
    i. Urinalysis
    j. Psychosocial assessment
    k. Not applicable
    l. Unknown
18. Medication assessment (Insert text):
19. Cardiac assessment (Choose one or more answers)
    a. Blood pressure
    b. Pulse
    c. 12 lead ECG
    d. Cardiac biomarkers
    e. Cardiac auscultation
    f. Echocardiogram
    g. Not applicable
    h. Unknown.
20. Cardiac assessment comments (Insert text):
21. Healthcare professionals who performed assessment (Choose one or more answers)
    a. Physician/medical officer
    b. Midwife
    c. Cardiac specialist nurse
    d. Obstetrician
    e. Not applicable
    f. Unknown
    g. Other:
22. Comments on healthcare professional who completed assessment (Insert text):
23. Hypertension management (Choose one answer)
    a. Not identified
    b. Identified and management optimised/reviewed
    c. Identified and management NOT optimised/reviewed
    d. Not applicable
    e. Unknown

24. Systolic blood pressure value:
25. Diastolic blood pressure value:
26. Arrhythmia management (Choose one answer)
    a. Not identified
    b. Identified and management optimised/reviewed
    c. Identified and management NOT optimised/reviewed
    d. Not applicable
    e. Unknown
27. Lifestyle factors identified (Choose one or more answers)
    a. Smoking
    b. Exercise tolerance
    c. Documented discussion with the woman, family and cardiologist re lifestyle factors
    d. Psychosocial evaluation (identify tool used)
    e. Not applicable
    f. ANRQ score
    g. Follow-up for response of 'Psychosocial evaluation (identify tool used) '...insert value and text
    h. EPPSD score
    i. Follow-up for response of 'Psychosocial evaluation (identify tool used) '...insert value and text

Preconception cardiac education

28. Documentation of cardiac education (Choose one answer)
    a. Yes
    b. No
    c. Not applicable
29. Patient informed regarding the potential expected outcomes (Choose one or more answers)
    a. spontaneous miscarriage
    b. live birth
    c. death
    d. antenatal care
    e. anaesthesia
    f. proposed care plan for pregnancy
    g. medications in the Peripartum management
    h. genetic counselling
    i. Not applicable
    j. Unknown

Antenatal management

30. Antenatal management offered (Choose one or more answers)
    a. Routine visits within 10-12 weeks
    b. Early ultrasound to establish estimated date of confirmation (EDC)
    c. Documented multidisciplinary team management that includes obstetrician,
    d. cardiologist, obstetric physician, anaesthetist, intensivist
    e. If applicable -fortnightly antenatal visits in high-risk medical clinic dependant on severity of disease.
    f. Not applicable high-risk antenatal visits
    g. Avoid anaemia+ regular Hb checks.
    h. Iron supplements + prenatal vitamins and dietary counselling
    i. Anaesthetic review before 28 weeks
    j. Unknown

Clinical assessment

31. Maternal age
32. Gestational age
33. Gravida
34. Parity
35. NYHA functional classification (Choose one answer)
    a. Documented
    b. Not documented
    c. Unknown

d. Not applicable

36. Comorbid conditions (Choose one or more answers)
    a. Previous cardiac events
    b. Previous cardiac surgery
    c. Previous cardiac interventions
    d. Past/current cardiac lesions
    e. Past/current cyanosis (Sa) 2 <90%)
    f. Medication history
    g. Use of cigarettes and/or alcohol
    h. Not applicable
    i. Unknown
37. Cardiac events additional information (Insert text)
38. Cardiac surgery additional information (Insert text)
39. Cardiac interventions additional information (Insert text)
40. Past/current cardiac lesions additional information (Insert text)
41. Past/current cyanosis additional information (Insert text)
42. Medication history additional information (Insert text)
43. Use of cigarettes and/or alcohol additional information (Insert text)

Clinical assessment: Investigations

44. 12 lead ECG findings
45. Echocardiogram findings
46. Fetal wellbeing/risks (Choose one or more answers)
    a. Regular (fortnightly) ultrasound assessment of fetal wellbeing
    b. Growth, umbilical artery Doppler, AFI
    c. Cardiotocograpghy (CTG) in third trimester
    d. Unknown
    e. Not applicable
47. Fetal risks (Choose one or more answers)
    a. Fetal echocardiogram at 20 weeks of gestation if woman on warfarin or identified cardiac fetal anomaly
    b. Amniocentesis with antibiotic prophylaxis
    c. Unknown

Planned care

48. Echocardiogram assessment (Choose one answer)
    a. Yes
    b. No
    c. Not applicable
    d. Unknown
49. Ongoing NYHA functional classification to assist with hospital choice (Choose one answer)
    a. Yes
    b. No
    c. Not applicable
    d. Unknown
50. Planned Care: Level of Hospital Care (comments):
51. Planned delivery mode (Choose one answer)
    a. Vaginal birth
    b. Caesarean section for obstetric emergency only
    c. Caesarean section for other
    d. Not applicable
    e. Unknown
52. Planned delivery mode (comments):

High risk management in labour

53. Identified as high risk (Choose one answer)
    a. Yes

b. No
c. Not applicable
d. Unknown

54. Labour and birth occurred in a hospital with adult intensive care or cardiac unit (Choose one answer)
    a. Yes
    b. No
    c. Not applicable
55. Documented plan of care in case notes (Choose one answer)
    a. Yes
    b. No
    c. Unknown
    d. Not applicable
56. Timing and labour of birth (Choose one answer)
    a. Multidisciplinary team discussion
    b. Cardiac state well stabilised
    c. At short notice in event of cardiac function and reserve altered
    d. Unknown
    e. Not applicable
57. During labour, the following multidisciplinary team members informed of impending birth and documented (Choose one or more answers)
    a. Cardiologist or physician
    b. Anaesthetist
    c. Paediatrician
    d. Not applicable
    e. Unknown
58. Appropriate antibiotic prophylaxis considered (Choose one answer)
    a. Yes
    b. No
    c. Not applicable
    d. Unknown
59. Planned cardiac drugs required in consultation with multidisciplinary team (Choose one answer)
    a. Yes
    b. No
    c. Not applicable
    d. Unknown
60. High risk management in labour comments (Insert text):
61. Was the second stage of birth shortened to avoid excessive maternal expulsive effort? (Choose one or more answers)
    a. No
    b. Yes with episiotomy
    c. Yes with forceps delivery
    d. Yes with no local anaesthetics with adrenaline being used
    e. Not applicable
    f. Unknown
62. Minimisation of cardiac compromise (Choose one or more answers)
    a. Consultation re avoiding the use of stirrups
    b. Assessment + prompt reporting of Tachycardia >130bpm
    c. Assessment + prompt reporting of Bradycardia < 40bpm
    d. Assessment + prompt reporting of respiratory rate >24 or < 5 bpm
    e. Assessment+ prompt reporting rapidly changing pulse or respiration rate (even if
    f. within threshold)
    g. Not applicable
    h. Unknown
63. Birth comments (Insert text)
64. Management in labour: Adult resuscitation equipment available? (Choose one answer)
    a. Yes
    b. No
65. Management in labour: Ability to perform perimortem Caesarean section within 5 minutes of cardiac arrest

(Choose one answer)

a. Yes
b. No

66. Multidisciplinary team included in management of labour (Choose one or more answers)
    a. Obstetrician
    b. Midwife
    c. Cardiologist
    d. Physician/ medical officer
    e. Anaesthetist
    f. Intensivist
    g. Other allied health professional
    h. Other:
67. Management in labour comments (Insert text):
68. Thromboembolism prophylaxis (Choose one or more answers)
    a. Use of anti- embolic stockings
    b. Subcutaneous LMWH or IV Unfractionated heparin
    c. Not applicable
    d. Unknown
69. Pain Management and Anaesthesia (Choose all that apply)
    a. Anaesthetic consultation regarding appropriate pain management undertaken
    b. Epidural considered
    c. Combined spinal-epidural anaesthesia to decrease preload and afterload
    d. Not applicable
    e. Other:
70. Pain management and anaesthesia comments (Insert text):

Preterm labour imminent

71. Cardiac consultation with cardiologist and physician advice sought (Choose one answer)
    a. Yes
    b. No
    c. Not applicable
    d. Unknown
72. Paediatric and neonatal staff available (Choose one answer)
    a. Yes
    b. No
    c. Unknown
73. Perinatal outcome of baby (Insert text comment)
74. Outcome of birth
75. Gestational age
76. Live baby weight grams
77. Baby's length at birth
78. Baby's Head circumference at birth
79. Apgar score at 1 min Bounds: 0 – 10 [inclusive]
80. Apgar at 5 min Bounds: 0 – 10 [inclusive]
81. Cardiac follow-up included in obstetric follow-up care

Checklist or nursing or medical documentation; include Text Comments

Table B1. Supplementary 1 code log for Auditmaker and SAS scoring for adherence to the Statewide Perinatal Guidelines

Auditmaker Variable	SPSS Variable name / SAS code	Coding instructions /SAS Scoring for Obstetric/Cardiac Guideline adherence.	Adherence score
1. Study ID	ID	The number assigned to each case note	NA
2. **Hospital site	Site	1=Tertiary Hospital level 5 care 2=Quaternary Hospital 3=Maternity stand-alone unit	NA
3. **Prenatal care:** Pre-conception counselling documented	Preconception	Where documented evidence of preconception counselling then **Total Score =+ 1 for Yes** 1=yes 2=No 3= Not applicable 4= Unknown	1
4. **Initial Antenatal Aassessment:** Comprehensive physical assessment where 10 Components included: 1. Weight 2. Height 3. BMI 4. Oral health 5. Respiratory examination (auscultation) 6. Breast Examination 7. Abdominal Examination 8. Vaginal Examination 9. Urinalysis 10. Psychosocial Assessment 11. Not applicable 12. Unknown	See subsequent rows where coded and scored separately as ANC 1, ANC2 and ANC 3.	1. Weight, Height, BMI. 2. Oral health /Respiratory (auscultation) Breast Examination 3. Abdominal /Vaginal Examination/Urinalysis 4. Psychosocial Assessment 5. Not applicable	*See below*
- Initial Antenatal assessment includes 1-3 components	ANC1	Weight, Height and BMI where ANC1 =3 then **Total Score =+1**	1
- Initial antenatal assessment includes components 4-6	ANC2	Oral health, respiratory and breast examination where ANC2=3 then **Total Score = +1**	1
- Initial Antenatal assessment includes 7-9	ANC3	Abdominal, vaginal, and urinalysis assessment where ANC3=3 then **Total Score = +1**	1
5. **Antenatal Mental Health assessment** - Psychosocial Assessment 1 recorded	ANRQ score recorded	Antenatal Risk Questionnaire score documented then **Total Score = +1**	1
- Psychosocial Assessment 2 recorded.	EPPSD score recorded	The Edinburgh Post Natal Depression Scale self-reported ten items documented then **Total Score = +1.**	1

- ANRQ score documented	ANRQ	Where ANRQ value documented =1 **Total Score =+ 1 for Yes** 1=yes / 2=No	1
6. *Antenatal Medication assessment:*	*ANM / medications string data only for separate coding for clinical outcomes*	*Comments: Documented prescribed and non prescribed medications or nil medications to be coded separately for clinical outcomes.*	NA
7. **Antenatal Cardiovascular Assessment** included: - BP - Pulse - 12 Lead ECG - Cardiac Biomarkers - Echocardiogram - Yes - Not applicable - Unknown	CVSA	Where all components completed, and assessment done sum =6 **Total Score =+1** 1. Yes 2. BP 3. Pulse 4. 12 Lead ECG 5. Cardiac Biomarkers (clinical indication) 6. Echocardiogram 7. Not applicable 8. Unknown	1
8. *Cardiac Assessment comments*	*String data only for separate coding for clinical outcomes*	*Comments to be coded for clinical outcome*	NA
9. **Health Professional who performed Cardiac Assessment** 1= Physician / medical officer 2= Midwife 3= Cardiac Specialist Nurse 4= Obstetrician 5= Not applicable 6= Unknown	HP.	Where health professional included sum = 3, Midwife/ Obstetrician ± Physician, Cardiac Specialist Nurse, then **Total Score =+1** 1= Physician /Medical officer 2= Midwife 3= Cardiac Specialist Nurse 4= Obstetrician 5= Not applicable 6= Unknown	1
10. *Health Professional who performed Cardiac Assessment comments*	*String data only for separate coding for clinical outcomes*	*Comments to be coded for clinical outcome*	NA
11. **Antenatal management** for Hypertension 1= Not Identified 2= Identified and management optimised /reviewed 3= Identified and management not optimised /reviewed 4= Not Applicable 5= unknown	HT	When hypertension Identified & management optimised /reviewed **Total Score =+1** 1= Not Identified 2= Identified and management optimised /reviewed 3= Identified and management not optimised /reviewed 4= Not Applicable 5= unknown	1
- *SBP = numerical value on admission*	*SBP*	*Numerical value to be coded separately for clinical outcomes*	NA
- *DBP = numerical value on admission*	*DBP*	*Numerical value to be coded separately for clinical outcomes*	NA

12. **Antenatal management** for Arrhythmias	Arrhythmia management	If Arrhythmia Identified & management optimised /reviewed then **Total score =+1** 1= Not Identified 2= Identified and management optimised /reviewed 3= Identified and management not optimised /reviewed 4= Not Applicable 5= No selection	1
13. **Antenatal management:** Lifestyle Factors Risk assessment total of 4 1= Smoking 2= Exercise Tolerance 3= Psychosocial Evaluation 4=Medical officer discussion re lifestyle with woman, family & cardiologist 5= Not Applicable	LSRA	Where the LSRA Sum= 4 then **Total score= +1** 1= Smoking 2= Exercise Tolerance 3= Psychosocial Evaluation 4= Cardiologist & Medical officer discussed Lifestyle factors with woman, family & cardiologist 5= Not Applicable	1
14. **Preconception Cardiac Education** 1=Yes 2 =No 3= Not Applicable 4= Unknown	PreEdu	Where documented evidence of pre-education then **Total Score =+ 1** 1=Yes 2 =No 3= Not Applicable 4= Unknown Documented discussion before conception, which is applicable to pre-existent cardiac group A only. For all others leave as Not applicable	1
15. **Patient Informed re total of 9** Content: 1. Miscarriage 2. Live birth 3. Death 4. Antenatal Care 5. Intensive Care 6. Anaesthesia 7. Proposed care plan for pregnancy 8. Medications in the Peri-partum management 9. Genetic Counselling 0= Not applicable 01=Unknown	PreEdu2	Documented evidence of pre-education of potential outcomes minimum proposed plan for pregnancy and medications in peripartum management if (7,8) then **Total Score =+1** 1. Miscarriage 2. Live birth 3. Death 4. Antenatal Care 5. Intensive Care 6. Anaesthesia 7. Proposed care plan for pregnancy 8. Medications in the Peri-partum management 9. Genetic Counselling 10= Not applicable 01=Unknown	1

16. **Antenatal Management offered**: total of 8 1. Routine Visits within 10-12 weeks 2. Early ultrasound to establish EDC 3. Documented Multi-Disciplinary Team management (Obstetrician, Cardiologist, HRP, anaesthetist, Intensivist) 4. If applicable: - fortnightly antenatal visits in High-Risk Medical clinic asper the severity of the disease. 5. Not applicable – High risk antenatal visits 6. Avoid anaemia and regular Hb checks 7. Iron supplements + prenatal vitamins and dietary counselling 8. Anaesthetic review before 28 weeks 9. Unknown	ANM	Where antenatal management included addition of **(6,7)** then **Total Score =+1** 1. Routine Visits within 10-12 weeks 2. Early ultrasound to establish EDC 3. Documented Multi-Disciplinary Team management (Obstetrician, Cardiologist, HRP, anaesthetist, Intensivist) 4. If applicable: - fortnightly antenatal visits in High Risk Medical clinic as per the severity of the disease. 5. Not applicable – High risk antenatal visits 6. Avoid anaemia and regular Hb checks 7. Iron supplements + prenatal vitamins and dietary counselling 8. Anaesthetic review before 28 weeks 9. Unknown	1
17. Maternal Age = numerical value	Maternalage	Numerical value	
18. Gestational Age on admission	Gestation	0-40+ weeks	
19. Gravida Numerical value for previous pregnancies	Gravida	Numerical value for previous pregnancies	
20. Parity: live babies from pregnancies	Parity	Numerical value for live babies from pregnancies	
21. **Antenatal management NYHFA documented** 1=yes 2=No 3= Unknown 4= Not applicable	NYHF	Where evidence NYHFA documented in case notes then **Total Score =+1 if documented: I II, III, IV** 1=Yes 2=No 3= Unknown 4= Not applicable	1
22. Comorbidities present *1. Previous cardiac history* *2. Previous cardiac surgery* *3. Previous cardiac interventions* *4. Previous cardiac lesions* *5. Past/Current Cyanosis with saO2 <90%* *6. Medication History* *7. Use of Alcohol and Cigarettes* *0=Not applicable* *8=Unknown*	*Comorbidities*	*String data with comments to be coded for clinical outcomes* *1. Previous cardiac history* *2. Previous cardiac surgery* *3. Previous cardiac interventions* *4. Previous cardiac lesions* *5. Past/Current Cyanosis with saO2 <90%* *6. Medication History* *7. Use of Alcohol and Cigarettes* *8. Not applicable* *9. Unknown*	
23. Previous cardiac history	*String data only for separate coding for clinical outcomes*	*Comments to be coded for clinical outcome*	

24. Previous cardiac surgery	*As above*	*Comments to be coded for clinical outcome*	
25. Previous cardiac interventions	*As above*	*Comments to be coded for clinical outcome*	
26. Previous cardiac lesions	*As above*	*Comments to be coded for clinical outcome*	
27. Past/Current Cyanosis with saO2 <90%	*As above*	*Comments to be coded for clinical outcome*	
28. Medication history	*As above*	*Comments to be coded for clinical outcome*	
29. Use of Alcohol and cigarettes	*As above*	*Comments to be coded for clinical outcome*	
30. 12 lead ECG findings	*As above*	*Comments to be coded for clinical outcome*	
31. Echocardiogram findings	*As above*	*Comments to be coded for clinical outcome*	
32. **Antenatal Management: Fetal Risk Assessment 1**. 3 components include; 1. Regular (Fortnightly)Ultrasound Assessment of fetal wellbeing 2. Growth, umbilical artery Doppler, AFI 3. Cardio topography (CTG) in Third Trimester 4. Unknown 5. Not applicable.	FetalRisk1	When documented evidence of 3 components sum= 3 then **Total Score =+ 1** 1. Regular (Fortnightly)Ultrasound Assessment of fetal wellbeing 2. Growth, umbilical artery Doppler, AFI 3. Cardio topography (CTG) in the Third Trimester 4. Unknown 5. Not applicable	1
33. **Fetal Risk Assessment 2**. 1= Fetal echocardiogram at 20 weeks of gestation (if women on warfarin: identified cardiac fetal anomaly) 2= Amniocentesis with antibiotic prophylaxis 3= Unknown	oetalRisk2	When documented evidence of two fetal risk assessment then **Total Score = +1 for sum of 2** 1= Fetal echocardiogram at 20 weeks of gestation (if women on warfarin: identified cardiac fetal anomaly) 2= Amniocentesis with antibiotic prophylaxis 3= Unknown	1
34. **Antenatal management** / assessment Planned care 1. Cardiac Echocardiogram 1= yes 2= No 3= Unknown 4= Not applicable	Plannedcare1	When documented evidence that echocardiogram was done then **Total Score =+ 1 for yes** 1= yes 2= No 3= Unknown 4=Not applicable	1
35. Planned Care 2 Ongoing NYHA to assist with hospital choice 1= Yes 2= No 3= Unknown 4= Not applicable	Plannedcare2	When NYHA determined hospital choice for planned care then **Total Score = +1 for yes** 1= Yes 2= No 3= Unknown 4= Not applicable	1
36. Planned Care: Level of Hospital Care comments	*String data only for separate coding for clinical outcomes*	*Comments to be coded for clinical outcome*	NA
37. Planned Care 3. Mode of delivery 1= NVD 2= Emergency LSCS 3= LSCS for other 4= Nil documented	Plannedcare 3	To be coded for clinical outcomes 1= NVD 2= Emergency LSCS 3= LSCS for other 4 = Nil documented	

38. Planned delivery mode comments	*Normal vaginal delivery/ assisted vaginal delivery / elective LSCS and non elective LSCS*	*Comments to be coded for clinical outcome*	
39. **High Risk Management During Labour 1** Identified as high Risk 1= Yes 2= No 3= Not applicable 4= Unknown	Highrisk1	When identified and documented as high risk then **Total Score =+1 for yes** 1= Yes 2= No 3= Not applicable 4= Unknown	1
40. **High Risk Management During Labour 2** Labour and Birth occurred in a hospital with Adult Intensive Care or Cardiac Unit 1= Yes 2= No 3= Unknown 4= Not applicable	Highrisk2	High Risk Management in Labour 2 then **Total Score =+ 1 for yes** Labour + Birth in ICU or CCU occurred in tertiary/ quaternary hospitals 1= Yes 2= No 3= Unknown 4= Not applicable	1
41. **High Risk Management During labour 3** Documented Plan of Care in case notes 1= yes 2= No 3= Unknown 4= Not applicable	Highrisk3	When documented evidence of Plan of Care in case notes then **Total Score =+1 for Yes.** 1= Yes 2= No 3= Unknown 4= Not applicable	1
42. **High Risk Management of labour** 4: Timing & labour of birth included the components of 1-3 Content 1. Multidisciplinary team Discussion 2. Cardiac state well stabilised 3. At short notice in the event of altered cardiac function & reserve 4. Unknown 5. Not applicable	Highrisk4	Where the timing and labour of birth included 1-3 then **Total Score =+1.** 1. Multidisciplinary team Discussion. 2. Cardiac state well stabilised 3. At short notice in the event of cardiac function and reserve altered 4. Unknown 5. Not applicable	1
43. **High Risk Management of labour** 5. The multidisciplinary team informed/ documentation of impending delivery: included 1-3 1. Anaesthetist 2. Cardiologist 3. Paediatrician 4. Unknown 5. Not applicable	Highrisk5	Multidisciplinary team communication for impending delivery then **Total Score =+1 for the sum of 3** 1. Anaesthetist 2. Cardiologist 3. Paediatrician 4. Unknown 5. Not applicable	1

44. **Management of labour** Paediatrician included in discussion e.g. impending delivery (IUGR & SFD)	Highrisk5.(3) Paediatrician included	Where explicit inclusion of paeditrician delivery then **Total Score =+1**	1
45. **Management of labour** Antibiotic Prophylaxis administered 1= Yes 2 = No 3= Not applicable 4= Unknown	Highrisk6	When prophylactic antibiotics administered then **Total Score =+1 for Yes** 1=Yes 2 = No 3= Unknown 4= Not applicable	1
46. **Management of labour** Planned Cardiac drugs in labour Collaboration with Multidisciplinary Team 1=Yes 2 = No 3= Unknown 4= Not applicable	Highrisk7	When cardiac drugs planned for use in labour with MDT discussion (documented) then **Total Score =+1 for Yes** 1=Yes 2 = No 3= Unknown 4= Not applicable	1
47. High Risk labour comments	*String data only for separate coding for clinical outcomes*	*Comments to be coded for clinical outcome*	NA
48. **Management of labour** The second stage of delivery is shortened to avoid excessive maternal expulsive effort 1= Yes, with Episiotomy 2 = Yes, With Forceps Delivery 3 = Yes, with local anaesthetics + adrenaline use 4= No 5 = Unknown 6 = Not applicable.	Highrisk8	When the 2nd stage shortened to avoid excessive maternal expulsive effort with following 1= Yes, with Episiotomy 2 = Yes, With Forceps Delivery 3 = Yes, local anaesthetics + adrenaline use 4= No 5 = Unknown 6 = Not applicable	
49. **Management of labour** with mminimisation of Cardiac compromise in labour score out of 4 1. Consultation re avoiding use of stirrups 2. Assessment + prompt reporting of Tachycardia >130bpm 3. Assessment + prompt reporting of Bradycardia < 40bpm 4. Assessment + prompt reporting of respiratory rate >24 or < 5 bpm 5. Assessment+ prompt reporting rapidly changing pulse or respiration rate (even if within the threshold) 6. Unknown 7. Not applicable	Highrisk 9 Compromise	Where sum of measures to minimise cardiac compromise in labour=4 then **Total Score =+ 1** 1. Consultation re avoiding the use of stirrups 2. Assessment + prompt reporting of Tachycardia >130bpm 3. Assessment + prompt reporting of Bradycardia < 40bpm 4. Assessment + prompt reporting of respiratory rate >24 or < 5 bpm 5. Assessment+ prompt reporting rapidly changing pulse or respiration rate (even if within threshold) 6. Unknown 7. Not applicable	1

50. Birth comments	*String data only for separate coding for clinical outcomes*	*Comments to be coded for clinical outcome*	NA
51. **Management in labour**: Adult resuscitation equipment available?	Management in Labour resuscitation equip	Where adult resuscitation equipment (note for WAS clinic etc.) available then **Total Score =+1 for Yes** 1=Yes 2= No 3 = Null	1
52. **Management in labour**: Ability to perform peri mortem Caesarean section within 5 minutes of cardiac arrest	Labour2/ Management in Labour 5 mins cardiac	Equipment & staff for emergency perimortem LSCS available then **Total Score =+1 for Yes** 1=Yes 2= No 3 = Null	1
53. **Management in labour** Multidisciplinary team included.	Team in labour/	If yes for Obstetrician**, SAS score=Total Score+1**	1
	Team 1 Obstetrician	if yes for Anaesthetist**, SAS score=Total Score+1**	1
	Team 5 Anaesthetist	If yes for Physician (medical officer) **SAS score=Total Score+1**	1
	Team 4 Physician (High Risk/ medical officer). Team sum where includes 5, 67	When MDT in labour included team sum includes *anaesthetist*, *intensivist, & allied health professional (5,6,7)* then **SAS score=Total Score +1** 1. Obstetrician 2. Midwife 3. Cardiologist 4. Medical officer 5. Anaesthetist 6. Intensivist 7. Other Allied health professionals 8. Other 9. Unknown	1
54. **Management in Labour** included cardiac consultation	Cardiac Consultation	Where cardiac consultation occurred for management in labour then **Total Score =+1 for Yes.**	1
55. Management in labour comments	*String data only for separate coding for clinical outcomes*	*Comments to be coded for clinical outcome*	NA
56. **Management in labour**: Thrombo-embolism prophylaxis	Thromboembolism sum of 2	**If the sum of 2 Total score =+ 1** 1= Use of anti- embolic stockings 2= Subcutaneous LMWH or IV Unfractionated heparin 3= Not applicable 4= Unknown	1
57. **Pain Management & Anaesthesia** 1. Anaesthetic consultation regarding appropriate pain management 2. Epidural considered 3. Combined spinal epidural to decrease preload and afterload 4. Not applicable 5. Other	Pain sum where, included anaesthetic consultation and epidural combined spinal	Pain management sum where, included anaesthetic consultation, epidural and /or combined spinal **Total score =+1** 1. Anaesthetic consultation regarding appropriate pain management 2. Epidural considered 3. Combined spinal epidural to decrease preload and afterload 4. Not applicable 5. Other	1

58. Pain Management and Anaesthesia comments	*String data only for separate coding for clinical outcomes*	*Comments to be coded for clinical outcome*	NA
59. **Management in labour** Cardiac collaboration /consultation with cardiologist /physician advice sought	Labour5/If Cardiac Consultation	Where documented cardiac consultation for labour then **Total Score =+1** 1=Yes 2= No 3 = Not applicable 4=Unknown 5=null	1
60. **Management in labour** Paediatric and neonatal staff available.	Labour6 /paediatric neonatal staff present	When paediatric neonatal staff present at delivery then **Total Score =+1** 1=Yes 2= No 3 = Not applicable 4=Unknown 5=No selection	1
61. Outcome of the birth	Outcomebirth	Alive & Well,	
62. Gestational Age	Gestationalage	Numeric	
63. Live baby weight	Newbornweight	Numeric	
64. Baby's length at birth	Newbornlength	Numeric	
65. Baby's Head circumference at birth	NewbornHC	Numeric	
66. Apgar score at 1 min	Apgarscore	Numeric	
67. Apgar at 5 min	Apgascore1	Numeric	
68. Cardiac follow-up included in obstetric follow-up care	*String data only for separate coding for clinical outcomes*	*Comments to be coded for clinical outcome*	
Total Adherence score			**40**

∗Please note that string data have not been included in the current code book as will be analysed for clinical outcomes. This tables provides an overview of the data collected and adherence scores calculation. The Auditmaker variables from audit tool reflect the South Australian Perinatal Practice Guidelines (SAPPGs). ∗∗Hospital sites tertiary, quaternary and Maternity Stand-alone unit as per SA Health: **Hospital 1** provided intermediate care (level five) that encompassed tertiary maternal services, maternal cardiac and intensive care and specialised neonatal care services excluding babies less than 32 weeks. **Hospital 2** provided (level six) care that included maternal cardiac, cardiothoracic surgical and intensive care, and neonatal intensive care services. **Hospital 3** provided a neonatal intensive care unit but no maternal cardiac or intensive care services.

B2. Assumption testing results for Publication Two

Model 1 Final Multivariable Logistic regression of Preconception versus Group, site and confounders

The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	Preconception

Number of Observations Read	271
Number of Observations Used	57
Number of Events	38
Number of Trials	57
Missing Values	214

Class Level Information

Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3
Cardiac_consultation	2	1.Yes 2.No

Response Profile

Ordered Value	*Preconception*	*Total Frequency*
1	Yes	38
2	No	19

PROC GENMOD is modelling the probability that Preconception='Yes'.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*	*Cardiac_consultation*
Prm1	Intercept			
Prm2	Revised_Groups	Acquired		
Prm3	Revised_Groups	Pre-existingt		
Prm4	Site		1	
Prm5	Site		2	
Prm6	Site		3	
Prm7	Cardiac_consultation			1.Yes
Prm8	Cardiac_consultation			2.No
Prm9	Gravida			

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-29.3365	
Full Log Likelihood		-29.3365	
AIC (smaller is better)		70.6731	
AICC (smaller is better)		72.3531	
BIC (smaller is better)		82.9314	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	-2.7521	1.3674	-5.4322	-0.0720	4.05	0.0442
Revised_Groups	Acquired	1	-0.8460	0.7327	-2.2821	0.5900	1.33	0.2482
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	-2.4282	1.5453	-5.4570	0.6005	2.47	0.1161
Site	2	1	-0.2579	0.6876	-1.6056	1.0897	0.14	0.7076
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Cardiac_consultation	1.Yes	1	2.9187	1.1276	0.7086	5.1288	6.70	0.0096
Cardiac_consultation	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Gravida		1	0.4757	0.2285	0.0279	0.9235	4.34	0.0373
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	1.33	0.2482
Site	2	2.48	0.2895
Cardiac_consultation	1	6.70	0.0096
Gravida	1	4.34	0.0373

Contrast Estimate Results

Label	Mean Estimate	Mean Confidence Limits		L'Beta Estimate	Standard Error	Alpha	L'Beta Confidence Limits		Chi-Square	Pr > ChiSq
Gravida	0.6167	0.5070	0.7157	0.4757	0.2285	0.05	0.0279	0.9235	4.34	0.0373
Exp(Gravida)				1.6091	0.3676	0.05	1.0283	2.5180		

Revised_Groups Least Squares Means

Revised_Groups	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
Acquired	-1.4985	0.9622	-1.56	0.1194	0.05	-3.3845	0.3874	0.2235	0.03389	1.4731
Pre-existing	-0.6525	0.6731	-0.97	0.3323	0.05	-1.9717	0.6667	0.5207	0.1392	1.9479

Differences of Revised_Groups Least Squares Means

Revised_ Groups	_Revised_ Groups	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
Acquired	Pre-existing	-0.8460	0.7327	-1.15	0.2482	0.05	-2.2821	0.5900	0.4291	0.1021	1.8041

Site Least Squares Means

Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	-2.6084	1.5875	-1.64	0.1004	0.05	-5.7199	0.5031	0.07365	0.003280	1.6539
2	-0.4381	0.6749	-0.65	0.5163	0.05	-1.7608	0.8846	0.6453	0.1719	2.4221
3	-0.1801	0.6206	-0.29	0.7716	0.05	-1.3964	1.0361	0.8352	0.2475	2.8183

Differences of Site Least Squares Means

Site	*_Site*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	2	-2.1703	1.4914	-1.46	0.1456	0.05	-5.0934	0.7528	0.1141	0.006137	2.1229
1	3	-2.4282	1.5453	-1.57	0.1161	0.05	-5.4570	0.6005	0.08819	0.004266	1.8231
2	3	-0.2579	0.6876	-0.38	0.7076	0.05	-1.6056	1.0897	0.7727	0.2008	2.9734

Cardiac_consultation Least Squares Means

Cardiac_ consultationx	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	0.3838	0.5554	0.69	0.4895	0.05	-0.7047	1.4724	1.4679	0.4942	4.3597
2.No	-2.5349	1.1991	-2.11	0.0345	0.05	-4.8851	-0.1847	0.07927	0.007559	0.8313

Differences of Cardiac_consultation Least Squares Means

Cardiac_ consultationx	*_Cardiac_ consultationx*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	2.No	2.9187	1.1276	2.59	0.0096	0.05	0.7086	5.1288	18.5177	2.0312	168.82

Model 17 Final Multivariable Ordinal logistic regression of ANC1 versus Group, site and confounders

The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Multinomial
Link Function	Cumulative Logit
Dependent Variable	ANC1

Number of Observations Read	271
Number of Observations Used	259
Missing Values	12

Class Level Information

Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3
ANRQ_scoreRECORDED	2	1.Yes 2.No

Response Profile

Ordered Value	*ANC1*	*Total Frequency*
1	3	172
2	2	32
3	1	25
4	0	30

PROC GENMOD is modelling the probabilities of levels of ANC1 having LOWER Ordered Values in the response profile table.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*	*ANRQ_scoreRECORDED*
Prm1	Revised_Groups	Acquired		
Prm2	Revised_Groups	Pre-existing		
Prm3	Site		1	
Prm4	Site		2	
Prm5	Site		3	
Prm6	ANRQ_scoreRECORDED			1.Yes
Prm7	ANRQ_scoreRECORDED			2.No
Prm8	Gestational_age_admi			

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-213.5324	
Full Log Likelihood		-213.5324	
AIC (smaller is better)		443.0649	
AICC (smaller is better)		443.6409	
BIC (smaller is better)		471.5195	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept1		1	-3.6725	1.3371	-6.2931	-1.0519	7.54	0.0060
Intercept2		1	-2.8125	1.3295	-5.4183	-0.2067	4.48	0.0344
Intercept3		1	-1.9564	1.3231	-4.5496	0.6368	2.19	0.1392
Revised_Groups	Acquired	1	0.0011	0.2963	-0.5797	0.5818	0.00	0.9972
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	-0.2097	0.5327	-1.2537	0.8344	0.15	0.6939
Site	2	1	1.5216	0.3694	0.7976	2.2457	16.97	<.0001
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
ANRQ_scoreRECORDED	1.Yes	1	2.4254	0.4489	1.5455	3.3052	29.19	<.0001
ANRQ_scoreRECORDED	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Gestational_age_admi		1	0.0850	0.0351	0.0163	0.1537	5.88	0.0153
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	0.00	0.9972
Site	2	18.52	<.0001
ANRQ_scoreRECORDED	1	29.19	<.0001
Gestational_age_admi	1	5.88	0.0153

Contrast Estimate Results

	Mean			L'Beta						
Label	*Mean Estimate*	*Confidence Limits*		*L'Beta Estimate*	*Standard Error*	*Alpha*	*Confidence Limits*		*Chi-Square*	*Pr > ChiSq*
Gestational_age_admission	0.5212	0.5041	0.5384	0.0850	0.0351	0.05	0.0163	0.1537	5.88	0.0153
Exp(Gestational_age_admission)				1.0887	0.0382	0.05	1.0164	1.1662		

Revised_Groups Least Squares Means

ANC1	*Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
3	Acquired	1.1249	0.2651	4.24	<.0001	0.05	0.6053	1.6446	3.0801	1.8318	5.1788
3	Pre-existing	1.1239	0.2662	4.22	<.0001	0.05	0.6022	1.6456	3.0768	1.8261	5.1843
2	Acquired	1.9849	0.2870	6.92	<.0001	0.05	1.4225	2.5474	7.2787	4.1473	12.7743
2	Pre-existing	1.9839	0.2865	6.92	<.0001	0.05	1.4224	2.5454	7.2710	4.1470	12.7483
1	Acquired	2.8410	0.3159	8.99	<.0001	0.05	2.2218	3.4603	17.1333	9.2237	31.8254
1	Pre-existing	2.8400	0.3184	8.92	<.0001	0.05	2.2159	3.4640	17.1152	9.1696	31.9459

Differences of Revised_Groups Least Squares Means

Revised_ Groups	*_Revised_ Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Pre-existing	0.001053	0.2963	0.00	0.9972	0.05	-0.5797	0.5818	1.0011	0.5600	1.7893

Site Least Squares Means

ANC1	*Site*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
3	1	0.4774	0.4621	1.03	0.3015	0.05	-0.4283	1.3831	1.6119	0.6516	3.9874
3	2	2.2087	0.3403	6.49	<.0001	0.05	1.5417	2.8757	9.1042	4.6727	17.7385
3	3	0.6871	0.2651	2.59	0.0095	0.05	0.1676	1.2066	1.9879	1.1825	3.3420
2	1	1.3374	0.4724	2.83	0.0046	0.05	0.4116	2.2632	3.8093	1.5093	9.6142
2	2	3.0687	0.3682	8.33	<.0001	0.05	2.3471	3.7903	21.5147	10.4555	44.2717
2	3	1.5471	0.2754	5.62	<.0001	0.05	1.0073	2.0869	4.6978	2.7381	8.0599
1	1	2.1935	0.4887	4.49	<.0001	0.05	1.2356	3.1514	8.9666	3.4406	23.3684
1	2	3.9248	0.3979	9.86	<.0001	0.05	3.1449	4.7048	50.6436	23.2167	110.47
1	3	2.4032	0.3041	7.90	<.0001	0.05	1.8071	2.9992	11.0581	6.0928	20.0699

Differences of Site Least Squares Means

Site	*_Site*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	2	-1.7313	0.5839	-2.96	0.0030	0.05	-2.8758	-0.5868	0.1771	0.05637	0.5561
1	3	-0.2097	0.5327	-0.39	0.6939	0.05	-1.2537	0.8344	0.8109	0.2854	2.3034
2	3	1.5216	0.3694	4.12	<.0001	0.05	0.7976	2.2457	4.5798	2.2202	9.4470

ANRQ_scoreRECORDED Least Squares Means

ANC1	*ANRQ_ scoreRECORDED*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
3	1.Yes	2.3371	0.3779	6.18	<.0001	0.05	1.5964	3.0779	10.3513	4.9350	21.7121
3	2.No	-0.08827	0.2349	-0.38	0.7071	0.05	-0.5486	0.3721	0.9155	0.5778	1.4507
2	1.Yes	3.1971	0.4023	7.95	<.0001	0.05	2.4087	3.9855	24.4617	11.1192	53.8145
2	2.No	0.7717	0.2439	3.16	0.0016	0.05	0.2938	1.2497	2.1635	1.3415	3.4893
1	1.Yes	4.0532	0.4291	9.45	<.0001	0.05	3.2122	4.8942	57.5805	24.8328	133.51
1	2.No	1.6278	0.2719	5.99	<.0001	0.05	1.0949	2.1607	5.0927	2.9888	8.6775

Differences of ANRQ_scoreRECORDED Least Squares Means

ANRQ_score RECORDED	*_ANRQ_Score RECORDED*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	2.No	2.4254	0.4489	5.40	<.0001	0.05	1.5455	3.3052	11.3065	4.6905	27.2542

Model 18 Final Multivariable Ordinal logistic regression of ANC2 versus Group, site and confounders

The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Multinomial
Link Function	Cumulative Logit
Dependent Variable	ANC2

Number of Observations Read	271
Number of Observations Used	64
Missing Values	207

Class Level Information

Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3
Highrisk1	2	1.Yes 2.No

Response Profile

Ordered Value	*ANC2*	*Total Frequency*
1	3	12
2	2	30
3	1	15
4	0	7

PROC GENMOD is modelling the probabilities of levels of ANC2 having LOWER Ordered Values in the response profile table.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*	*Highrisk1*
Prm1	Revised_Groups	Acquired		
Prm2	Revised_Groups	Pre-existing		
Prm3	Site		1	
Prm4	Site		2	
Prm5	Site		3	
Prm6	Highrisk1			1.Yes
Prm7	Highrisk1			2.No
Prm8	Babys_length_birth			
Prm9	ANRQ_score			

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-65.6960	
Full Log Likelihood		-65.6960	
AIC (smaller is better)		149.3919	
AICC (smaller is better)		152.7253	
BIC (smaller is better)		168.8219	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept1		1	4.6504	2.6541	-0.5515	9.8524	3.07	0.0797
Intercept2		1	7.5676	2.7838	2.1115	13.0238	7.39	0.0066
Intercept3		1	9.5519	2.8689	3.9290	15.1749	11.09	0.0009
Revised_Groups	Acquired	1	0.6688	0.5324	-0.3747	1.7123	1.58	0.2091
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	-0.7845	0.6738	-2.1051	0.5361	1.36	0.2443
Site	2	1	-1.3899	0.6625	-2.6884	-0.0914	4.40	0.0359
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Highrisk1	1.Yes	1	1.2366	0.5590	0.1411	2.3322	4.89	0.0269
Highrisk1	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Babys_length_birth		1	-0.1201	0.0544	-0.2268	-0.0134	4.87	0.0273
ANRQ_score		1	-0.0656	0.0205	-0.1058	-0.0255	10.26	0.0014
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	1.58	0.2091
Site	2	4.43	0.1092
Highrisk1	1	4.89	0.0269
Babys_length_birth	1	4.87	0.0273
ANRQ_score	1	10.26	0.0014

Contrast Estimate Results

	Mean			L'Beta						
Label	*Mean Estimate*	*Confidence Limits*		*L'Beta Estimate*	*Standard Error*	*Alpha*	*Confidence Limits*		*Chi-Square*	*Pr > ChiSq*
Babys_length_birth	0.4700	0.4435	0.4966	-0.1201	0.0544	0.05	-0.2268	-0.0134	4.87	0.0273
Exp(Babys_length_birth)				0.8868	0.0483	0.05	0.7971	0.9867		
ANRQ_score	0.4836	0.4736	0.4936	-0.0656	0.0205	0.05	-0.1058	-0.0255	10.26	0.0014
Exp(ANRQ_score)				0.9365	0.0192	0.05	0.8996	0.9748		

Revised_Groups Least Squares Means

ANC2	*Revised_ Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
3	Acquired	-1.8237	0.4440	-4.11	<.0001	0.05	-2.6940	-0.9534	0.1614	0.06761	0.3854
3	Pre-existing	-2.4925	0.5312	-4.69	<.0001	0.05	-3.5336	-1.4515	0.08270	0.02920	0.2342
2	Acquired	1.0934	0.4083	2.68	0.0074	0.05	0.2933	1.8936	2.9845	1.3408	6.6435
2	Pre-existing	0.4247	0.4546	0.93	0.3502	0.05	-0.4663	1.3156	1.5291	0.6273	3.7271
1	Acquired	3.0778	0.5692	5.41	<.0001	0.05	1.9622	4.1934	21.7098	7.1146	66.2464
1	Pre-existing	2.4090	0.5519	4.36	<.0001	0.05	1.3272	3.4907	11.1227	3.7706	32.8101

Differences of Revised_Groups Least Squares Means

Revised_ Groups	*_Revised_ Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Pre-existing	0.6688	0.5324	1.26	0.2091	0.05	-0.3747	1.7123	1.9519	0.6875	5.5415

Site Least Squares Means

ANC2	*Site*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
3	1	-2.2178	0.5451	-4.07	<.0001	0.05	-3.2861	-1.1495	0.1088	0.03740	0.3168
3	2	-2.8232	0.5552	-5.09	<.0001	0.05	-3.9114	-1.7351	0.05941	0.02001	0.1764
3	3	-1.4333	0.5590	-2.56	0.0103	0.05	-2.5289	-0.3377	0.2385	0.07975	0.7134
2	1	0.6994	0.4716	1.48	0.1380	0.05	-0.2249	1.6236	2.0125	0.7986	5.0713
2	2	0.09394	0.4226	0.22	0.8241	0.05	-0.7344	0.9223	1.0985	0.4798	2.5150
2	3	1.4839	0.5982	2.48	0.0131	0.05	0.3114	2.6563	4.4100	1.3654	14.2432
1	1	2.6837	0.6062	4.43	<.0001	0.05	1.4955	3.8719	14.6390	4.4614	48.0342
1	2	2.0783	0.5190	4.00	<.0001	0.05	1.0610	3.0956	7.9905	2.8891	22.0996
1	3	3.4682	0.7105	4.88	<.0001	0.05	2.0757	4.8607	32.0785	7.9698	129.12

Differences of Site Least Squares Means

Site	*_Site*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	2	0.6054	0.5842	1.04	0.3000	0.05	-0.5396	1.7504	1.8320	0.5830	5.7572
1	3	-0.7845	0.6738	-1.16	0.2443	0.05	-2.1051	0.5361	0.4563	0.1218	1.7094
2	3	-1.3899	0.6625	-2.10	0.0359	0.05	-2.6884	-0.09145	0.2491	0.06799	0.9126

Highrisk1 Least Squares Means

ANC2	*Highrisk1*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
3	1.Yes	-1.5398	0.3947	-3.90	<.0001	0.05	-2.3134	-0.7662	0.2144	0.09893	0.4648
3	2.No	-2.7764	0.5814	-4.78	<.0001	0.05	-3.9160	-1.6369	0.06226	0.01992	0.1946
2	1.Yes	1.3774	0.4037	3.41	0.0006	0.05	0.5861	2.1686	3.9645	1.7970	8.7460
2	2.No	0.1407	0.4742	0.30	0.7666	0.05	-0.7886	1.0701	1.1511	0.4545	2.9157
1	1.Yes	3.3617	0.5917	5.68	<.0001	0.05	2.2020	4.5213	28.8380	9.0434	91.9593
1	2.No	2.1251	0.5413	3.93	<.0001	0.05	1.0641	3.1860	8.3734	2.8982	24.1922

Differences of Highrisk1 Least Squares Means

Highrisk1	*_Highrisk1*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	2.No	1.2366	0.5590	2.21	0.0269	0.05	0.1411	2.3322	3.4440	1.1515	10.3003

Model 19 Final Multivariable Ordinal logistic regression of ANC3 versus Group, site and confounders

The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Multinomial
Link Function	Cumulative Logit
Dependent Variable	ANC3

Number of Observations Read	271
Number of Observations Used	232
Missing Values	39

Class Level Information

Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3
Highrisk1	2	1.Yes 2.No
Highrisk3	2	1.Yes 2.No

Response Profile

Ordered Value	*ANC3*	*Total Frequency*
1	3	23
2	2	86
3	1	87
4	0	36

PROC GENMOD is modelling the probabilities of levels of ANC3 having LOWER Ordered Values in the response profile table.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*	*Highrisk1*	*Highrisk3*
Prm1	Revised_Groups	Acquired			
Prm2	Revised_Groups	Pre-existing			
Prm3	Site		1		
Prm4	Site		2		
Prm5	Site		3		
Prm6	Highrisk1			1.Yes	
Prm7	Highrisk1			2.No	
Prm8	Highrisk3				1.Yes
Prm9	Highrisk3				2.No

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-283.5509	
Full Log Likelihood		-283.5509	
AIC (smaller is better)		583.1019	
AICC (smaller is better)		583.7476	
BIC (smaller is better)		610.6758	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept1		1	-3.4221	0.4828	-4.3683	-2.4760	50.25	<.0001
Intercept2		1	-1.2686	0.4361	-2.1234	-0.4138	8.46	0.0036
Intercept3		1	0.6327	0.4317	-0.2134	1.4789	2.15	0.1428
Revised_Groups	Acquired	1	0.1680	0.2652	-0.3518	0.6878	0.40	0.5265
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	0.0790	0.4687	-0.8396	0.9976	0.03	0.8661
Site	2	1	-0.2259	0.2646	-0.7445	0.2927	0.73	0.3932
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Highrisk1	1.Yes	1	0.5423	0.2625	0.0277	1.0569	4.27	0.0389
Highrisk1	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Highrisk3	1.Yes	1	0.9564	0.4113	0.1503	1.7625	5.41	0.0200
Highrisk3	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	0.40	0.5265
Site	2	0.90	0.6365
Highrisk1	1	4.27	0.0389
Highrisk3	1	5.41	0.0200

Revised_Groups Least Squares Means

ANC3	Revised_ Groups	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
3	Acquired	-2.5538	0.3243	-7.87	<.0001	0.05	-3.1894	-1.9182	0.07779	0.04120	0.1469
3	Pre-existing	-2.7218	0.3313	-8.22	<.0001	0.05	-3.3711	-2.0724	0.06576	0.03435	0.1259
2	Acquired	-0.4002	0.2694	-1.49	0.1375	0.05	-0.9283	0.1279	0.6702	0.3952	1.1364
2	Pre-existing	-0.5682	0.2727	-2.08	0.0372	0.05	-1.1027	-0.03362	0.5666	0.3320	0.9669
1	Acquired	1.5011	0.2877	5.22	<.0001	0.05	0.9373	2.0649	4.4866	2.5531	7.8847
1	Pre-existing	1.3331	0.2887	4.62	<.0001	0.05	0.7674	1.8989	3.7929	2.1541	6.6784

Differences of Revised_Groups Least Squares Means

Revised_ Groups	_Revised_ Groups	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
Acquired	Pre-existing	0.1680	0.2652	0.63	0.5265	0.05	-0.3518	0.6878	1.1829	0.7034	1.9893

Site Least Squares Means

ANC3	Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
3	1	-2.5098	0.4933	-5.09	<.0001	0.05	-3.4767	-1.5429	0.08128	0.03091	0.2138
3	2	-2.8147	0.3213	-8.76	<.0001	0.05	-3.4444	-2.1850	0.05992	0.03192	0.1125
3	3	-2.5888	0.3059	-8.46	<.0001	0.05	-3.1883	-1.9893	0.07511	0.04124	0.1368
2	1	-0.3562	0.4611	-0.77	0.4398	0.05	-1.2599	0.5474	0.7003	0.2837	1.7288
2	2	-0.6611	0.2554	-2.59	0.0096	0.05	-1.1618	-0.1605	0.5163	0.3129	0.8517

Site Least Squares Means

ANC3	Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
2	3	-0.4352	0.2458	-1.77	0.0766	0.05	-0.9169	0.04648	0.6471	0.3997	1.0476
1	1	1.5451	0.4731	3.27	0.0011	0.05	0.6179	2.4723	4.6884	1.8550	11.8499
1	2	1.2402	0.2678	4.63	<.0001	0.05	0.7154	1.7650	3.4562	2.0450	5.8415
1	3	1.4661	0.2671	5.49	<.0001	0.05	0.9425	1.9896	4.3322	2.5665	7.3128

Differences of Site Least Squares Means

Site	_Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	2	0.3049	0.4710	0.65	0.5174	0.05	-0.6182	1.2280	1.3565	0.5389	3.4145
1	3	0.07901	0.4687	0.17	0.8661	0.05	-0.8396	0.9976	1.0822	0.4319	2.7117
2	3	-0.2259	0.2646	-0.85	0.3932	0.05	-0.7445	0.2927	0.7978	0.4750	1.3400

Highrisk1 Least Squares Means

ANC3	Highrisk1	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
3	1.Yes	-2.3666	0.3171	-7.46	<.0001	0.05	-2.9882	-1.7450	0.09380	0.05038	0.1746
3	2.No	-2.9089	0.3371	-8.63	<.0001	0.05	-3.5697	-2.2482	0.05453	0.02816	0.1056
2	1.Yes	-0.2130	0.2661	-0.80	0.4233	0.05	-0.7345	0.3084	0.8081	0.4797	1.3613
2	2.No	-0.7553	0.2747	-2.75	0.0060	0.05	-1.2938	-0.2168	0.4699	0.2742	0.8051
1	1.Yes	1.6883	0.2921	5.78	<.0001	0.05	1.1157	2.2608	5.4101	3.0518	9.5909
1	2.No	1.1460	0.2829	4.05	<.0001	0.05	0.5915	1.7004	3.1455	1.8067	5.4764

Differences of Highrisk1 Least Squares Means

Highrisk1	_Highrisk1	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	0.5423	0.2625	2.07	0.0389	0.05	0.02774	1.0569	1.7200	1.0281	2.8773

Highrisk3 Least Squares Means

ANC3	Highrisk3	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
3	1.Yes	-2.1596	0.2558	-8.44	<.0001	0.05	-2.6610	-1.6581	0.1154	0.06988	0.1905
3	2.No	-3.1160	0.4460	-6.99	<.0001	0.05	-3.9901	-2.2419	0.04434	0.01850	0.1063
2	1.Yes	-0.00598	0.1886	-0.03	0.9747	0.05	-0.3757	0.3637	0.9940	0.6868	1.4387
2	2.No	-0.9624	0.4010	-2.40	0.0164	0.05	-1.7483	-0.1764	0.3820	0.1741	0.8382
1	1.Yes	1.8953	0.2330	8.13	<.0001	0.05	1.4387	2.3520	6.6547	4.2150	10.5065
1	2.No	0.9389	0.4015	2.34	0.0194	0.05	0.1520	1.7258	2.5572	1.1642	5.6171

Differences of Highrisk3 Least Squares Means

Highrisk3	_Highrisk3	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	0.9564	0.4113	2.33	0.0200	0.05	0.1503	1.7625	2.6023	1.1622	5.8269

Model 2 Final Multivariable Logistic regression of ANCQ versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	ANCQ

Number of Observations Read	271
Number of Observations Used	253
Number of Events	167
Number of Trials	253
Missing Values	18

Class Level Information		
Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3
EPPSD_scoreRECORDED	2	1.Yes 2.No

Response Profile		
Ordered Value	*ANCQ*	*Total Frequency*
1	1	167
2	0	86

PROC GENMOD is modelling the probability that ANCQ='1'.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*	*EPPSD_scoreRECORDED*
Prm1	Intercept			
Prm2	Revised_Groups	Acquired		
Prm3	Revised_Groups	Pre-existing		
Prm4	Site		1	
Prm5	Site		2	
Prm6	Site		3	
Prm7	EPPSD_scoreRECORDED			1.Yes
Prm8	EPPSD_scoreRECORDED			2.No
Prm9	Live_baby_weight			

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-91.7271	
Full Log Likelihood		-91.7271	
AIC (smaller is better)		195.4542	
AICC (smaller is better)		195.7957	
BIC (smaller is better)		216.6546	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	1.4071	0.8562	-0.2709	3.0852	2.70	0.1003
Revised_Groups	Acquired	1	-0.9397	0.3823	-1.6890	-0.1904	6.04	0.0140
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	0.9360	0.8065	-0.6448	2.5168	1.35	0.2458
Site	2	1	1.3011	0.3881	0.5404	2.0618	11.24	0.0008
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
EPPSD_scoreRECORDED	1.Yes	1	4.3183	0.7602	2.8283	5.8084	32.26	<.0001
EPPSD_scoreRECORDED	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Live_baby_weight		1	-0.0006	0.0003	-0.0011	-0.0001	5.64	0.0176
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	6.04	0.0140
Site	2	11.57	0.0031
EPPSD_scoreRECORDED	1	32.26	<.0001
Live_baby_weight	1	5.64	0.0176

Contrast Estimate Results

	Mean			L'Beta						
Label	*Mean Estimate*	*Confidence Limits*		*L'Beta Estimate*	*Standard Error*	*Alpha*	*Confidence Limits*		*Chi-Square*	*Pr > ChiSq*
Live_baby_weight	0.4998	0.4997	0.5000	-0.0006	0.0003	0.05	-0.0011	-0.0001	5.64	0.0176
Exp(Live_baby_weight)				0.9994	0.0003	0.05	0.9989	0.9999		

Revised_Groups Least Squares Means

Revised_Groups	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	1.4831	0.4304	3.45	0.0006	0.05	0.6396	2.3266	4.4066	1.8958	10.2429
Pre-existing	2.4228	0.4740	5.11	<.0001	0.05	1.4937	3.3519	11.2776	4.4538	28.5568

Differences of Revised_Groups Least Squares Means

Revised_ Groups	*_Revised _Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Pre-existing	-0.9397	0.3823	-2.46	0.0140	0.05	-1.6890	-0.1904	0.3907	0.1847	0.8266

Site Least Squares Means

Site	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	2.1433	0.7914	2.71	0.0068	0.05	0.5921	3.6944	8.5273	1.8078	40.2219
2	2.5084	0.4491	5.58	<.0001	0.05	1.6281	3.3887	12.2849	5.0940	29.6271
3	1.2072	0.4178	2.89	0.0039	0.05	0.3884	2.0260	3.3443	1.4747	7.5840

Differences of Site Least Squares Means

Site	_Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	2	-0.3651	0.8312	-0.44	0.6605	0.05	-1.9942	1.2640	0.6941	0.1361	3.5397
1	3	0.9360	0.8065	1.16	0.2458	0.05	-0.6448	2.5168	2.5498	0.5248	12.3892
2	3	1.3011	0.3881	3.35	0.0008	0.05	0.5404	2.0618	3.6734	1.7167	7.8604

EPPSD_scoreRECORDED Least Squares Means

EPPSD_ scoreRECORDED	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	4.1121	0.7351	5.59	<.0001	0.05	2.6714	5.5528	61.0765	14.4605	257.97
2.No	-0.2062	0.2924	-0.71	0.4807	0.05	-0.7793	0.3669	0.8137	0.4587	1.4432

Differences of EPPSD_scoreRECORDED Least Squares Means

EPPSD_ scoreRECORDED	_EPPSD_ scoreRECORDED	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	4.3183	0.7602	5.68	<.0001	0.05	2.8283	5.8084	75.0630	16.9163	333.08

Model 20 Final Multivariable Ordinal logistic regression of FetalRisk1_sum versus Group, site and confounders

The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Multinomial
Link Function	Cumulative Logit
Dependent Variable	FetalRisk1_sum

Number of Observations Read	271
Number of Observations Used	133
Missing Values	138

Class Level Information

Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3
Highrisk1	2	1.Yes 2.No
Highrisk7	2	1.Yes 2.No

Response Profile

Ordered Value	*FetalRisk1_sum*	*Total Frequency*
1	3	98
2	2	26
3	1	9

PROC GENMOD is modelling the probabilities of levels of FetalRisk1_sum having LOWER Ordered Values in the response profile table.

Parameter Information					
Parameter	*Effect*	*Revised_Groups*	*Site*	*Highrisk1*	*Highrisk7*
Prm1	Revised_Groups	Acquired			
Prm2	Revised_Groups	Pre-existing			
Prm3	Site		1		
Prm4	Site		2		
Prm5	Site		3		
Prm6	Highrisk1			1.Yes	
Prm7	Highrisk1			2.No	
Prm8	Highrisk7				1.Yes
Prm9	Highrisk7				2.No

Criteria For Assessing Goodness Of Fit			
Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-76.7630	
Full Log Likelihood		-76.7630	
AIC (smaller is better)		167.5260	
AICC (smaller is better)		168.4220	
BIC (smaller is better)		187.7584	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept1		1	-1.4178	0.4913	-2.3808	-0.4549	8.33	0.0039
Intercept2		1	0.6557	0.4916	-0.3077	1.6191	1.78	0.1822
Revised_Groups	Acquired	1	-0.0279	0.4523	-0.9144	0.8587	0.00	0.9509
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	0.8848	0.8506	-0.7824	2.5520	1.08	0.2983
Site	2	1	1.4718	0.5413	0.4108	2.5329	7.39	0.0066
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Highrisk1	1.Yes	1	1.4584	0.5089	0.4610	2.4558	8.21	0.0042
Highrisk1	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Highrisk7	1.Yes	1	1.3284	0.5231	0.3031	2.3537	6.45	0.0111
Highrisk7	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	0.00	0.9509
Site	2	7.78	0.0204
Highrisk1	1	8.21	0.0042
Highrisk7	1	6.45	0.0111

Revised_Groups Least Squares Means

FetalRisk1_sum	*Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
3	Acquired	0.7332	0.4267	1.72	0.0857	0.05	-0.1030	1.5695	2.0818	0.9021	4.8041
3	Pre-existing	0.7611	0.3856	1.97	0.0484	0.05	0.005414	1.5168	2.1406	1.0054	4.5575
2	Acquired	2.8068	0.5307	5.29	<.0001	0.05	1.7666	3.8469	16.5564	5.8510	46.8493
2	Pre-existing	2.8346	0.4980	5.69	<.0001	0.05	1.8587	3.8106	17.0241	6.4151	45.1772

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Pre-existing	-0.02786	0.4523	-0.06	0.9509	0.05	-0.9144	0.8587	0.9725	0.4008	2.3600

Site Least Squares Means

FetalRisk1_sum	*Site*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
3	1	0.8464	0.8200	1.03	0.3020	0.05	-0.7607	2.4536	2.3313	0.4673	11.6296
3	2	1.4335	0.4635	3.09	0.0020	0.05	0.5250	2.3419	4.1932	1.6905	10.4012
3	3	-0.03838	0.2918	-0.13	0.8953	0.05	-0.6102	0.5334	0.9623	0.5432	1.7048
2	1	2.9199	0.8796	3.32	0.0009	0.05	1.1960	4.6438	18.5403	3.3070	103.94
2	2	3.5070	0.5890	5.95	<.0001	0.05	2.3526	4.6614	33.3481	10.5127	105.79
2	3	2.0352	0.3875	5.25	<.0001	0.05	1.2757	2.7946	7.6534	3.5811	16.3567

Differences of Site Least Squares Means

Site	_Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	2	-0.5871	0.9341	-0.63	0.5297	0.05	-2.4179	1.2438	0.5560	0.08911	3.4687
1	3	0.8848	0.8506	1.04	0.2983	0.05	-0.7824	2.5520	2.4225	0.4573	12.8331
2	3	1.4718	0.5413	2.72	0.0066	0.05	0.4108	2.5329	4.3573	1.5081	12.5894

Highrisk1 Least Squares Means

FetalRisk1_sum	Highrisk1	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
3	1.Yes	1.4764	0.4265	3.46	0.0005	0.05	0.6404	2.3123	4.3770	1.8973	10.0977
3	2.No	0.01797	0.4195	0.04	0.9658	0.05	-0.8042	0.8401	1.0181	0.4475	2.3167
2	1.Yes	3.5499	0.5632	6.30	<.0001	0.05	2.4460	4.6538	34.8095	11.5417	104.99
2	2.No	2.0915	0.4894	4.27	<.0001	0.05	1.1322	3.0508	8.0971	3.1026	21.1319

Differences of Highrisk1 Least Squares Means

Highrisk1	_Highrisk1	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	1.4584	0.5089	2.87	0.0042	0.05	0.4610	2.4558	4.2990	1.5857	11.6554

Highrisk7 Least Squares Means

FetalRisk1_sum	Highrisk7	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
3	1.Yes	1.4114	0.3608	3.91	<.0001	0.05	0.7042	2.1185	4.1015	2.0222	8.3188
3	2.No	0.08297	0.4848	0.17	0.8641	0.05	-0.8673	1.0332	1.0865	0.4201	2.8100
2	1.Yes	3.4849	0.5083	6.86	<.0001	0.05	2.4886	4.4812	32.6190	12.0442	88.3413
2	2.No	2.1565	0.5529	3.90	<.0001	0.05	1.0728	3.2402	8.6409	2.9235	25.5398

Differences of Highrisk7 Least Squares Means

Highrisk7	_Highrisk7	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	1.3284	0.5231	2.54	0.0111	0.05	0.3031	2.3537	3.7750	1.3540	10.5245

Model 21 Final Multivariable Logistic regression of FetalRisk2_sum versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	FetalRisk2_sum

Number of Observations Read	271
Number of Observations Used	85
Number of Events	21
Number of Trials	85
Missing Values	186

Class Level Information

Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3

Response Profile

Ordered Value	*FetalRisk2_sum*	*Total Frequency*
1	2	21
2	1	64

PROC GENMOD is modelling the probability that FetalRisk2_sum='2'.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*
Prm1	Intercept		
Prm2	Revised_Groups	Acquired	
Prm3	Revised_Groups	Pre-exising	
Prm4	Site		1
Prm5	Site		2
Prm6	Site		3

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-47.2074	
Full Log Likelihood		-47.2074	
AIC (smaller is better)		102.4147	
AICC (smaller is better)		102.9147	
BIC (smaller is better)		112.1853	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	-1.0323	0.4130	-1.8417	-0.2228	6.25	0.0124
Revised_Groups	Acquired	1	-0.3416	0.5440	-1.4078	0.7247	0.39	0.5301
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	-0.0551	0.7581	-1.5409	1.4308	0.01	0.9421
Site	2	1	0.1561	0.5562	-0.9340	1.2462	0.08	0.7790
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	0.39	0.5301
Site	2	0.11	0.9488

Revised_Groups Least Squares Means

Revised_Groups	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	-1.3402	0.4328	-3.10	0.0020	0.05	-2.1885	-0.4918	0.2618	0.1121	0.6115
Pre-existing	-0.9986	0.3591	-2.78	0.0054	0.05	-1.7024	-0.2948	0.3684	0.1822	0.7447

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Pre-existing	-0.3416	0.5440	-0.63	0.5301	0.05	-1.4078	0.7247	0.7106	0.2447	2.0641

Site Least Squares Means

Site	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	-1.2581	0.6551	-1.92	0.0548	0.05	-2.5420	0.02577	0.2842	0.07871	1.0261
2	-1.0470	0.4390	-2.38	0.0171	0.05	-1.9074	-0.1866	0.3510	0.1485	0.8298
3	-1.2031	0.3709	-3.24	0.0012	0.05	-1.9300	-0.4761	0.3003	0.1451	0.6212

Differences of Site Least Squares Means

Site	*_Site*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	2	-0.2112	0.7979	-0.26	0.7913	0.05	-1.7750	1.3527	0.8096	0.1695	3.8679
1	3	-0.05506	0.7581	-0.07	0.9421	0.05	-1.5409	1.4308	0.9464	0.2142	4.1821
2	3	0.1561	0.5562	0.28	0.7790	0.05	-0.9340	1.2462	1.1689	0.3930	3.4769

Model 3 Final Multivariable Logistic regression of Plannedcare1 versus Group, site and confounders

The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	Plannedcare1

Number of Observations Read	271
Number of Observations Used	197
Number of Events	159
Number of Trials	197
Missing Values	74

Class Level Information		
Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3
Highrisk1	2	1.Yes 2.No
Highrisk3	2	1.Yes 2.No

Response Profile		
Ordered Value	*Plannedcare1*	*Total Frequency*
1	Yes	159
2	No	38

PROC GENMOD is modelling the probability that Plannedcare1='Yes'.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*	*Highrisk1*	*Highrisk3*
Prm1	Intercept				
Prm2	Revised_Groups	Acquired			
Prm3	Revised_Groups	Pre-existing			
Prm4	Site		1		
Prm5	Site		2		
Prm6	Site		3		
Prm7	Highrisk1			1.Yes	
Prm8	Highrisk1			2.No	
Prm9	Highrisk3				1.Yes
Prm10	Highrisk3				2.No

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-78.6963	
Full Log Likelihood		-78.6963	
AIC (smaller is better)		169.3927	
AICC (smaller is better)		169.8348	
BIC (smaller is better)		189.0919	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	-1.0108	0.5867	-2.1607	0.1391	2.97	0.0849
Revised_Groups	Acquired	1	-0.6683	0.4353	-1.5214	0.1849	2.36	0.1247
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	24.6415	84674.54	-165934	165983.7	0.00	0.9998
Site	2	1	0.4068	0.4206	-0.4176	1.2312	0.94	0.3335
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Highrisk1	1.Yes	1	0.9403	0.4312	0.0951	1.7854	4.75	0.0292
Highrisk1	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Highrisk3	1.Yes	1	2.2374	0.5631	1.1337	3.3411	15.79	<.0001
Highrisk3	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	2.36	0.1247
Site	2	0.94	0.6265
Highrisk1	1	4.75	0.0292
Highrisk3	1	15.79	<.0001

Revised_Groups Least Squares Means

Revised_Groups	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
Acquired	8.2592	28225	0.00	0.9998	0.05	-55311	55328	3862.96	0	Infty
Pre-existing	8.9274	28225	0.00	0.9997	0.05	-55311	55329	7535.97	0	Infty

Differences of Revised_Groups Least Squares Means

Revised_Groups	_Revised_Groups	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
Acquired	Pre-existing	-0.6683	0.4353	-1.54	0.1247	0.05	-1.5214	0.1849	0.5126	0.2184	1.2031

Site Least Squares Means

Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	24.8854	84675	0.00	0.9998	0.05	-165934	165984	6.421E10	0	Infty
2	0.6507	0.3572	1.82	0.0685	0.05	-0.04944	1.3508	1.9169	0.9518	3.8606
3	0.2439	0.3471	0.70	0.4823	0.05	-0.4364	0.9242	1.2762	0.6463	2.5199

Differences of Site Least Squares Means

Site	_Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	2	24.2347	84675	0.00	0.9998	0.05	-165935	165983	3.35E10	0	Infty
1	3	24.6415	84675	0.00	0.9998	0.05	-165934	165984	5.031E10	0	Infty
2	3	0.4068	0.4206	0.97	0.3335	0.05	-0.4176	1.2312	1.5020	0.6586	3.4254

Highrisk1 Least Squares Means

Highrisk1	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	9.0635	28225	0.00	0.9997	0.05	-55311	55329	8633.96	0	Infty
2.No	8.1232	28225	0.00	0.9998	0.05	-55312	55328	3371.70	0	Infty

Differences of Highrisk1 Least Squares Means

Highrisk1	_Highrisk1	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	0.9403	0.4312	2.18	0.0292	0.05	0.09513	1.7854	2.5607	1.0998	5.9622

Highrisk3 Least Squares Means

Highrisk3	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	9.7120	28225	0.00	0.9997	0.05	-55310	55329	16515	0	Infty
2.No	7.4746	28225	0.00	0.9998	0.05	-55312	55327	1762.74	0	Infty

Differences of Highrisk3 Least Squares Means

Highrisk3	_Highrisk3	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	2.2374	0.5631	3.97	<.0001	0.05	1.1337	3.3411	9.3688	3.1070	28.2506

Model 4 Final Multivariable Logistic regression of Plannedcare2 versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	Plannedcare2

Number of Observations Read	271
Number of Observations Used	81
Number of Events	14
Number of Trials	81
Missing Values	190

Class Level Information		
Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3
Highrisk1	2	1.Yes 2.No

Response Profile		
Ordered Value	*Plannedcare2*	*Total Frequency*
1	Yes	14
2	No	67

PROC GENMOD is modelling the probability that Plannedcare2='Yes'.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*	*Highrisk1*
Prm1	Intercept			
Prm2	Revised_Groups	Acquired		
Prm3	Revised_Groups	Pre-existing		
Prm4	Site		1	
Prm5	Site		2	
Prm6	Site		3	
Prm7	Highrisk1			1.Yes
Prm8	Highrisk1			2.No
Prm9	Parity			

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-31.0770	
Full Log Likelihood		-31.0770	
AIC (smaller is better)		74.1541	
AICC (smaller is better)		75.2892	
BIC (smaller is better)		88.5208	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	-3.5006	0.9487	-5.3601	-1.6411	13.61	0.0002
Revised_Groups	Acquired	1	0.4062	0.6989	-0.9636	1.7759	0.34	0.5611
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	-0.0460	1.4826	-2.9519	2.8599	0.00	0.9753
Site	2	1	-0.2160	0.6851	-1.5587	1.1267	0.10	0.7525
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Highrisk1	1.Yes	1	1.6620	0.8449	0.0061	3.3179	3.87	0.0492
Highrisk1	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Parity		1	0.4665	0.2296	0.0165	0.9164	4.13	0.0421
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	0.34	0.5611
Site	2	0.10	0.9506
Highrisk1	1	3.87	0.0492
Parity	1	4.13	0.0421

Contrast Estimate Results

	Mean			L'Beta						
Label	*Mean Estimate*	*Confidence Limits*		*L'Beta Estimate*	*Standard Error*	*Alpha*	*Confidence Limits*		*Chi-Square*	*Pr > ChiSq*
Parity	0.6145	0.5041	0.7143	0.4665	0.2296	0.05	0.0165	0.9164	4.13	0.0421
Exp(Parity)				1.5944	0.3660	0.05	1.0167	2.5002		

Revised_Groups Least Squares Means

Revised_Groups	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	-1.7000	0.8393	-2.03	0.0428	0.05	-3.3450	-0.05504	0.1827	0.03526	0.9464
Pre-existing	-2.1062	0.6224	-3.38	0.0007	0.05	-3.3261	-0.8863	0.1217	0.03593	0.4122

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Pre-existing	0.4062	0.6989	0.58	0.5611	0.05	-0.9636	1.7759	1.5011	0.3815	5.9058

Site Least Squares Means

Site	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	-1.8618	1.5021	-1.24	0.2152	0.05	-4.8058	1.0823	0.1554	0.008182	2.9513
2	-2.0318	0.5389	-3.77	0.0002	0.05	-3.0879	-0.9756	0.1311	0.04560	0.3770
3	-1.8158	0.5864	-3.10	0.0020	0.05	-2.9650	-0.6665	0.1627	0.05156	0.5135

Differences of Site Least Squares Means

Site	_Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	2	0.1700	1.4798	0.11	0.9085	0.05	-2.7304	3.0704	1.1853	0.06520	21.5501
1	3	-0.04599	1.4826	-0.03	0.9753	0.05	-2.9519	2.8599	0.9550	0.05224	17.4594
2	3	-0.2160	0.6851	-0.32	0.7525	0.05	-1.5587	1.1267	0.8057	0.2104	3.0854

Highrisk1 Least Squares Means

Highrisk1	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	-1.0721	0.5614	-1.91	0.0562	0.05	-2.1725	0.02830	0.3423	0.1139	1.0287
2.No	-2.7341	0.9430	-2.90	0.0037	0.05	-4.5823	-0.8859	0.06495	0.01023	0.4124

Differences of Highrisk1 Least Squares Means

Highrisk1	_Highrisk1	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	1.6620	0.8449	1.97	0.0492	0.05	0.006088	3.3179	5.2697	1.0061	27.6012

Model 4 Final Multivariable Logistic regression of Plannedcare2 versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	Plannedcare3x

Number of Observations Read	271
Number of Observations Used	198
Number of Events	98
Number of Trials	198
Missing Values	73

Class Level Information		
Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3
Highrisk5_sum	3	1 2 3

Response Profile		
Ordered Value	*Plannedcare3x*	*Total Frequency*
1	Vaginal	98
2	Caesarean	100

PROC GENMOD is modelling the probability that Plannedcare3x='Vaginal'.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*	*Highrisk5_sum*
Prm1	Intercept			
Prm2	Revised_Groups	Acquired		
Prm3	Revised_Groups	Pre-existing		
Prm4	Site		1	
Prm5	Site		2	
Prm6	Site		3	
Prm7	Highrisk5_sum			1
Prm8	Highrisk5_sum			2
Prm9	Highrisk5_sum			3
Prm10	team_sum			

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-112.2955	
Full Log Likelihood		-112.2955	
AIC (smaller is better)		238.5910	
AICC (smaller is better)		239.1805	
BIC (smaller is better)		261.6089	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	1.8388	0.7264	0.4150	3.2626	6.41	0.0114
Revised_Groups	Acquired	1	-0.1068	0.3393	-0.7719	0.5583	0.10	0.7530
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	-0.1021	0.6074	-1.2926	1.0885	0.03	0.8666
Site	2	1	-0.5026	0.3583	-1.2049	0.1997	1.97	0.1607
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Highrisk5_sum	1	1	2.0169	0.8080	0.4333	3.6005	6.23	0.0126
Highrisk5_sum	2	1	0.9905	0.3867	0.2326	1.7484	6.56	0.0104
Highrisk5_sum	3	0	0.0000	0.0000	0.0000	0.0000	.	.
team_sum		1	-0.5816	0.1695	-0.9139	-0.2493	11.77	0.0006
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	0.10	0.7530
Site	2	2.04	0.3601
Highrisk5_sum	2	11.04	0.0040
team_sum	1	11.77	0.0006

Contrast Estimate Results

	Mean			L'Beta						
Label	*Mean Estimate*	*Confidence Limits*		*L'Beta Estimate*	*Standard Error*	*Alpha*	*Confidence Limits*		*Chi-Square*	*Pr > ChiSq*
team_sum	0.3586	0.2862	0.4380	-0.5816	0.1695	0.05	-0.9139	-0.2493	11.77	0.0006
Exp(team_sum)				0.5590	0.0948	0.05	0.4009	0.7793		

Revised_Groups Least Squares Means

Revised_Groups	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	0.5765	0.3683	1.57	0.1175	0.05	-0.1453	1.2984	1.7798	0.8647	3.6634
Pre-existing	0.6833	0.3471	1.97	0.0490	0.05	0.003121	1.3635	1.9805	1.0031	3.9100

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Pre-existing	-0.1068	0.3393	-0.31	0.7530	0.05	-0.7719	0.5583	0.8987	0.4621	1.7477

Site Least Squares Means

Site	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	0.7294	0.5909	1.23	0.2171	0.05	-0.4288	1.8876	2.0739	0.6513	6.6035
2	0.3289	0.3469	0.95	0.3431	0.05	-0.3511	1.0088	1.3894	0.7039	2.7424
3	0.8315	0.3397	2.45	0.0144	0.05	0.1656	1.4973	2.2967	1.1801	4.4698

Differences of Site Least Squares Means

Site	_Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	2	0.4005	0.6035	0.66	0.5069	0.05	-0.7823	1.5833	1.4926	0.4574	4.8712
1	3	-0.1021	0.6074	-0.17	0.8666	0.05	-1.2926	1.0885	0.9030	0.2746	2.9697
2	3	-0.5026	0.3583	-1.40	0.1607	0.05	-1.2049	0.1997	0.6050	0.2997	1.2210

Highrisk5_sum Least Squares Means

Highrisk5_sum	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	1.6443	0.7825	2.10	0.0356	0.05	0.1107	3.1780	5.1776	1.1171	23.9976
2	0.6180	0.3558	1.74	0.0824	0.05	-0.07940	1.3153	1.8552	0.9237	3.7261
3	-0.3725	0.2466	-1.51	0.1308	0.05	-0.8558	0.1107	0.6890	0.4249	1.1171

Differences of Highrisk5_sum Least Squares Means

Highrisk5_sum	_Highrisk5_sum	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	2	1.0264	0.8386	1.22	0.2210	0.05	-0.6173	2.6700	2.7909	0.5394	14.4405
1	3	2.0169	0.8080	2.50	0.0126	0.05	0.4333	3.6005	7.5149	1.5423	36.6173
2	3	0.9905	0.3867	2.56	0.0104	0.05	0.2326	1.7484	2.6926	1.2619	5.7455

Model 6 Final Multivariable Logistic regression of compromise_3Respiratory versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	compromise_3Respiratory

Number of Observations Read	271
Number of Observations Used	174
Number of Events	169
Number of Trials	174
Missing Values	97

Class Level Information		
Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3

Response Profile		
Ordered Value	*compromise_3Respiratory*	*Total Frequency*
1	1	169
2	0	5

PROC GENMOD is modelling the probability that compromise_3Respiratory='1'.

Parameter Information			
Parameter	*Effect*	*Revised_Groups*	*Site*
Prm1	Intercept		
Prm2	Revised_Groups	Acquired	
Prm3	Revised_Groups	Pre-existing	
Prm4	Site		1
Prm5	Site		2
Prm6	Site		3
Prm7	Apgar_5min		

Criteria For Assessing Goodness Of Fit			
Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-16.9642	
Full Log Likelihood		-16.9642	
AIC (smaller is better)		43.9284	
AICC (smaller is better)		44.2855	
BIC (smaller is better)		59.7237	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	27.8560	9.8780	8.4955	47.2164	7.95	0.0048
Revised_Groups	Acquired	1	-1.9629	1.1649	-4.2462	0.3203	2.84	0.0920
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	22.9556	241272.5	-472863	472908.4	0.00	0.9999
Site	2	1	-0.5702	1.0486	-2.6255	1.4851	0.30	0.5866
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Apgar_5min		1	-2.4747	1.0059	-4.4463	-0.5031	6.05	0.0139
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	2.84	0.0920
Site	2	0.30	0.8626
Apgar_5min	1	6.05	0.0139

Contrast Estimate Results

	Mean			L'Beta						
Label	*Mean Estimate*	*Confidence Limits*		*L'Beta Estimate*	*Standard Error*	*Alpha*	*Confidence Limits*		*Chi-Square*	*Pr > ChiSq*
Apgar_5min	0.0777	0.0116	0.3768	-2.4747	1.0059	0.05	-4.4463	-0.5031	6.05	0.0139
Exp(Apgar_5min)				0.0842	0.0847	0.05	0.0117	0.6046		

Revised_Groups Least Squares Means

Revised_Groups	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	11.6656	80424	0.00	0.9999	0.05	-157617	157640	116496	0	Infty
Pre-existing	13.6285	80424	0.00	0.9999	0.05	-157615	157642	829462	0	Infty

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Pre-existing	-1.9629	1.1649	-1.68	0.0920	0.05	-4.2462	0.3203	0.1404	0.01432	1.3776

Site Least Squares Means

Site	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	28.1409	241273	0.00	0.9999	0.05	-472857	472914	1.665E12	0	Infty
2	4.6151	1.0195	4.53	<.0001	0.05	2.6168	6.6133	101.00	13.6920	744.96
3	5.1853	1.1844	4.38	<.0001	0.05	2.8639	7.5066	178.62	17.5295	1820.06

Differences of Site Least Squares Means

Site	*_Site*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	2	23.5258	241273	0.00	0.9999	0.05	-472862	472909	1.649E10	0	Infty
1	3	22.9556	241273	0.00	0.9999	0.05	-472863	472908	9.3219E9	0	Infty
2	3	-0.5702	1.0486	-0.54	0.5866	0.05	-2.6255	1.4851	0.5654	0.07241	4.4154

Model 22 Final Multivariable Ordinal logistic regression of compromise_sum versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Multinomial
Link Function	Cumulative Logit
Dependent Variable	compromise_sum

Number of Observations Read	271
Number of Observations Used	176
Missing Values	95

Class Level Information		
Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3

Response Profile		
Ordered Value	*compromise_sum*	*Total Frequency*
1	4	163
2	3	9
3	2	1
4	1	3

PROC GENMOD is modelling the probabilities of levels of compromise_sum having LOWER Ordered Values in the response profile table.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*
Prm1	Revised_Groups	Acquired	
Prm2	Revised_Groups	Pre-existing	
Prm3	Site		1
Prm4	Site		2
Prm5	Site		3

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-55.5528	
Full Log Likelihood		-55.5528	
AIC (smaller is better)		123.1055	
AICC (smaller is better)		123.6026	
BIC (smaller is better)		142.1284	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept1		1	2.3725	0.5279	1.3378	3.4071	20.20	<.0001
Intercept2		1	3.6108	0.6705	2.2966	4.9250	29.00	<.0001
Intercept3		1	3.9052	0.7310	2.4725	5.3379	28.54	<.0001
Revised_Groups	Acquired	1	-0.1148	0.6012	-1.2932	1.0636	0.04	0.8486
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	23.3251	107108.8	-209906	209952.7	0.00	0.9998
Site	2	1	0.2615	0.6004	-0.9152	1.4383	0.19	0.6631
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	0.04	0.8486
Site	2	0.19	0.9095

Revised_Groups Least Squares Means

compromise_sum	*Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
4	Acquired	10.1199	35703	0.00	0.9998	0.05	-69966	69987	24832	0	Infty
4	Pre-existing	10.2347	35703	0.00	0.9998	0.05	-69966	69987	27853	0	Infty
3	Acquired	11.3582	35703	0.00	0.9997	0.05	-69965	69988	85669	0	Infty
3	Pre-existing	11.4730	35703	0.00	0.9997	0.05	-69965	69988	96090	0	Infty
2	Acquired	11.6526	35703	0.00	0.9997	0.05	-69965	69988	114991	0	Infty
2	Pre-existing	11.7674	35703	0.00	0.9997	0.05	-69965	69988	128979	0	Infty

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Pre-existing	-0.1148	0.6012	-0.19	0.8486	0.05	-1.2932	1.0636	0.8915	0.2744	2.8967

Site Least Squares Means

compromise_sum	Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
4	1	25.6402	107109	0.00	0.9998	0.05	-209904	209955	1.366E11	0	Infty
4	2	2.5766	0.4369	5.90	<.0001	0.05	1.7203	3.4330	13.1527	5.5861	30.9687
4	3	2.3151	0.3991	5.80	<.0001	0.05	1.5328	3.0974	10.1257	4.6311	22.1395
3	1	26.8785	107109	0.00	0.9998	0.05	-209902	209956	4.712E11	0	Infty
3	2	3.8150	0.6048	6.31	<.0001	0.05	2.6297	5.0003	45.3760	13.8694	148.46
3	3	3.5534	0.5746	6.18	<.0001	0.05	2.4273	4.6796	34.9331	11.3280	107.73
2	1	27.1729	107109	0.00	0.9998	0.05	-209902	209957	6.325E11	0	Infty
2	2	4.1093	0.6698	6.14	<.0001	0.05	2.7966	5.4221	60.9070	16.3885	226.36
2	3	3.8478	0.6431	5.98	<.0001	0.05	2.5873	5.1083	46.8898	13.2941	165.39

Differences of Site Least Squares Means

Site	_Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	2	23.0635	107109	0.00	0.9998	0.05	-209906	209952	1.038E10	0	Infty
1	3	23.3251	107109	0.00	0.9998	0.05	-209906	209953	1.349E10	0	Infty
2	3	0.2615	0.6004	0.44	0.6631	0.05	-0.9152	1.4383	1.2989	0.4004	4.2136

Model 7 Final Multivariable Logistic regression of compromise_4Changing versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	compromise_4Changing

Number of Observations Read	271
Number of Observations Used	176
Number of Events	165
Number of Trials	176
Missing Values	95

Class Level Information		
Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3

Response Profile		
Ordered Value	*compromise_4Changing*	*Total Frequency*
1	1	165
2	0	11

PROC GENMOD is modelling the probability that compromise_4Changing='1'.

Parameter Information			
Parameter	*Effect*	*Revised_Groups*	*Site*
Prm1	Intercept		
Prm2	Revised_Groups	Acquired	
Prm3	Revised_Groups	Pre-existing	
Prm4	Site		1
Prm5	Site		2
Prm6	Site		3

Criteria For Assessing Goodness Of Fit			
Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-40.2079	
Full Log Likelihood		-40.2079	
AIC (smaller is better)		88.4159	
AICC (smaller is better)		88.6498	
BIC (smaller is better)		101.0978	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	2.4757	0.5654	1.3676	3.5838	19.17	<.0001
Revised_Groups	Acquired	1	-0.0083	0.6503	-1.2828	1.2662	0.00	0.9898
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	23.8931	153307.3	-300453	300500.7	0.00	0.9999
Site	2	1	0.3242	0.6495	-0.9487	1.5971	0.25	0.6177
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	0.00	0.9898
Site	2	0.25	0.8829

Revised_Groups Least Squares Means

Revised_Groups	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	10.5398	51102	0.00	0.9998	0.05	-100148	100169	37789	0	Infty
Pre-existing	10.5481	51102	0.00	0.9998	0.05	-100148	100169	38106	0	Infty

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Pre-existing	-0.00833	0.6503	-0.01	0.9898	0.05	-1.2828	1.2662	0.9917	0.2773	3.5472

Site Least Squares Means

Site	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	26.3646	153307	0.00	0.9999	0.05	-300450	300503	2.818E11	0	Infty
2	2.7957	0.4766	5.87	<.0001	0.05	1.8616	3.7298	16.3742	6.4339	41.6722
3	2.4715	0.4278	5.78	<.0001	0.05	1.6330	3.3100	11.8405	5.1195	27.3851

Differences of Site Least Squares Means

Site	*_Site*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	2	23.5689	153307	0.00	0.9999	0.05	-300453	300500	1.721E10	0	Infty
1	3	23.8931	153307	0.00	0.9999	0.05	-300453	300501	2.38E10	0	Infty
2	3	0.3242	0.6495	0.50	0.6177	0.05	-0.9487	1.5971	1.3829	0.3872	4.9387

Model 8 Final Multivariable Logistic regression of thromboembolism_sum versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	thromboembolism_sum

Number of Observations Read	271
Number of Observations Used	118
Number of Events	59
Number of Trials	118
Missing Values	153

Class Level Information		
Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3
team_5Anaesthetist	2	0 1

Response Profile		
Ordered Value	*thromboembolism_sum*	*Total Frequency*
1	2	59
2	1	59

PROC GENMOD is modelling the probability that thromboembolism_sum='2'.

Parameter Information				
Parameter	*Effect*	*Revised_Groups*	*Site*	*team_5Anaesthetist*
Prm1	Intercept			
Prm2	Revised_Groups	Acquired		
Prm3	Revised_Groups	Pre-existing		
Prm4	Site		1	
Prm5	Site		2	
Prm6	Site		3	
Prm7	team_5Anaesthetist			0
Prm8	team_5Anaesthetist			1

Criteria For Assessing Goodness Of Fit			
Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-72.4554	
Full Log Likelihood		-72.4554	
AIC (smaller is better)		154.9108	
AICC (smaller is better)		155.4465	
BIC (smaller is better)		168.7642	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	0.0526	0.4407	-0.8112	0.9165	0.01	0.9049
Revised_Groups	Acquired	1	-0.5391	0.4189	-1.3602	0.2820	1.66	0.1981
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	-0.9850	0.8823	-2.7142	0.7443	1.25	0.2642
Site	2	1	0.7058	0.4506	-0.1774	1.5889	2.45	0.1173
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
team_5Anaesthetist	0	1	-1.6782	0.8128	-3.2713	-0.0851	4.26	0.0390
team_5Anaesthetist	1	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	1.66	0.1981
Site	2	5.45	0.0656
team_5Anaesthetist	1	4.26	0.0390

Revised_Groups Least Squares Means

Revised_Groups	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	-1.4186	0.5026	-2.82	0.0048	0.05	-2.4037	-0.4336	0.2420	0.09039	0.6482
Pre-existing	-0.8795	0.5141	-1.71	0.0871	0.05	-1.8871	0.1281	0.4150	0.1515	1.1366

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Pre-existing	-0.5391	0.4189	-1.29	0.1981	0.05	-1.3602	0.2820	0.5833	0.2566	1.3257

Site Least Squares Means

Site	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	-2.0410	0.8768	-2.33	0.0199	0.05	-3.7594	-0.3226	0.1299	0.02330	0.7243
2	-0.3502	0.4430	-0.79	0.4292	0.05	-1.2185	0.5180	0.7045	0.2957	1.6787
3	-1.0560	0.4955	-2.13	0.0331	0.05	-2.0271	-0.08493	0.3478	0.1317	0.9186

Differences of Site Least Squares Means

Site	*_Site*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	2	-1.6908	0.8478	-1.99	0.0461	0.05	-3.3525	-0.02902	0.1844	0.03500	0.9714
1	3	-0.9850	0.8823	-1.12	0.2642	0.05	-2.7142	0.7443	0.3734	0.06626	2.1049
2	3	0.7058	0.4506	1.57	0.1173	0.05	-0.1774	1.5889	2.0254	0.8374	4.8986

team_5Anaesthetist Least Squares Means

team_5Anaesthetist	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
0	-1.9882	0.8141	-2.44	0.0146	0.05	-3.5838	-0.3925	0.1369	0.02777	0.6753
1	-0.3100	0.3109	-1.00	0.3187	0.05	-0.9193	0.2993	0.7335	0.3988	1.3489

Differences of team_5Anaesthetist Least Squares Means

team_5Anaesthetist	_team_5Anaesthetist	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
0	1	-1.6782	0.8128	-2.06	0.0390	0.05	-3.2713	-0.08512	0.1867	0.03796	0.9184

Model 9 Final Multivariable Logistic regression of thromboembolism_1stockings versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	thromboembolism_1stockings

Number of Observations Read	271
Number of Observations Used	115
Number of Events	74
Number of Trials	115
Missing Values	156

Class Level Information		
Class	*Levels*	*Values*
Revised_Groups	2	Acquired Pre-existing
Site	3	1 2 3

Response Profile		
Ordered Value	*thromboembolism_1stockings*	*Total Frequency*
1	1	74
2	0	41

PROC GENMOD is modelling the probability that thromboembolism_1stockings='1'.

Parameter Information			
Parameter	*Effect*	*Revised_Groups*	*Site*
Prm1	Intercept		
Prm2	Revised_Groups	Acquired	
Prm3	Revised_Groups	Pre-existing	
Prm4	Site		1
Prm5	Site		2
Prm6	Site		3
Prm7	Live_baby_weight		

Criteria For Assessing Goodness Of Fit			
Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-68.6009	
Full Log Likelihood		-68.6009	
AIC (smaller is better)		147.2019	
AICC (smaller is better)		147.7523	
BIC (smaller is better)		160.9265	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	2.8485	0.9684	0.9504	4.7466	8.65	0.0033
Revised_Groups	Acquired	1	-0.2226	0.4387	-1.0825	0.6372	0.26	0.6118
Revised_Groups	Preexisting	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	-1.3663	0.7259	-2.7891	0.0564	3.54	0.0598
Site	2	1	0.0658	0.4763	-0.8678	0.9995	0.02	0.8901
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Live_baby_weight		1	-0.0007	0.0003	-0.0012	-0.0001	5.68	0.0171
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	0.26	0.6118
Site	2	4.42	0.1098
Live_baby_weight	1	5.68	0.0171

Contrast Estimate Results

	Mean			L'Beta						
Label	*Mean Estimate*	*Confidence Limits*		*L'Beta Estimate*	*Standard Error*	*Alpha*	*Confidence Limits*		*Chi-Square*	*Pr > ChiSq*
Live_baby_weight per 1kg increase	0.3393	0.2290	0.4704	-0.6662	0.2795	0.05	-1.2140	-0.1184	5.68	0.0171
Exp(Live_baby_weight per 1kg increase)				0.5137	0.1436	0.05	0.2970	0.8883		

Revised_Groups Least Squares Means

Revised_Groups	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	0.1993	0.3317	0.60	0.5479	0.05	-0.4508	0.8495	1.2206	0.6371	2.3384
Preexiseant	0.4219	0.3489	1.21	0.2265	0.05	-0.2619	1.1058	1.5249	0.7696	3.0215

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Preexisting	-0.2226	0.4387	-0.51	0.6118	0.05	-1.0825	0.6372	0.8004	0.3388	1.8912

Site Least Squares Means

Site	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	-0.6222	0.6281	-0.99	0.3219	0.05	-1.8533	0.6089	0.5368	0.1567	1.8384
2	0.8100	0.2864	2.83	0.0047	0.05	0.2487	1.3713	2.2479	1.2823	3.9404
3	0.7441	0.3748	1.99	0.0471	0.05	0.009592	1.4787	2.1046	1.0096	4.3871

Differences of Site Least Squares Means

Site	*_Site*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	2	-1.4322	0.6981	-2.05	0.0402	0.05	-2.8004	-0.06393	0.2388	0.06078	0.9381
1	3	-1.3663	0.7259	-1.88	0.0598	0.05	-2.7891	0.05639	0.2550	0.06148	1.0580
2	3	0.06585	0.4763	0.14	0.8901	0.05	-0.8678	0.9995	1.0681	0.4199	2.7168

Model 10 Final Multivariable Logistic regression of thromboembolism_2heparin versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	thromboembolism_2heparin

Number of Observations Read	271
Number of Observations Used	75
Number of Events	67
Number of Trials	75
Missing Values	196

Class Level Information		
Class	*Levels*	*Values*
Revised_Groups	2	Acquired Preexisting
Site	3	1 2 3
Cardiac_consultation	2	1.Yes 2.No

Response Profile		
Ordered Value	*thromboembolism_2heparin*	*Total Frequency*
1	1	67
2	0	8

PROC GENMOD is modelling the probability that thromboembolism_2heparin='1'.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*	*Cardiac_consultation*
Prm1	Intercept			
Prm2	Revised_Groups	Acquired		
Prm3	Revised_Groups	Preexisting		
Prm4	Site		1	
Prm5	Site		2	
Prm6	Site		3	
Prm7	Cardiac_consultation			1.Yes
Prm8	Cardiac_consultation			2.No
Prm9	Parity			

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-13.9821	
Full Log Likelihood		-13.9821	
AIC (smaller is better)		39.9642	
AICC (smaller is better)		41.1995	
BIC (smaller is better)		53.8692	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	2.8790	1.8895	-0.8243	6.5824	2.32	0.1276
Revised_Groups	Acquired	1	-3.4841	1.5998	-6.6198	-0.3485	4.74	0.0294
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	26.7358	295367.2	-578882	578935.9	0.00	0.9999
Site	2	1	-0.5984	1.1270	-2.8074	1.6105	0.28	0.5954
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Cardiac_consultation	1.Yes	1	4.1792	1.4730	1.2922	7.0662	8.05	0.0046
Cardiac_consultation	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Parity		1	-0.8501	0.3437	-1.5236	-0.1765	6.12	0.0134
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	4.74	0.0294
Site	2	0.28	0.8685
Cardiac_consultation	1	8.05	0.0046
Parity	1	6.12	0.0134

Contrast Estimate Results

	Mean			L'Beta					
Label	*Mean Estimate*	*Confidence Limits*		*L'Beta Estimate*	*Standard Error*	*Alpha*	*Confidence Limits*		*Chi-Square*	*Pr > ChiSq*
Parity	0.2994	0.1789	0.4560	-0.8501	0.3437	0.05	-1.5236	-0.1765	6.12	0.0134
Exp(Parity)				0.4274	0.1469	0.05	0.2179	0.8382		

Revised_Groups Least Squares Means

Revised_Groups	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	8.8709	98456	0.00	0.9999	0.05	-192961	192979	7121.39	0	Infty
Pre-existing	12.3550	98456	0.00	0.9999	0.05	-192957	192982	232118	0	Infty

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Pre-existing	-3.4841	1.5998	-2.18	0.0294	0.05	-6.6198	-0.3485	0.03068	0.001334	0.7057

Site Least Squares Means

Site	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	28.6363	295367	0.00	0.9999	0.05	-578880	578938	2.733E12	0	Infty
2	1.3020	0.7441	1.75	0.0802	0.05	-0.1564	2.7605	3.6768	0.8552	15.8075
3	1.9005	1.0369	1.83	0.0668	0.05	-0.1317	3.9327	6.6891	0.8766	51.0435

Differences of Site Least Squares Means

Site	*_Site*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	2	27.3342	295367	0.00	0.9999	0.05	-578882	578936	7.432E11	0	Infty
1	3	26.7358	295367	0.00	0.9999	0.05	-578882	578936	4.085E11	0	Infty
2	3	-0.5984	1.1270	-0.53	0.5954	0.05	-2.8074	1.6105	0.5497	0.06036	5.0055

Cardiac_consultation Least Squares Means

Cardiac_consultationx	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	12.7025	98456	0.00	0.9999	0.05	-192957	192982	328582	0	Infty
2.No	8.5233	98456	0.00	0.9999	0.05	-192961	192978	5030.72	0	Infty

Differences of Cardiac_consultation Least Squares Means

Cardiac_consultationx	*_Cardiac_consultationx*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	2.No	4.1792	1.4730	2.84	0.0046	0.05	1.2922	7.0662	65.3152	3.6409	1171.72

Model 23 Final Multivariable Ordinal logistic regression of Pain_sum versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Multinomial
Link Function	Cumulative Logit
Dependent Variable	Pain_sum

Number of Observations Read	271
Number of Observations Used	204
Missing Values	67

Class Level Information

Class	*Levels*	*Values*
Revised_Groups	2	Acquired Preexisting
Site	3	1 2 3
team_1Obstetricianx	2	1.Yes 2.No
team_5Anaesthetistx	2	1.Yes 2.No

Response Profile

Ordered Value	*Pain_sum*	*Total Frequency*
1	4	28
2	3	40
3	2	73
4	1	63

PROC GENMOD is modelling the probabilities of levels of Pain_sum having LOWER Ordered Values in the response profile table.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*	*team_1Obstetricianx*	*team_5Anaesthetistx*
Prm1	Revised_Groups	Acquired			
Prm2	Revised_Groups	Preexisting			
Prm3	Site		1		
Prm4	Site		2		
Prm5	Site		3		
Prm6	team_1Obstetricianx			1.Yes	
Prm7	team_1Obstetricianx			2.No	
Prm8	team_5Anaesthetistx				1.Yes
Prm9	team_5Anaesthetistx				2.No
Prm10	Live_baby_weight				

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-241.6578	
Full Log Likelihood		-241.6578	
AIC (smaller is better)		501.3155	
AICC (smaller is better)		502.2433	
BIC (smaller is better)		531.1786	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept1		1	-0.5695	0.7391	-2.0181	0.8792	0.59	0.4410
Intercept2		1	0.7420	0.7447	-0.7177	2.2016	0.99	0.3191
Intercept3		1	2.5696	0.7662	1.0679	4.0713	11.25	0.0008
Revised_Groups	Acquired	1	-0.9690	0.2879	-1.5333	-0.4047	11.33	0.0008
Revised_Groups	Preexistingt	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	-0.6022	0.4734	-1.5299	0.3256	1.62	0.2033
Site	2	1	-0.7536	0.3078	-1.3569	-0.1503	5.99	0.0144
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
team_1Obstetricianx	1.Yes	1	1.0321	0.3595	0.3274	1.7367	8.24	0.0041
team_1Obstetricianx	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
team_5Anaesthetistx	1.Yes	1	1.0374	0.4439	0.1674	1.9073	5.46	0.0194
team_5Anaesthetistx	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Live_baby_weight		1	-0.0008	0.0002	-0.0012	-0.0004	17.66	<.0001
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	11.33	0.0008
Site	2	6.36	0.0416
team_1Obstetricianx	1	8.24	0.0041
team_5Anaesthetistx	1	5.46	0.0194
Live_baby_weight	1	17.66	<.0001

Contrast Estimate Results

	Mean			L'Beta						
Label	*Mean Estimate*	*Confidence Limits*		*L'Beta Estimate*	*Standard Error*	*Alpha*	*Confidence Limits*		*Chi-Square*	*Pr > ChiSq*
Live_baby_weight per 1kg increase	0.3132	0.2403	0.3968	-0.7850	0.1868	0.05	-1.1511	-0.4188	17.66	<.0001
Exp(Live_baby_weight per 1kg increase)				0.4561	0.0852	0.05	0.3163	0.6578		

Revised_Groups Least Squares Means

Pain_sum	*Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
4	Acquired	-3.3519	0.3641	-9.21	<.0001	0.05	-4.0655	-2.6383	0.03502	0.01715	0.07148
4	Pre-existing	-2.3829	0.3130	-7.61	<.0001	0.05	-2.9964	-1.7695	0.09228	0.04997	0.1704
3	Acquired	-2.0405	0.3173	-6.43	<.0001	0.05	-2.6624	-1.4186	0.1300	0.06978	0.2421
3	Pre-existing	-1.0715	0.2787	-3.85	0.0001	0.05	-1.6177	-0.5253	0.3425	0.1984	0.5914
2	Acquired	-0.2129	0.2833	-0.75	0.4524	0.05	-0.7681	0.3424	0.8083	0.4639	1.4083
2	Preexisting	0.7561	0.2792	2.71	0.0068	0.05	0.2089	1.3034	2.1300	1.2323	3.6818

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Preexisting	-0.9690	0.2879	-3.37	0.0008	0.05	-1.5333	-0.4047	0.3795	0.2158	0.6672

Site Least Squares Means

Pain_sum	Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
4	1	-3.0177	0.4962	-6.08	<.0001	0.05	-3.9902	-2.0451	0.04892	0.01850	0.1294
4	2	-3.1691	0.3520	-9.00	<.0001	0.05	-3.8591	-2.4792	0.04204	0.02109	0.08381
4	3	-2.4155	0.3139	-7.70	<.0001	0.05	-3.0307	-1.8003	0.08932	0.04828	0.1653
3	1	-1.7062	0.4689	-3.64	0.0003	0.05	-2.6252	-0.7872	0.1815	0.07242	0.4551
3	2	-1.8577	0.3058	-6.08	<.0001	0.05	-2.4569	-1.2584	0.1560	0.08570	0.2841
3	3	-1.1041	0.2777	-3.98	<.0001	0.05	-1.6483	-0.5599	0.3315	0.1924	0.5713
2	1	0.1214	0.4565	0.27	0.7903	0.05	-0.7734	1.0162	1.1291	0.4614	2.7626
2	2	-0.03006	0.2772	-0.11	0.9137	0.05	-0.5733	0.5132	0.9704	0.5636	1.6707
2	3	0.7235	0.2739	2.64	0.0082	0.05	0.1868	1.2603	2.0617	1.2054	3.5265

Differences of Site Least Squares Means

Site	_Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	2	0.1514	0.4862	0.31	0.7554	0.05	-0.8015	1.1044	1.1635	0.4486	3.0175
1	3	-0.6022	0.4734	-1.27	0.2033	0.05	-1.5299	0.3256	0.5476	0.2166	1.3849
2	3	-0.7536	0.3078	-2.45	0.0144	0.05	-1.3569	-0.1503	0.4707	0.2575	0.8604

team_1Obstetricianx Least Squares Means

Pain_sum	*team_1Obstetricianx*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
4	1.Yes	-2.3514	0.3370	-6.98	<.0001	0.05	-3.0120	-1.6908	0.09524	0.04919	0.1844
4	2.No	-3.3835	0.3743	-9.04	<.0001	0.05	-4.1171	-2.6498	0.03393	0.01629	0.07066
3	1.Yes	-1.0400	0.3010	-3.46	0.0006	0.05	-1.6299	-0.4500	0.3535	0.1959	0.6376
3	2.No	-2.0720	0.3331	-6.22	<.0001	0.05	-2.7248	-1.4192	0.1259	0.06556	0.2419
2	1.Yes	0.7877	0.2978	2.65	0.0082	0.05	0.2040	1.3713	2.1982	1.2263	3.9405
2	2.No	-0.2444	0.3045	-0.80	0.4222	0.05	-0.8413	0.3525	0.7832	0.4312	1.4226

Differences of team_1Obstetricianx Least Squares Means

team_1Obstetricianx	*_team_1Obstetricianx*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	2.No	1.0321	0.3595	2.87	0.0041	0.05	0.3274	1.7367	2.8068	1.3873	5.6786

team_5Anaesthetistx Least Squares Means

Pain_sum	*team_5Anaesthetistx*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
4	1.Yes	-2.3487	0.2738	-8.58	<.0001	0.05	-2.8855	-1.8120	0.09549	0.05583	0.1633
4	2.No	-3.3861	0.4611	-7.34	<.0001	0.05	-4.2898	-2.4824	0.03384	0.01371	0.08354
3	1.Yes	-1.0373	0.2250	-4.61	<.0001	0.05	-1.4784	-0.5963	0.3544	0.2280	0.5509
3	2.No	-2.0747	0.4298	-4.83	<.0001	0.05	-2.9172	-1.2322	0.1256	0.05409	0.2917
2	1.Yes	0.7903	0.2247	3.52	0.0004	0.05	0.3499	1.2307	2.2041	1.4190	3.4236
2	2.No	-0.2471	0.4060	-0.61	0.5428	0.05	-1.0427	0.5486	0.7811	0.3525	1.7309

Differences of team_5Anaesthetistx Least Squares Means

team_5Anaesthetistx	*_team_5Anaesthetistx*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	2.No	1.0374	0.4439	2.34	0.0194	0.05	0.1674	1.9073	2.8218	1.1822	6.7350

Model 11 Final Multivariable Logistic regression of Pain_1Anaesthetic versus Group, site and confounders

The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	Pain_1Anaesthetic

Number of Observations Read	271
Number of Observations Used	193
Number of Events	91
Number of Trials	193
Missing Values	78

Class Level Information

Class	*Levels*	*Values*
Revised_Groups	2	Acquired Preexisting
Site	3	1 2 3
Highrisk1	2	1.Yes 2.No
team_5Anaesthetistx	2	1.Yes 2.No

Response Profile

Ordered Value	*Pain_1Anaesthetic*	*Total Frequency*
1	1	91
2	0	102

PROC GENMOD is modelling the probability that Pain_1Anaesthetic='1'.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*	*Highrisk1*	*team_5Anaesthetistx*
Prm1	Intercept				
Prm2	Revised_Groups	Acquired			
Prm3	Revised_Groups	Preexisting			
Prm4	Site		1		
Prm5	Site		2		
Prm6	Site		3		
Prm7	Highrisk1			1.Yes	
Prm8	Highrisk1			2.No	
Prm9	team_5Anaesthetistx				1.Yes
Prm10	team_5Anaesthetistx				2.No
Prm11	Live_baby_weight				

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-114.2735	
Full Log Likelihood		-114.2735	
AIC (smaller is better)		242.5470	
AICC (smaller is better)		243.1524	
BIC (smaller is better)		265.3859	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	1.2085	0.9792	-0.7107	3.1277	1.52	0.2171
Revised_Groups	Acquired	1	-0.9199	0.3484	-1.6028	-0.2370	6.97	0.0083
Revised_Groups	Preexisting	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	-0.4199	0.5836	-1.5636	0.7239	0.52	0.4718
Site	2	1	-0.6504	0.3493	-1.3350	0.0342	3.47	0.0626
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Highrisk1	1.Yes	1	0.9424	0.3616	0.2337	1.6511	6.79	0.0092
Highrisk1	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
team_5Anaesthetistx	1.Yes	1	1.0283	0.4907	0.0664	1.9901	4.39	0.0361
team_5Anaesthetistx	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Live_baby_weight		1	-0.0007	0.0002	-0.0012	-0.0002	8.20	0.0042
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	6.97	0.0083
Site	2	3.49	0.1745
Highrisk1	1	6.79	0.0092

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
team_5Anaesthetistx	1	4.39	0.0361
Live_baby_weight	1	8.20	0.0042

Contrast Estimate Results

	Mean			*L'Beta*					
Label	*Mean Estimate*	*Confidence Limits*		*L'Beta Estimate*	*Standard Error*	*Alpha*	*Confidence Limits*		*Chi-Square*	*Pr > ChiSq*
Live_baby_weight per 1kg increase	0.3328	0.2365	0.4454	-0.6956	0.2429	0.05	-1.1718	-0.2195	8.20	0.0042
Exp(Live_baby_weight per 1kg increase)				0.4988	0.1212	0.05	0.3098	0.8030		

Revised_Groups Least Squares Means

Revised_Groups	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	-1.1995	0.3600	-3.33	0.0009	0.05	-1.9051	-0.4939	0.3013	0.1488	0.6103
Preexisting	-0.2796	0.3062	-0.91	0.3612	0.05	-0.8798	0.3206	0.7561	0.4149	1.3779

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Preexisting	-0.9199	0.3484	-2.64	0.0083	0.05	-1.6028	-0.2370	0.3986	0.2013	0.7890

Site Least Squares Means

Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	-0.8027	0.5595	-1.43	0.1514	0.05	-1.8992	0.2938	0.4481	0.1497	1.3416
2	-1.0332	0.3176	-3.25	0.0011	0.05	-1.6556	-0.4108	0.3559	0.1910	0.6631
3	-0.3828	0.3115	-1.23	0.2191	0.05	-0.9934	0.2278	0.6819	0.3703	1.2558

Differences of Site Least Squares Means

Site	_Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	2	0.2305	0.5814	0.40	0.6917	0.05	-0.9090	1.3700	1.2592	0.4029	3.9354
1	3	-0.4199	0.5836	-0.72	0.4718	0.05	-1.5636	0.7239	0.6571	0.2094	2.0624
2	3	-0.6504	0.3493	-1.86	0.0626	0.05	-1.3350	0.03424	0.5218	0.2632	1.0348

Highrisk1 Least Squares Means

Highrisk1	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	-0.2684	0.2977	-0.90	0.3674	0.05	-0.8519	0.3152	0.7646	0.4266	1.3705
2.No	-1.2108	0.3734	-3.24	0.0012	0.05	-1.9426	-0.4789	0.2980	0.1433	0.6195

Differences of Highrisk1 Least Squares Means

Highrisk1	_Highrisk1	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	0.9424	0.3616	2.61	0.0092	0.05	0.2337	1.6511	2.5661	1.2633	5.2127

team_5Anaesthetistx Least Squares Means

team_5Anaesthetistx	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	-0.2254	0.2368	-0.95	0.3411	0.05	-0.6896	0.2387	0.7982	0.5018	1.2696
2.No	-1.2537	0.4765	-2.63	0.0085	0.05	-2.1876	-0.3198	0.2854	0.1122	0.7263

Differences of team_5Anaesthetistx Least Squares Means

team_5Anaesthetistx	*_team_5Anaesthetistx*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	2.No	1.0283	0.4907	2.10	0.0361	0.05	0.06645	1.9901	2.7962	1.0687	7.3161

Model 12 Final Multivariable Logistic regression of Pain_2Epidural versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	Pain_2Epidural

Number of Observations Read	271
Number of Observations Used	203
Number of Events	157
Number of Trials	203
Missing Values	68

Class Level Information		
Class	*Levels*	*Values*
Revised_Groups	2	Acquired Preexisting
Site	3	1 2 3
team_5Anaesthetistx	2	1.Yes 2.No

Response Profile		
Ordered Value	*Pain_2Epidural*	*Total Frequency*
1	1	157
2	0	46

PROC GENMOD is modelling the probability that Pain_2Epidural='1'.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*	*team_5Anaesthetistx*
Prm1	Intercept			
Prm2	Revised_Groups	Acquired		
Prm3	Revised_Groups	Preexisting		
Prm4	Site		1	
Prm5	Site		2	
Prm6	Site		3	
Prm7	team_5Anaesthetistx			1.Yes
Prm8	team_5Anaesthetistx			2.No
Prm9	Apgar_1min			

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-91.6808	
Full Log Likelihood		-91.6808	
AIC (smaller is better)		195.3615	
AICC (smaller is better)		195.7901	
BIC (smaller is better)		215.2408	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	-2.2675	0.9241	-4.0788	-0.4563	6.02	0.0141
Revised_Groups	Acquired	1	-0.7592	0.3896	-1.5228	0.0045	3.80	0.0514
Revised_Groups	Preexisting	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	0.1179	0.6831	-1.2209	1.4567	0.03	0.8630
Site	2	1	-0.3128	0.4152	-1.1266	0.5011	0.57	0.4513
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
team_5Anaesthetistx	1.Yes	1	1.9225	0.4410	1.0582	2.7869	19.00	<.0001
team_5Anaesthetistx	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Apgar_1min		1	0.3244	0.0875	0.1530	0.4959	13.75	0.0002
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	3.80	0.0514
Site	2	0.74	0.6897
team_5Anaesthetistx	1	19.00	<.0001
Apgar_1min	1	13.75	0.0002

Contrast Estimate Results

	Mean			L'Beta						
Label	*Mean Estimate*	*Confidence Limits*		*L'Beta Estimate*	*Standard Error*	*Alpha*	*Confidence Limits*		*Chi-Square*	*Pr > ChiSq*
Apgar_1min	0.5804	0.5382	0.6215	0.3244	0.0875	0.05	0.1530	0.4959	13.75	0.0002
Exp(Apgar_1min)				1.3832	0.1210	0.05	1.1653	1.6419		

Revised_Groups Least Squares Means

Revised_Groups	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	0.4393	0.3140	1.40	0.1617	0.05	-0.1760	1.0547	1.5517	0.8386	2.8711
Preexisting	1.1985	0.3349	3.58	0.0003	0.05	0.5422	1.8548	3.3151	1.7198	6.3905

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Pre-existing	-0.7592	0.3896	-1.95	0.0514	0.05	-1.5228	0.004458	0.4681	0.2181	1.0045

Site Least Squares Means

Site	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	1.0018	0.6221	1.61	0.1073	0.05	-0.2175	2.2210	2.7230	0.8045	9.2170
2	0.5711	0.2964	1.93	0.0540	0.05	-0.00981	1.1520	1.7702	0.9902	3.1646
3	0.8839	0.3105	2.85	0.0044	0.05	0.2754	1.4924	2.4203	1.3171	4.4476

Differences of Site Least Squares Means

Site	_Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	2	0.4306	0.6842	0.63	0.5291	0.05	-0.9103	1.7716	1.5382	0.4024	5.8801
1	3	0.1179	0.6831	0.17	0.8630	0.05	-1.2209	1.4567	1.1251	0.2950	4.2917
2	3	-0.3128	0.4152	-0.75	0.4513	0.05	-1.1266	0.5011	0.7314	0.3241	1.6505

team_5Anaesthetistx Least Squares Means

team_5Anaesthetistx	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	1.7802	0.2821	6.31	<.0001	0.05	1.2273	2.3331	5.9310	3.4119	10.3098
2.No	-0.1424	0.3905	-0.36	0.7154	0.05	-0.9077	0.6230	0.8673	0.4035	1.8645

Differences of team_5Anaesthetistx Least Squares Means

team_5Anaesthetistx	_team_5Anaesthetistx	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	1.9225	0.4410	4.36	<.0001	0.05	1.0582	2.7869	6.8383	2.8811	16.2310

Model 13 Final Multivariable Logistic regression of Pain_3Combined versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	Pain_3Combined

Number of Observations Read	271
Number of Observations Used	192
Number of Events	70
Number of Trials	192
Missing Values	79

Class Level Information		
Class	*Levels*	*Values*
Revised_Groups	2	Acquired Preexisting
Site	3	1 2 3
Highrisk3	2	1.Yes 2.No
Highrisk9_4Nox	2	1.Yes 2.No
team_1Obstetricianx	2	1.Yes 2.No
team_4Physicianx	2	1.Yes 2.No
team_5Anaesthetistx	2	1.Yes 2.No

Response Profile		
Ordered Value	*Pain_3Combined*	*Total Frequency*
1	1	70
2	0	122

PROC GENMOD is modelling the probability that Pain_3Combined='1'.

Parameter Information								
Parameter	*Effect*	*Revised_Groups*	*Site*	*Highrisk3*	*Highrisk9_4Nox*	*team_1Obstetricianx*	*team_4Physicianx*	*team_5Anaesthetistx*
Prm1	Intercept							
Prm2	Revised_Groups	Acquired						
Prm3	Revised_Groups	Preexisting						
Prm4	Site		1					
Prm5	Site		2					
Prm6	Site		3					
Prm7	Highrisk3			1.Yes				
Prm8	Highrisk3			2.No				
Prm9	Highrisk9_4Nox				1.Yes			
Prm10	Highrisk9_4Nox				2.No			
Prm11	team_1Obstetricianx					1.Yes		
Prm12	team_1Obstetricianx					2.No		
Prm13	team_4Physicianx						1.Yes	
Prm14	team_4Physicianx						2.No	
Prm15	team_5Anaesthetistx							1.Yes
Prm16	team_5Anaesthetistx							2.No

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-97.4691	
Full Log Likelihood		-97.4691	
AIC (smaller is better)		212.9381	
AICC (smaller is better)		213.9271	
BIC (smaller is better)		242.2556	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	-7.7783	1.6731	-11.0575	-4.4991	21.61	<.0001
Revised_Groups	Acquired	1	0.3455	0.3760	-0.3914	1.0825	0.84	0.3581
Revised_Groups	Preexisting	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	-1.3970	0.8613	-3.0852	0.2912	2.63	0.1048
Site	2	1	0.0834	0.4199	-0.7396	0.9064	0.04	0.8425
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Highrisk3	1.Yes	1	2.2568	1.0912	0.1180	4.3955	4.28	0.0386
Highrisk3	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Highrisk9_4Nox	1.Yes	1	1.3559	0.6099	0.1606	2.5513	4.94	0.0262
Highrisk9_4Nox	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
team_1Obstetricianx	1.Yes	1	1.2921	0.6265	0.0643	2.5200	4.25	0.0392
team_1Obstetricianx	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
team_4Physicianx	1.Yes	1	0.7859	0.3876	0.0263	1.5456	4.11	0.0426
team_4Physicianx	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
team_5Anaesthetistx	1.Yes	1	2.4502	1.0689	0.3552	4.5452	5.25	0.0219
team_5Anaesthetistx	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	0.84	0.3581
Site	2	3.18	0.2040
Highrisk3	1	4.28	0.0386
Highrisk9_4Nox	1	4.94	0.0262
team_1Obstetricianx	1	4.25	0.0392
team_4Physicianx	1	4.11	0.0426
team_5Anaesthetistx	1	5.25	0.0219

Revised_Groups Least Squares Means

Revised_Groups	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	-3.8002	0.8736	-4.35	<.0001	0.05	-5.5124	-2.0880	0.02237	0.004037	0.1239
Preexisting	-4.1457	0.8727	-4.75	<.0001	0.05	-5.8562	-2.4352	0.01583	0.002862	0.08758

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Pre-existing	0.3455	0.3760	0.92	0.3581	0.05	-0.3914	1.0825	1.4128	0.6761	2.9520

Site Least Squares Means

Site	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	-4.9321	1.1553	-4.27	<.0001	0.05	-7.1965	-2.6678	0.007211	0.000749	0.06941
2	-3.4516	0.8558	-4.03	<.0001	0.05	-5.1290	-1.7743	0.03169	0.005923	0.1696
3	-3.5351	0.8069	-4.38	<.0001	0.05	-5.1165	-1.9536	0.02916	0.005997	0.1418

Differences of Site Least Squares Means

Site	*_Site*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	2	-1.4805	0.8324	-1.78	0.0753	0.05	-3.1119	0.1510	0.2275	0.04451	1.1630
1	3	-1.3970	0.8613	-1.62	0.1048	0.05	-3.0852	0.2912	0.2473	0.04572	1.3380
2	3	0.08342	0.4199	0.20	0.8425	0.05	-0.7396	0.9064	1.0870	0.4773	2.4755

Highrisk3 Least Squares Means

Highrisk3	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	-2.8445	0.6687	-4.25	<.0001	0.05	-4.1551	-1.5340	0.05816	0.01568	0.2157
2.No	-5.1013	1.2658	-4.03	<.0001	0.05	-7.5823	-2.6203	0.006089	0.000509	0.07278

Differences of Highrisk3 Least Squares Means

Highrisk3	_Highrisk3	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	2.2568	1.0912	2.07	0.0386	0.05	0.1180	4.3955	9.5524	1.1253	81.0881

Highrisk9_4Nox Least Squares Means

Highrisk9_4Nox	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	-3.2950	0.8051	-4.09	<.0001	0.05	-4.8728	-1.7171	0.03707	0.007652	0.1796
2.No	-4.6509	0.9960	-4.67	<.0001	0.05	-6.6030	-2.6988	0.009553	0.001356	0.06728

Differences of Highrisk9_4Nox Least Squares Means

Highrisk9_4Nox	_Highrisk9_4Nox	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	1.3559	0.6099	2.22	0.0262	0.05	0.1606	2.5513	3.8804	1.1742	12.8236

team_1Obstetricianx Least Squares Means

team_1Obstetricianx	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	-3.3269	0.8436	-3.94	<.0001	0.05	-4.9804	-1.6734	0.03590	0.006871	0.1876
2.No	-4.6190	0.9688	-4.77	<.0001	0.05	-6.5178	-2.7202	0.009863	0.001477	0.06586

Differences of team_1Obstetricianx Least Squares Means

team_1Obstetricianx	_team_1Obstetricianx	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	1.2921	0.6265	2.06	0.0392	0.05	0.06427	2.5200	3.6405	1.0664	12.4283

team_4Physicianx Least Squares Means

team_4Physicianx	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	-3.5800	0.8777	-4.08	<.0001	0.05	-5.3003	-1.8597	0.02788	0.004990	0.1557
2.No	-4.3659	0.8711	-5.01	<.0001	0.05	-6.0732	-2.6586	0.01270	0.002304	0.07005

Differences of team_4Physicianx Least Squares Means

team_4Physicianx	_team_4Physicianx	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	0.7859	0.3876	2.03	0.0426	0.05	0.02628	1.5456	2.1944	1.0266	4.6906

team_5Anaesthetistx Least Squares Means

team_5Anaesthetistx	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	-2.7479	0.7033	-3.91	<.0001	0.05	-4.1263	-1.3695	0.06406	0.01614	0.2542
2.No	-5.1980	1.2372	-4.20	<.0001	0.05	-7.6230	-2.7731	0.005527	0.000489	0.06247

Differences of team_5Anaesthetistx Least Squares Means

team_5Anaesthetistx	*_team_5Anaesthetistx*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	2.No	2.4502	1.0689	2.29	0.0219	0.05	0.3552	4.5452	11.5902	1.4264	94.1748

Model 14 Final Multivariable Logistic regression of Pain_4Other versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	Pain_4Other

Number of Observations Read	271
Number of Observations Used	194
Number of Events	113
Number of Trials	194
Missing Values	77

Class Level Information		
Class	*Levels*	*Values*
Revised_Groups	2	Acquired Preexisting
Site	3	1 2 3
Highrisk1	2	1.Yes 2.No

Response Profile		
Ordered Value	*Pain_4Other*	*Total Frequency*
1	1	113
2	0	81

PROC GENMOD is modelling the probability that Pain_4Other='1'.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*	*Highrisk1*
Prm1	Intercept			
Prm2	Revised_Groups	Acquired		
Prm3	Revised_Groups	Pre-existing		
Prm4	Site		1	
Prm5	Site		2	
Prm6	Site		3	
Prm7	Highrisk1			1.Yes
Prm8	Highrisk1			2.No
Prm9	Live_baby_weight			

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-122.4862	
Full Log Likelihood		-122.4862	
AIC (smaller is better)		256.9725	
AICC (smaller is better)		257.4216	
BIC (smaller is better)		276.5796	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	1.9477	0.8536	0.2747	3.6208	5.21	0.0225
Revised_Groups	Acquired	1	-0.6735	0.3234	-1.3073	-0.0397	4.34	0.0373
Revised_Groups	Preexisting	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	-0.3252	0.5539	-1.4108	0.7604	0.34	0.5571
Site	2	1	-0.2343	0.3310	-0.8830	0.4144	0.50	0.4791
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Highrisk1	1.Yes	1	0.7068	0.3357	0.0489	1.3647	4.43	0.0352
Highrisk1	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Live_baby_weight		1	-0.0005	0.0002	-0.0010	-0.0001	5.25	0.0219
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	4.34	0.0373
Site	2	0.65	0.7209
Highrisk1	1	4.43	0.0352
Live_baby_weight	1	5.25	0.0219

Contrast Estimate Results

	Mean			L'Beta						
Label	*Mean Estimate*	*Confidence Limits*		*L'Beta Estimate*	*Standard Error*	*Alpha*	*Confidence Limits*		*Chi-Square*	*Pr > ChiSq*
Live_baby_weight per 1kg increase	0.3700	0.2714	0.4808	-0.5321	0.2322	0.05	-0.9873	-0.0770	5.25	0.0219
Exp(Live_baby_weight per 1kg increase)				0.5874	0.1364	0.05	0.3726	0.9259		

Revised_Groups Least Squares Means

Revised_Groups	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	-0.1783	0.2778	-0.64	0.5210	0.05	-0.7229	0.3662	0.8367	0.4853	1.4423
Preexisting	0.4952	0.2480	2.00	0.0459	0.05	0.009030	0.9813	1.6408	1.0091	2.6680

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Preexisting	-0.6735	0.3234	-2.08	0.0373	0.05	-1.3073	-0.03969	0.5099	0.2705	0.9611

Site Least Squares Means

Site	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	0.01968	0.5078	0.04	0.9691	0.05	-0.9757	1.0150	1.0199	0.3769	2.7595
2	0.1107	0.2329	0.48	0.6347	0.05	-0.3458	0.5672	1.1170	0.7076	1.7632
3	0.3449	0.2412	1.43	0.1527	0.05	-0.1278	0.8176	1.4119	0.8801	2.2651

Differences of Site Least Squares Means

Site	*_Site*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	2	-0.09098	0.5529	-0.16	0.8693	0.05	-1.1746	0.9926	0.9130	0.3090	2.6983
1	3	-0.3252	0.5539	-0.59	0.5571	0.05	-1.4108	0.7604	0.7224	0.2439	2.1391
2	3	-0.2343	0.3310	-0.71	0.4791	0.05	-0.8830	0.4144	0.7912	0.4136	1.5135

Highrisk1 Least Squares Means

Highrisk1	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	0.5118	0.2256	2.27	0.0233	0.05	0.06964	0.9540	1.6683	1.0721	2.5961
2.No	-0.1950	0.3031	-0.64	0.5200	0.05	-0.7891	0.3991	0.8228	0.4543	1.4905

Differences of Highrisk1 Least Squares Means

Highrisk1	*_Highrisk1*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	2.No	0.7068	0.3357	2.11	0.0352	0.05	0.04891	1.3647	2.0275	1.0501	3.9146

Model 16 Final Multivariable Logistic regression of Paediatric_neonatal_staff versus Group, site and confounders
The GENMOD Procedure

Model Information	
Data Set	WORK.CARDIAC2
Distribution	Binomial
Link Function	Logit
Dependent Variable	Paediatric_neonatal_staff

Number of Observations Read	271
Number of Observations Used	195
Number of Events	154
Number of Trials	195
Missing Values	76

Class Level Information

Class	*Levels*	*Values*
Revised_Groups	2	Acquired Preexisting
Site	3	1 2 3
Highrisk5_3Paediatri	2	1.Yes 2.No
team_4Physicianx	2	1.Yes 2.No

Response Profile

Ordered Value	*Paediatric_neonatal_staff*	*Total Frequency*
1	Yes	154
2	No	41

PROC GENMOD is modelling the probability that Paediatric_neonatal_staff='Yes'.

Parameter Information

Parameter	*Effect*	*Revised_Groups*	*Site*	*Highrisk5_3Paediatri*	*team_4Physicianx*
Prm1	Intercept				
Prm2	Revised_Groups	Acquired			
Prm3	Revised_Groups	Preexisting			
Prm4	Site		1		
Prm5	Site		2		
Prm6	Site		3		
Prm7	Highrisk5_3Paediatri			1.Yes	
Prm8	Highrisk5_3Paediatri			2.No	
Prm9	team_4Physicianx				1.Yes
Prm10	team_4Physicianx				2.No
Prm11	Live_baby_weight				

Criteria For Assessing Goodness Of Fit

Criterion	*DF*	*Value*	*Value/DF*
Log Likelihood		-58.6168	
Full Log Likelihood		-58.6168	
AIC (smaller is better)		131.2336	
AICC (smaller is better)		131.8325	
BIC (smaller is better)		154.1446	

Algorithm converged.

Analysis Of Maximum Likelihood Parameter Estimates

Parameter		*DF*	*Estimate*	*Standard Error*	*Wald 95% Confidence Limits*		*Wald Chi-Square*	*Pr > ChiSq*
Intercept		1	1.2456	1.4245	-1.5463	4.0375	0.76	0.3819
Revised_Groups	Acquired	1	-0.4550	0.5032	-1.4412	0.5311	0.82	0.3658
Revised_Groups	Pre-existing	0	0.0000	0.0000	0.0000	0.0000	.	.
Site	1	1	0.2018	0.8950	-1.5524	1.9559	0.05	0.8216
Site	2	1	0.4128	0.5886	-0.7409	1.5664	0.49	0.4831
Site	3	0	0.0000	0.0000	0.0000	0.0000	.	.
Highrisk5_3Paediatri	1.Yes	1	2.7886	0.5275	1.7547	3.8224	27.94	<.0001
Highrisk5_3Paediatri	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
team_4Physicianx	1.Yes	1	1.9718	0.5801	0.8349	3.1087	11.56	0.0007
team_4Physicianx	2.No	0	0.0000	0.0000	0.0000	0.0000	.	.
Live_baby_weight		1	-0.0008	0.0004	-0.0016	-0.0000	3.92	0.0476
Scale		0	1.0000	0.0000	1.0000	1.0000		

Note: The scale parameter was held fixed.

Wald Statistics For Type 3 Analysis

Source	*DF*	*Chi-Square*	*Pr > ChiSq*
Revised_Groups	1	0.82	0.3658
Site	2	0.50	0.7804
Highrisk5_3Paediatri	1	27.94	<.0001
team_4Physicianx	1	11.56	0.0007
Live_baby_weight	1	3.92	0.0476

Contrast Estimate Results

	Mean			L'Beta						
Label	*Mean Estimate*	*Confidence Limits*		*L'Beta Estimate*	*Standard Error*	*Alpha*	*Confidence Limits*		*Chi-Square*	*Pr > ChiSq*
Live_baby_weight per 1kg increase	0.3073	0.1656	0.4979	-0.8127	0.4103	0.05	-1.6169	-0.0084	3.92	0.0476
Exp(Live_baby_weight per 1kg increase)				0.4437	0.1821	0.05	0.1985	0.9916		

Revised_Groups Least Squares Means

Revised_Groups	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	0.9207	0.4281	2.15	0.0315	0.05	0.08166	1.7597	2.5110	1.0851	5.8109
Preexisteant	1.3757	0.4197	3.28	0.0010	0.05	0.5532	2.1983	3.9580	1.7389	9.0092

Differences of Revised_Groups Least Squares Means

Revised_Groups	*_Revised_Groups*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
Acquired	Preexisting	-0.4550	0.5032	-0.90	0.3658	0.05	-1.4412	0.5311	0.6344	0.2366	1.7009

Site Least Squares Means

Site	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1	1.1451	0.8205	1.40	0.1628	0.05	-0.4631	2.7533	3.1429	0.6294	15.6948
2	1.3562	0.4667	2.91	0.0037	0.05	0.4415	2.2709	3.8813	1.5550	9.6878
3	0.9434	0.3762	2.51	0.0122	0.05	0.2059	1.6808	2.5686	1.2287	5.3699

Differences of Site Least Squares Means

Site	_Site	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1	2	-0.2110	0.9502	-0.22	0.8242	0.05	-2.0734	1.6513	0.8098	0.1258	5.2140
1	3	0.2018	0.8950	0.23	0.8216	0.05	-1.5524	1.9559	1.2236	0.2117	7.0703
2	3	0.4128	0.5886	0.70	0.4831	0.05	-0.7409	1.5664	1.5110	0.4767	4.7895

Highrisk5_3Paediatri Least Squares Means

Highrisk5_3Paediatricianx	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.5425	0.4283	5.94	<.0001	0.05	1.7030	3.3820	12.7114	5.4905	29.4289
2.No	-0.2461	0.4341	-0.57	0.5709	0.05	-1.0969	0.6048	0.7819	0.3339	1.8309

Differences of Highrisk5_3Paediatri Least Squares Means

Highrisk5_3Paedix	_Highrisk5_3Paediatricianx	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.No	2.7886	0.5275	5.29	<.0001	0.05	1.7547	3.8224	16.2575	5.7815	45.7160

team_4Physicianx Least Squares Means

team_4Physicianx	Estimate	Standard Error	z Value	Pr > |z|	Alpha	Lower	Upper	Exponentiated	Exponentiated Lower	Exponentiated Upper
1.Yes	2.1341	0.4932	4.33	<.0001	0.05	1.1675	3.1007	8.4496	3.2140	22.2144
2.No	0.1623	0.3972	0.41	0.6828	0.05	-0.6162	0.9409	1.1762	0.5400	2.5622

Differences of team_4Physicianx Least Squares Means

team_4Physicianx	*_team_4Physicianx*	*Estimate*	*Standard Error*	*z Value*	*Pr > |z|*	*Alpha*	*Lower*	*Upper*	*Exponentiated*	*Exponentiated Lower*	*Exponentiated Upper*
1.Yes	2.No	1.9718	0.5801	3.40	0.0007	0.05	0.8349	3.1087	7.1836	2.3046	22.3919

B3. S3 Linear regressions of total score versus various predictors

Model number	*Predictor*	*Comparison*	*Estimate (95% CI)*	*Comparison P value*	*Global P value*
1	Revised_Groups	Acquired vs Pre-existing	-2.31 (-3.88, -0.74)		0.0039
2	Plannedcare3x	Caesarean vs Vaginal	6.04 (4.58, 7.49)		<.0001
3	RaceC	ATSI vs Asian	1.84 (-2.19, 5.87)	0.3706	0.1298
		ATSI vs Caucasian	2.65 (0.25, 5.05)	0.0305	
		ATSI vs Other	5.11 (-1.12, 11.33)	0.1077	
		Asian vs Caucasian	0.81 (-2.66, 4.28)	0.6473	
		Asian vs Other	3.27 (-3.44, 9.97)	0.3398	
		Caucasian vs Other	2.46 (-3.42, 8.33)	0.4126	
4	Site	1 vs 2	-3.42 (-5.95, -0.88)	0.0082	<0.0001
		1 vs 3	0.53 (-2.00, 3.06)	0.6832	
		2 vs 3	3.94 (2.32, 5.56)	<.0001	
5	PC	Metropolitan vs Remote	-5.05 (-8.87, -1.24)	0.0095	0.0009
		Metropolitan vs Rural	-3.13 (-5.21, -1.05)	0.0031	
		Remote vs Rural	1.92 (-2.24, 6.08)	0.3649	
6	Status	De facto/ living with partner versus Divorced/Separated	0.22 (-5.33, 5.78)	0.9381	0.1814
		De facto/ living with partner versus Married	1.79 (-0.21, 3.79)	0.0789	
		De facto/ living with partner versus Never married	2.87 (0.03, 5.71)	0.0473	
		Divorced/Separated vs Married	1.57 (-3.80, 6.95)	0.5663	
		Divorced/Separated vs Never Married	2.65 (-3.09, 8.39)	0.3652	
		Married vs Never married	1.08 (-1.39, 3.54)	0.3912	
7	Highrisk9_1episiotom	No vs Yes	-0.96 (-5.22, 3.29)		0.6571
8	Highrisk9_2forcepsx	Yes vs No	2.39 (-0.28, 5.06)		0.0798
9	Highrisk9_4No	No vs Yes	0.97 (-1.46, 3.40)		0.4354
10	Prev_preg_cardiac	No vs Yes	-1.66 (-3.25, -0.07)		0.0404
11	COBB	Born in Australia vs Born overseas	1.15 (-0.90, 3.21)		0.2715
12	Cause_1Rheumatic	No vs Yes	-1.08 (-3.43, 1.26)		0.3654
13	Cause_2Congenital	No vs Yes	-1.96 (-3.85, -0.07)		0.0416
14	Cause_3Arrhythmias	No vs Yes	0.24 (-1.54, 2.02)		0.7935

Model number	*Predictor*	*Comparison*	*Estimate (95% CI)*	*Comparison P value*	*Global P value*
15	Cause_4Ischaemic	No vs Yes	0.20 (-4.03, 4.43)		0.9256
16	Cause_5Failure	No vs Yes	-2.19 (-4.75, 0.38)		0.0952
17	Cause_6Arrest	No vs Yes	1.28 (-3.74, 6.31)		0.6164
18	Cause_7Conduction	No vs Yes	13.44 (0.39, 26.50)		0.0436
19	Cause_8PE	No vs Yes	2.70 (0.06, 5.35)		0.0452
20	Cause_9Hypertension	No vs Yes	-0.42 (-4.65, 3.81)		0.8452
21	Cause_9Hypertension	No vs Yes	-0.42 (-4.65, 3.81)		0.8452
22	Cause_11Other	No vs Yes	1.37 (-0.83, 3.57)		0.2222
23	Age		0.03 (-0.10, 0.16)		0.6728
24	Weight		0.03 (-0.01, 0.07)		0.1999
25	Height		-0.14 (-0.25, -0.03)		0.0162
26	BMI		0.13 (0.02, 0.25)		0.0256
27	SBP		0.01 (-0.04, 0.06)		0.6602
28	DBP		0.00 (-0.05, 0.06)		0.9031
29	ANRQ_score		0.01 (-0.09, 0.10)		0.8875
30	EPPSD_score		0.15 (-0.05, 0.36)		0.1413
31	Maternal_age		0.03 (-0.10, 0.16)		0.6640
32	Gestational_age_admission		-0.05 (-0.24, 0.15)		0.6365
33	Gravida		-0.02 (-0.40, 0.36)		0.9145
34	Parity		-0.25 (-0.70, 0.20)		0.2796
35	Gestational_age		-0.14 (-0.37, 0.08)		0.2033
36	Live_baby_weight per 100g increase		-0.24 (-0.33, -0.17)		<.0001
37	Babys_length_birth		-0.38 (-0.58, -0.17)		0.0003
38	Babys_Head_circ_birth		-0.38 (-0.71, -0.05)		0.0256
39	Apgar_1min		-0.66 (-1.09, -0.23)		0.0027
40	Apgar_5min		-1.02 (-1.73, -0.31)		0.0051

B4. Univariate regression results

STUDY OF CARDIAC PROBLEMS DURING PREGNANCY – PART 3: UNIVARIATE REGRESSIONS FURTHER CORRECTED
Researcher: Sindy Millington
Statistician: Suzanne Edwards
Date: 23 May 2019

The following outcomes were investigated: preconception, ANC1, ANC2, ANC3, ANCQ, Fetal risk 1_sum, Fetal risk 2_sum, Planned care 1, Planned care 2, Planned care 3, Compromise_sum, Compromise_1Tachycardia, Compromise_2Bradycardia, Compromise_3Respiratory, Compromise_4Changing, Thromboembolism_sum, Thromboembolism_1stockings, Thromboembolism_2heparin, Pain_sum, Pain_1Anaesthetic, Pain_2Epidural, Pain_3Combined, Pain_4Other, Cardiac consultation, and Paediatric neonatal staff. Manage labour resuscitation equipment and Management labour 5 mins cardiac arrest were not included because only for the first, No=2/284 and for the second, No=1/283 so a logistic regression model would not converge.

The following predictors were investigated: Group, Site, High risk 1, High risk 2, High risk 3, High risk 4, High risk 6, High risk 7, High risk 5_sum, High risk 5_1Anaesthetist, High risk 5_2Cardiologist, High risk 5_3Paediatrician, High risk 9_1episiotomy, High risk 9_2forceps, High risk9_4No, team_sum, team_1Obstetrician, team_2Midwife, team_3Cardologist, team_4Physician. team_5Anaesthetist, team_6Intensivist, team_8Other, Cardiac consultation ANRQ score recorded (zero score is No), EPPSD score recorded, Age, Weight, Live baby weight, Baby's length birth, Baby's head circumference birth, ANRQ score (zero score is missing), EPPSD score, Gestational age admission, Gravida, Parity, Gestational age, Apgar 1 minute, and Apgar 5 minutes.

Univariate binary logistic regressions were performed for each binary outcome versus each predictor. Global P values are given in Table 2. Univariate ordinal logistic regressions were performed for each ordinal outcome versus each predictor. Global P values are given in Table 3.

The statistical software used was SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Table 1. Frequency table of revised groups

Revised_Groups	*Frequency*	*Percent*	*Cumulative Frequency*	*Cumulative Percent*
Acquired	128	47.23	128	47.23
Pre-existing	143	52.77	271	100.00

Table 2. Univariate binary logistic regression results

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
1	preconception	Revised_Groups	0.9959
2	preconception	Site	0.5744
3	preconception	Highrisk1	0.0064
4	preconception	Highrisk2	0.6888
5	preconception	Highrisk3	0.0407
6	preconception	Highrisk4	0.0570
7	preconception	Highrisk6	0.1678
8	preconception	Highrisk7	0.0004
9	preconception	Highrisk5_sum	0.0316
10	preconception	Highrisk5_1Anaesthet	.
11	preconception	Highrisk5_2Cardiolog	0.0373
12	preconception	Highrisk5_3Paediatri	0.0351
13	preconception	Highrisk9_1episiotom	.
14	preconception	Highrisk9_2forceps	0.6189
15	preconception	Highrisk9_4No	0.8050
16	Preconception	team_sum	0.1784
17	Preconception	team_1Obstetrician	0.3052
18	Preconception	team_2Midwife	.
19	Preconception	team_3Cardiologist	0.2038
20	Preconception	team_4Physician	0.1644
21	Preconception	team_5Anaesthetist	0.5981
22	Preconception	team_6Intensivist	0.1556
24	Preconception	team_8Other	0.9373
25	Preconception	Cardiac_consultation	0.0346
26	Preconception	ANRQ_scoreRECORDED	0.2062
27	preconception	EPPSD_scoreRECORDED	0.6733
28	preconception	Age	0.5986
29	preconception	Weight	0.8116
31	preconception	BMI	0.4987
34	preconception	Live_baby_weight	0.1138
35	preconception	Babys_length_birth	0.2062
36	preconception	Babys_Head_circ_birth	0.4218
37	preconception	ANRQ_score	0.1449
38	preconception	EPPSD_score	0.5997
39	preconception	Gestational_age_admission	0.3907
40	preconception	Gravida	0.0064

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
41	preconception	Parity	0.0300
42	preconception	Gestational_age	0.2004
43	preconception	Apgar_1min	0.1904
44	preconception	Apgar_5min	0.1046
1	ANCQ	Revised_Groups	0.0002
2	ANCQ	Site	<.0001
3	ANCQ	Highrisk1	0.2053
4	ANCQ	Highrisk2	<.0001
5	ANCQ	Highrisk3	0.0382
6	ANCQ	Highrisk4	0.0265
6	ANCQ	Highrisk4	0.0265
6	ANCQ	Highrisk4	0.0265
7	ANCQ	Highrisk6	0.1155
8	ANCQ	Highrisk7	0.2681
9	ANCQ	Highrisk5_sum	0.5050
10	ANCQ	Highrisk5_1Anaesthet	0.2252
11	ANCQ	Highrisk5_2Cardiolog	0.5919
12	ANCQ	Highrisk5_3Paediatri	0.6763
13	ANCQ	Highrisk9_1episiotom	.
14	ANCQ	Highrisk9_2forceps	0.6661
15	ANCQ	Highrisk9_4No	0.2434
16	ANCQ	team_sum	0.5665
17	ANCQ	team_1Obstetrician	0.4031
18	ANCQ	team_2Midwife	0.8791
19	ANCQ	team_3Cardiologist	0.4568
20	ANCQ	team_4Physician	0.1166
21	ANCQ	team_5Anaesthetist	0.6020
22	ANCQ	team_6Intensivist	0.3457
24	ANCQ	team_8Other	0.8277
25	ANCQ	Cardiac_consultation	0.0359
26	ANCQ	ANRQ_scoreRECORDED	<.0001
27	ANCQ	EPPSD_scoreRECORDED	<.0001
28	ANCQ	Age	0.3341
29	ANCQ	Weight	0.5589
31	ANCQ	BMI	0.1603
34	ANCQ	Live_baby_weight	0.0212
35	ANCQ	Babys_length_birth	0.0120

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
36	ANCQ	Babys_Head_circ_birth	0.9100
37	ANCQ	ANRQ_score	0.3664
38	ANCQ	EPPSD_score	0.1680
39	ANCQ	Gestational_age_admission	0.4354
40	ANCQ	Gravida	0.7751
41	ANCQ	Parity	0.5044
42	ANCQ	Gestational_age	0.2061
43	ANCQ	Apgar_1min	0.3682
44	ANCQ	Apgar_5min	0.4192
1	FetalRisk2_sum	Revised_Groups	0.4736
2	FetalRisk2_sum	Site	0.8924
3	FetalRisk2_sum	Highrisk1	0.6230
4	FetalRisk2_sum	Highrisk2	0.6500
5	FetalRisk2_sum	Highrisk3	0.6258
6	FetalRisk2_sum	Highrisk4	<.0001
7	FetalRisk2_sum	Highrisk6	.
8	FetalRisk2_sum	Highrisk7	0.4611
9	FetalRisk2_sum	Highrisk5_sum	0.9360
10	FetalRisk2_sum	Highrisk5_1Anaesthet	0.4218
11	FetalRisk2_sum	Highrisk5_2Cardiolog	0.5902
12	FetalRisk2_sum	Highrisk5_3Paediatri	0.5192
13	FetalRisk2_sum	Highrisk9_1episiotom	0.9456
14	FetalRisk2_sum	Highrisk9_2forceps	0.3585
15	FetalRisk2_sum	Highrisk9_4No	0.6821
16	FetalRisk2_sum	team_sum	0.8127
17	FetalRisk2_sum	team_1Obstetrician	0.8285
18	FetalRisk2_sum	team_2Midwife	0.7262
19	FetalRisk2_sum	team_3Cardiologist	0.8048
20	FetalRisk2_sum	team_4Physician	0.4156
21	FetalRisk2_sum	team_5Anaesthetist	0.8573
22	FetalRisk2_sum	team_6Intensivist	0.6392
24	FetalRisk2_sum	team_8Other	0.9889
25	FetalRisk2_sum	Cardiac_consultation	0.2012
26	FetalRisk2_sum	ANRQ_scoreRECORDED	0.7571
27	FetalRisk2_sum	EPPSD_scoreRECORDED	0.5739
28	FetalRisk2_sum	Age	0.1355
29	FetalRisk2_sum	Weight	0.9198

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
31	FetalRisk2_sum	BMI	0.9669
34	FetalRisk2_sum	Live_baby_weight	0.7901
35	FetalRisk2_sum	Babys_length_birth	0.6583
36	FetalRisk2_sum	Babys_Head_circ_birth	0.7096
37	FetalRisk2_sum	ANRQ_score	0.8734
38	FetalRisk2_sum	EPPSD_score	0.8194
39	FetalRisk2_sum	Gestational_age_admission	0.3897
40	FetalRisk2_sum	Gravida	0.6335
41	FetalRisk2_sum	Parity	0.5617
42	FetalRisk2_sum	Gestational_age	0.4715
43	FetalRisk2_sum	Apgar_1min	0.3404
44	FetalRisk2_sum	Apgar_5min	0.8797
1	Plannedcare1	Revised_Groups	0.1902
2	Plannedcare1	Site	0.2330
3	Plannedcare1	Highrisk1	0.0032
4	Plannedcare1	Highrisk2	0.0740
5	Plannedcare1	Highrisk3	<.0001
6	Plannedcare1	Highrisk4	<.0001
7	Plannedcare1	Highrisk6	0.0661
8	Plannedcare1	Highrisk7	0.0002
9	Plannedcare1	Highrisk5_sum	0.0326
10	Plannedcare1	Highrisk5_1Anaesthet	0.0036
11	Plannedcare1	Highrisk5_2Cardiolog	0.1872
12	Plannedcare1	Highrisk5_3Paediatri	0.1486
13	Plannedcare1	Highrisk9_1episiotom	0.0253
14	Plannedcare1	Highrisk9_2forceps	0.2251
15	Plannedcare1	Highrisk9_4No	0.9771
16	Plannedcare1	team_sum	0.0147
17	Plannedcare1	team_1Obstetrician	0.0139
18	Plannedcare1	team_2Midwife	0.6513
19	Plannedcare1	team_3Cardiologist	.
20	Plannedcare1	team_4Physician	0.6317
21	Plannedcare1	team_5Anaesthetist	0.0145
22	Plannedcare1	team_6Intensivist	.
24	Plannedcare1	team_8Other	0.9465
25	Plannedcare1	Cardiac_consultation	<.0001
26	Plannedcare1	ANRQ_scoreRECORDED	0.9440

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
27	Plannedcare1	EPPSD_scoreRECORDED	0.2897
28	Plannedcare1	Age	0.3543
29	Plannedcare1	Weight	0.9166
31	Plannedcare1	BMI	0.7396
34	Plannedcare1	Live_baby_weight	0.6693
35	Plannedcare1	Babys_length_birth	0.6329
36	Plannedcare1	Babys_Head_circ_birth	0.3931
37	Plannedcare1	ANRQ_score	0.6211
38	Plannedcare1	EPPSD_score	0.9771
39	Plannedcare1	Gestational_age_admission	0.9473
40	Plannedcare1	Gravida	0.1260
41	Plannedcare1	Parity	0.1626
42	Plannedcare1	Gestational_age	0.7758
43	Plannedcare1	Apgar_1min	0.1830
44	Plannedcare1	Apgar_5min	0.1293
1	Plannedcare2	Revised_Groups	0.4320
2	Plannedcare2	Site	0.8166
3	Plannedcare2	Highrisk1	0.0172
4	Plannedcare2	Highrisk2	0.2999
5	Plannedcare2	Highrisk3	.
6	Plannedcare2	Highrisk4	0.0735
7	Plannedcare2	Highrisk6	0.5601
8	Plannedcare2	Highrisk7	.
9	Plannedcare2	Highrisk5_sum	<.0001
10	Plannedcare2	Highrisk5_1Anaesthet	.
11	Plannedcare2	Highrisk5_2Cardiolog	.
12	Plannedcare2	Highrisk5_3Paediatri	0.1864
13	Plannedcare2	Highrisk9_1episiotom	.
14	Plannedcare2	Highrisk9_2forceps	.
15	Plannedcare2	Highrisk9_4No	.
16	Plannedcare2	team_sum	0.3790
17	Plannedcare2	team_1Obstetrician	0.5975
18	Plannedcare2	team_2Midwife	0.1070
19	Plannedcare2	team_3Cardiologist	0.4169
20	Plannedcare2	team_4Physician	0.7781
21	Plannedcare2	team_5Anaesthetist	0.1823
22	Plannedcare2	team_6Intensivist	0.0793

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
24	Plannedcare2	team_8Other	.
25	Plannedcare2	Cardiac_consultation	.
26	Plannedcare2	ANRQ_scoreRECORDED	0.5502
27	Plannedcare2	EPPSD_scoreRECORDED	0.9395
28	Plannedcare2	Age	0.4794
29	Plannedcare2	Weight	0.6809
31	Plannedcare2	BMI	0.8773
34	Plannedcare2	Live_baby_weight	0.0373
35	Plannedcare2	Babys_length_birth	0.9338
36	Plannedcare2	Babys_Head_circ_birth	0.9342
37	Plannedcare2	ANRQ_score	0.5530
38	Plannedcare2	EPPSD_score	0.4655
39	Plannedcare2	Gestational_age_admission	0.1911
40	Plannedcare2	Gravida	0.2525
41	Plannedcare2	Parity	0.0137
42	Plannedcare2	Gestational_age	0.0227
43	Plannedcare2	Apgar_1min	0.1772
44	Plannedcare2	Apgar_5min	0.2124
1	Plannedcare3x	Revised_Groups	0.9368
2	Plannedcare3x	Site	0.3874
3	Plannedcare3x	Highrisk1	<.0001
4	Plannedcare3x	Highrisk2	0.4857
5	Plannedcare3x	Highrisk3	0.0034
6	Plannedcare3x	Highrisk4	<.0001
7	Plannedcare3x	Highrisk6	0.0012
8	Plannedcare3x	Highrisk7	0.1221
9	Plannedcare3x	Highrisk5_sum	<.0001
10	Plannedcare3x	Highrisk5_1Anaesthet	0.0166
11	Plannedcare3x	Highrisk5_2Cardiolog	0.0205
12	Plannedcare3x	Highrisk5_3Paediatri	<.0001
13	Plannedcare3x	Highrisk9_1episiotom	.
14	Plannedcare3x	Highrisk9_2forceps	0.7089
15	Plannedcare3x	Highrisk9_4No	0.0019
16	Plannedcare3x	team_sum	<.0001
17	Plannedcare3x	team_1Obstetrician	<.0001
18	Plannedcare3x	team_2Midwife	0.0408
19	Plannedcare3x	team_3Cardiologist	0.2994

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
20	Plannedcare3x	team_4Physician	<.0001
21	Plannedcare3x	team_5Anaesthetist	<.0001
22	Plannedcare3x	team_6Intensivist	0.0035
24	Plannedcare3x	team_8Other	0.3503
25	Plannedcare3x	Cardiac_consultation	0.0409
26	Plannedcare3x	ANRQ_scoreRECORDED	0.1078
27	Plannedcare3x	EPPSD_scoreRECORDED	0.4008
28	Plannedcare3x	Age	0.4435
29	Plannedcare3x	Weight	0.4122
31	Plannedcare3x	BMI	0.0511
34	Plannedcare3x	Live_baby_weight	0.0001
35	Plannedcare3x	Babys_length_birth	0.0169
36	Plannedcare3x	Babys_Head_circ_birth	0.0350
37	Plannedcare3x	ANRQ_score	0.6978
38	Plannedcare3x	EPPSD_score	0.2757
39	Plannedcare3x	Gestational_age_admission	0.0016
40	Plannedcare3x	Gravida	0.4471
41	Plannedcare3x	Parity	0.6649
42	Plannedcare3x	Gestational_age	<.0001
43	Plannedcare3x	Apgar_1min	0.0002
44	Plannedcare3x	Apgar_5min	0.0013
1	compromise_1Tachycardia	Revised_Groups	0.9999
3	compromise_1Tachycardia	Highrisk1	.
4	compromise_1Tachycardia	Highrisk2	.
5	compromise_1Tachycardia	Highrisk3	.
5	compromise_1Tachycardia	Highrisk3	.
7	compromise_1Tachycardia	Highrisk6	.
8	compromise_1Tachycardia	Highrisk7	1.0000
9	compromise_1Tachycardia	Highrisk5_sum	1.0000
10	compromise_1Tachycardia	Highrisk5_1Anaesthet	.
11	compromise_1Tachycardia	Highrisk5_2Cardiolog	.
12	compromise_1Tachycardia	Highrisk5_3Paediatri	.
13	compromise_1Tachycardia	Highrisk9_1episiotom	0.9999
14	compromise_1Tachycardia	Highrisk9_2forceps	1.0000
15	compromise_1Tachycardia	Highrisk9_4No	1.0000
44	Plannedcare3x	Apgar_5min	0.0013
17	compromise_1Tachycardia	team_1Obstetrician	0.9999

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
18	compromise_1Tachycardia	team_2Midwife	.
19	compromise_1Tachycardia	team_3Cardiologist	.
20	compromise_1Tachycardia	team_4Physician	0.9999
21	compromise_1Tachycardia	team_5Anaesthetist	0.9999
22	compromise_1Tachycardia	team_6Intensivist	.
24	compromise_1Tachycardia	team_8Other	.
25	compromise_1Tachycardia	Cardiac_consultation	0.9999
26	compromise_1Tachycardia	ANRQ_scoreRECORDED	0.9999
27	compromise_1Tachycardia	EPPSD_scoreRECORDED	.
28	compromise_1Tachycardia	Age	0.3991
29	compromise_1Tachycardia	Weight	0.1339
31	compromise_1Tachycardia	BMI	0.2292
34	compromise_1Tachycardia	Live_baby_weight	0.2020
35	compromise_1Tachycardia	Babys_length_birth	0.2999
36	compromise_1Tachycardia	Babys_Head_circ_birth	0.4368
.		Babys_Head_circ_birt	0.4368
36	compromise_1Tachycardia	Babys_Head_circ_birth	.
38	compromise_1Tachycardia	EPPSD_score	1.0000
39	compromise_1Tachycardia	Gestational_age_admission	0.1841
40	compromise_1Tachycardia	Gravida	0.5801
41	compromise_1Tachycardia	Parity	0.7616
42	compromise_1Tachycardia	Gestational_age	0.1081
43	compromise_1Tachycardia	Apgar_1min	0.5567
43	compromise_1Tachycardia	Apgar_1min	0.5567
1	compromise_2Bradycardia	Revised_Groups	0.9999
2	compromise_2Bradycardia	Site	<.0001
3	compromise_2Bradycardia	Highrisk1	.
4	compromise_2Bradycardia	Highrisk2	0.8374
5	compromise_2Bradycardia	Highrisk3	0.0936
5	compromise_2Bradycardia	Highrisk3	0.0936
7	compromise_2Bradycardia	Highrisk6	0.2630
8	compromise_2Bradycardia	Highrisk7	.
9	compromise_2Bradycardia	Highrisk5_sum	1.0000
10	compromise_2Bradycardia	Highrisk5_1Anaesthet	.
11	compromise_2Bradycardia	Highrisk5_2Cardiolog	.
12	compromise_2Bradycardia	Highrisk5_3Paediatri	.
13	compromise_2Bradycardia	Highrisk9_1episiotom	1.0000

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
14	compromise_2Bradycardia	Highrisk9_2forceps	1.0000
15	compromise_2Bradycardia	Highrisk9_4No	.
16	compromise_2Bradycardia	team_sum	0.3825
17	compromise_2Bradycardia	team_1Obstetrician	.
18	compromise_2Bradycardia	team_2Midwife	.
19	compromise_2Bradycardia	team_3Cardiologist	.
20	compromise_2Bradycardia	team_4Physician	0.9999
21	compromise_2Bradycardia	team_5Anaesthetist	0.5442
22	compromise_2Bradycardia	team_6Intensivist	.
24	compromise_2Bradycardia	team_8Other	.
25	compromise_2Bradycardia	Cardiac_consultation	.
26	compromise_2Bradycardia	ANRQ_scoreRECORDED	0.7739
27	compromise_2Bradycardia	EPPSD_scoreRECORDED	0.7739
28	compromise_2Bradycardia	Age	0.0491
29	compromise_2Bradycardia	Weight	0.5421
31	compromise_2Bradycardia	BMI	0.2235
34	compromise_2Bradycardia	Live_baby_weight	0.1913
35	compromise_2Bradycardia	Babys_length_birth	0.3584
36	compromise_2Bradycardia	Babys_Head_circ_birth	0.7262
37	compromise_2Bradycardia	ANRQ_score	0.5055
38	compromise_2Bradycardia	EPPSD_score	0.0998
39	compromise_2Bradycardia	Gestational_age_admission	0.1608
40	compromise_2Bradycardia	Gravida	0.2407
41	compromise_2Bradycardia	Parity	0.5458
42	compromise_2Bradycardia	Gestational_age	0.1721
43	compromise_2Bradycardia	Apgar_1min	0.5282
44	compromise_2Bradycardia	Apgar_5min	0.2710
1	compromise_3Respiratory	Revised_Groups	0.1310
2	compromise_3Respiratory	Site	<.0001
3	compromise_3Respiratory	Highrisk1	0.7581
4	compromise_3Respiratory	Highrisk2	0.3447
5	compromise_3Respiratory	Highrisk3	0.0170
6	compromise_3Respiratory	Highrisk4	<.0001
7	compromise_3Respiratory	Highrisk6	0.5457
8	compromise_3Respiratory	Highrisk7	0.2475
9	compromise_3Respiratory	Highrisk5_sum	0.5366
10	compromise_3Respiratory	Highrisk5_1Anaesthet	0.0671

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
11	compromise_3Respiratory	Highrisk5_2Cardiolog	.
12	compromise_3Respiratory	Highrisk5_3Paediatri	0.4914
13	compromise_3Respiratory	Highrisk9_1episiotom	0.0044
14	compromise_3Respiratory	Highrisk9_2forceps	0.1907
15	compromise_3Respiratory	Highrisk9_4No	0.1249
16	compromise_3Respiratory	team_sum	0.0544
17	compromise_3Respiratory	team_1Obstetrician	0.1225
18	compromise_3Respiratory	team_2Midwife	.
19	compromise_3Respiratory	team_3Cardiologist	.
20	compromise_3Respiratory	team_4Physician	0.1727
21	compromise_3Respiratory	team_5Anaesthetist	0.2548
22	compromise_3Respiratory	team_6Intensivist	.
24	compromise_3Respiratory	team_8Other	.
25	compromise_3Respiratory	Cardiac_consultation	0.2970
26	compromise_3Respiratory	ANRQ_scoreRECORDED	0.9458
27	compromise_3Respiratory	EPPSD_scoreRECORDED	0.3441
28	compromise_3Respiratory	Age	0.0502
29	compromise_3Respiratory	Weight	0.0901
31	compromise_3Respiratory	BMI	0.6285
34	compromise_3Respiratory	Live_baby_weight	0.1662
35	compromise_3Respiratory	Babys_length_birth	0.5267
36	compromise_3Respiratory	Babys_Head_circ_birth	0.8825
37	compromise_3Respiratory	ANRQ_score	0.6331
38	compromise_3Respiratory	EPPSD_score	0.0998
39	compromise_3Respiratory	Gestational_age_admission	0.0858
40	compromise_3Respiratory	Gravida	0.6049
41	compromise_3Respiratory	Parity	0.4934
42	compromise_3Respiratory	Gestational_age	0.0533
43	compromise_3Respiratory	Apgar_1min	0.4477
44	compromise_3Respiratory	Apgar_5min	0.0131
1	compromise_4Changing	Revised_Groups	0.8752
2	compromise_4Changing	Site	<.0001
3	compromise_4Changing	Highrisk1	0.5850
4	compromise_4Changing	Highrisk2	0.2848
5	compromise_4Changing	Highrisk3	0.0251
6	compromise_4Changing	Highrisk4	<.0001
7	compromise_4Changing	Highrisk6	0.8862

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
8	compromise_4Changing	Highrisk7	0.6465
9	compromise_4Changing	Highrisk5_sum	0.7750
10	compromise_4Changing	Highrisk5_1Anaesthet	0.3494
11	compromise_4Changing	Highrisk5_2Cardiolog	0.7194
12	compromise_4Changing	Highrisk5_3Paediatri	0.6880
13	compromise_4Changing	Highrisk9_1episiotom	0.0011
14	compromise_4Changing	Highrisk9_2forceps	0.4834
15	compromise_4Changing	Highrisk9_4No	0.7104
16	compromise_4Changing	team_sum	0.5753
17	compromise_4Changing	team_1Obstetrician	0.4875
18	compromise_4Changing	team_2Midwife	.
19	compromise_4Changing	team_3Cardiologist	0.8979
20	compromise_4Changing	team_4Physician	0.9069
21	compromise_4Changing	team_5Anaesthetist	0.4937
22	compromise_4Changing	team_6Intensivist	0.8510
24	compromise_4Changing	team_8Other	.
25	compromise_4Changing	Cardiac_consultation	0.7432
26	compromise_4Changing	ANRQ_scoreRECORDED	0.7824
27	compromise_4Changing	EPPSD_scoreRECORDED	0.3312
28	compromise_4Changing	Age	0.3334
29	compromise_4Changing	Weight	0.4179
31	compromise_4Changing	BMI	0.9420
34	compromise_4Changing	Live_baby_weight	0.6195
35	compromise_4Changing	Babys_length_birth	0.6210
36	compromise_4Changing	Babys_Head_circ_birth	0.2864
37	compromise_4Changing	ANRQ_score	0.4206
38	compromise_4Changing	EPPSD_score	0.0289
39	compromise_4Changing	Gestational_age_admission	0.3465
40	compromise_4Changing	Gravida	0.4391
41	compromise_4Changing	Parity	0.8540
42	compromise_4Changing	Gestational_age	0.3385
43	compromise_4Changing	Apgar_1min	0.8849
44	compromise_4Changing	Apgar_5min	0.3269
1	thromboembolism_sum	Revised_Groups	0.0229
2	thromboembolism_sum	Site	0.0148
3	thromboembolism_sum	Highrisk1	0.0531
4	thromboembolism_sum	Highrisk2	0.0838

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
5	thromboembolism_sum	Highrisk3	0.5769
6	thromboembolism_sum	Highrisk4	<.0001
7	thromboembolism_sum	Highrisk6	0.1041
8	thromboembolism_sum	Highrisk7	0.0833
9	thromboembolism_sum	Highrisk5_sum	0.5007
10	thromboembolism_sum	Highrisk5_1Anaesthet	.
11	thromboembolism_sum	Highrisk5_2Cardiolog	0.5964
12	thromboembolism_sum	Highrisk5_3Paediatri	0.3058
13	thromboembolism_sum	Highrisk9_1episiotom	.
14	thromboembolism_sum	Highrisk9_2forceps	0.4560
15	thromboembolism_sum	Highrisk9_4No	0.2840
16	thromboembolism_sum	team_sum	0.0105
17	thromboembolism_sum	team_1Obstetrician	0.0084
18	thromboembolism_sum	team_2Midwife	0.6977
19	thromboembolism_sum	team_3Cardiologist	0.5441
20	thromboembolism_sum	team_4Physician	0.7079
21	thromboembolism_sum	team_5Anaesthetist	0.0119
22	thromboembolism_sum	team_6Intensivist	0.0250
24	thromboembolism_sum	team_8Other	.
25	thromboembolism_sum	Cardiac_consultation	0.1039
26	thromboembolism_sum	ANRQ_scoreRECORDED	0.6525
27	thromboembolism_sum	EPPSD_scoreRECORDED	0.9157
28	thromboembolism_sum	Age	0.1472
29	thromboembolism_sum	Weight	0.1049
31	thromboembolism_sum	BMI	0.3093
34	thromboembolism_sum	Live_baby_weight	0.0419
35	thromboembolism_sum	Babys_length_birth	0.1773
36	thromboembolism_sum	Babys_Head_circ_birth	0.2620
37	thromboembolism_sum	ANRQ_score	0.8864
38	thromboembolism_sum	EPPSD_score	0.1926
39	thromboembolism_sum	Gestational_age_admission	0.4325
40	thromboembolism_sum	Gravida	0.0966
41	thromboembolism_sum	Parity	0.1144
42	thromboembolism_sum	Gestational_age	0.7165
43	thromboembolism_sum	Apgar_1min	0.2286
44	thromboembolism_sum	Apgar_5min	0.1340
1	thromboembolism_1stockings	Revised_Groups	0.1828

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
2	thromboembolism_1stockings	Site	0.0661
3	thromboembolism_1stockings	Highrisk1	0.1214
4	thromboembolism_1stockings	Highrisk2	0.4971
5	thromboembolism_1stockings	Highrisk3	0.7703
6	thromboembolism_1stockings	Highrisk4	<.0001
6	thromboembolism_1stockings	Highrisk4	<.0001
6	thromboembolism_1stockings	Highrisk4	<.0001
7	thromboembolism_1stockings	Highrisk6	0.0943
8	thromboembolism_1stockings	Highrisk7	0.3623
9	thromboembolism_1stockings	Highrisk5_sum	0.5503
10	thromboembolism_1stockings	Highrisk5_1Anaesthet	.
11	thromboembolism_1stockings	Highrisk5_2Cardiolog	0.7500
12	thromboembolism_1stockings	Highrisk5_3Paediatri	0.1220
13	thromboembolism_1stockings	Highrisk9_1episiotom	.
14	thromboembolism_1stockings	Highrisk9_2forceps	0.2455
15	thromboembolism_1stockings	Highrisk9_4No	0.8404
16	thromboembolism_1stockings	team_sum	0.0461
17	thromboembolism_1stockings	team_1Obstetrician	0.1328
18	thromboembolism_1stockings	team_2Midwife	0.7169
19	thromboembolism_1stockings	team_3Cardiologist	0.3904
20	thromboembolism_1stockings	team_4Physician	0.8482
21	thromboembolism_1stockings	team_5Anaesthetist	0.0279
22	thromboembolism_1stockings	team_6Intensivist	0.0206
24	thromboembolism_1stockings	team_8Other	.
25	thromboembolism_1stockings	Cardiac_consultation	0.9186
26	thromboembolism_1stockings	ANRQ_scoreRECORDED	0.3958
27	thromboembolism_1stockings	EPPSD_scoreRECORDED	0.5448
28	thromboembolism_1stockings	Age	0.2137
29	thromboembolism_1stockings	Weight	0.0478
31	thromboembolism_1stockings	BMI	0.2059
34	thromboembolism_1stockings	Live_baby_weight	0.0132
35	thromboembolism_1stockings	Babys_length_birth	0.1577
36	thromboembolism_1stockings	Babys_Head_circ_birth	0.2523
37	thromboembolism_1stockings	ANRQ_score	0.3812
38	thromboembolism_1stockings	EPPSD_score	0.5188
39	thromboembolism_1stockings	Gestational_age_admission	0.2586
40	thromboembolism_1stockings	Gravida	0.6399

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
41	thromboembolism_1stockings	Parity	0.9268
42	thromboembolism_1stockings	Gestational_age	0.4309
43	thromboembolism_1stockings	Apgar_1min	0.2211
44	thromboembolism_1stockings	Apgar_5min	0.1033
1	thromboembolism_2heparin	Revised_Groups	0.1462
2	thromboembolism_2heparin	Site	0.0802
3	thromboembolism_2heparin	Highrisk1	0.4845
4	thromboembolism_2heparin	Highrisk2	0.1100
5	thromboembolism_2heparin	Highrisk3	0.6811
6	thromboembolism_2heparin	Highrisk4	<.0001
7	thromboembolism_2heparin	Highrisk6	0.8558
8	thromboembolism_2heparin	Highrisk7	0.1246
9	thromboembolism_2heparin	Highrisk5_sum	0.9537
10	thromboembolism_2heparin	Highrisk5_1Anaesthet	.
11	thromboembolism_2heparin	Highrisk5_2Cardiolog	0.7373
12	thromboembolism_2heparin	Highrisk5_3Paediatri	0.5457
13	thromboembolism_2heparin	Highrisk9_1episiotom	.
14	thromboembolism_2heparin	Highrisk9_2forceps	0.5247
15	thromboembolism_2heparin	Highrisk9_4No	0.0699
16	thromboembolism_2heparin	team_sum	0.3191
17	thromboembolism_2heparin	team_1Obstetrician	0.0482
18	thromboembolism_2heparin	team_2Midwife	0.9539
19	thromboembolism_2heparin	team_3Cardiologist	0.7408
20	thromboembolism_2heparin	team_4Physician	0.4167
21	thromboembolism_2heparin	team_5Anaesthetist	0.3662
22	thromboembolism_2heparin	team_6Intensivist	0.5963
24	thromboembolism_2heparin	team_8Other	.
25	thromboembolism_2heparin	Cardiac_consultation	0.0114
26	thromboembolism_2heparin	ANRQ_scoreRECORDED	0.5920
27	thromboembolism_2heparin	EPPSD_scoreRECORDED	0.3178
28	thromboembolism_2heparin	Age	0.7045
29	thromboembolism_2heparin	Weight	0.6728
31	thromboembolism_2heparin	BMI	0.7646
34	thromboembolism_2heparin	Live_baby_weight	0.5877
35	thromboembolism_2heparin	Babys_length_birth	0.9831
36	thromboembolism_2heparin	Babys_Head_circ_birth	0.9697
37	thromboembolism_2heparin	ANRQ_score	0.1380

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
38	thromboembolism_2heparin	EPPSD_score	0.2508
39	thromboembolism_2heparin	Gestational_age_admission	0.6548
40	thromboembolism_2heparin	Gravida	0.0792
41	thromboembolism_2heparin	Parity	0.0351
42	thromboembolism_2heparin	Gestational_age	0.5651
43	thromboembolism_2heparin	Apgar_1min	0.9549
44	thromboembolism_2heparin	Apgar_5min	0.9098
1	Pain_1Anaesthetic	Revised_Groups	0.0550
2	Pain_1Anaesthetic	Site	0.4731
3	Pain_1Anaesthetic	Highrisk1	0.0002
4	Pain_1Anaesthetic	Highrisk2	0.5434
5	Pain_1Anaesthetic	Highrisk3	0.3008
6	Pain_1Anaesthetic	Highrisk4	0.1538
6	Pain_1Anaesthetic	Highrisk4	0.1538
6	Pain_1Anaesthetic	Highrisk4	0.1538
7	Pain_1Anaesthetic	Highrisk6	0.0241
8	Pain_1Anaesthetic	Highrisk7	0.8940
9	Pain_1Anaesthetic	Highrisk5_sum	0.3133
10	Pain_1Anaesthetic	Highrisk5_1Anaesthet	1.0000
11	Pain_1Anaesthetic	Highrisk5_2Cardiolog	0.5887
12	Pain_1Anaesthetic	Highrisk5_3Paediatri	0.0417
13	Pain_1Anaesthetic	Highrisk9_1episiotom	0.6688
14	Pain_1Anaesthetic	Highrisk9_2forceps	0.0776
15	Pain_1Anaesthetic	Highrisk9_4No	0.1983
16	Pain_1Anaesthetic	team_sum	0.0105
17	Pain_1Anaesthetic	team_1Obstetrician	0.0704
18	Pain_1Anaesthetic	team_2Midwife	0.2045
19	Pain_1Anaesthetic	team_3Cardiologist	0.0553
20	Pain_1Anaesthetic	team_4Physician	0.3941
21	Pain_1Anaesthetic	team_5Anaesthetist	0.0242
22	Pain_1Anaesthetic	team_6Intensivist	0.0669
24	Pain_1Anaesthetic	team_8Other	0.5557
25	Pain_1Anaesthetic	Cardiac_consultation	0.3211
26	Pain_1Anaesthetic	ANRQ_scoreRECORDED	0.0767
27	Pain_1Anaesthetic	EPPSD_scoreRECORDED	0.6117
28	Pain_1Anaesthetic	Age	0.6775
29	Pain_1Anaesthetic	Weight	0.1274

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
31	Pain_1Anaesthetic	BMI	0.1755
34	Pain_1Anaesthetic	Live_baby_weight	<.0001
35	Pain_1Anaesthetic	Babys_length_birth	0.0599
36	Pain_1Anaesthetic	Babys_Head_circ_birth	0.0053
37	Pain_1Anaesthetic	ANRQ_score	0.7158
38	Pain_1Anaesthetic	EPPSD_score	0.2038
39	Pain_1Anaesthetic	Gestational_age_admission	0.0220
40	Pain_1Anaesthetic	Gravida	0.0926
41	Pain_1Anaesthetic	Parity	0.0601
42	Pain_1Anaesthetic	Gestational_age	0.0049
43	Pain_1Anaesthetic	Apgar_1min	0.3058
44	Pain_1Anaesthetic	Apgar_5min	0.4685
1	Pain_2Epidural	Revised_Groups	0.0484
2	Pain_2Epidural	Site	0.7973
3	Pain_2Epidural	Highrisk1	0.1834
4	Pain_2Epidural	Highrisk2	0.4142
5	Pain_2Epidural	Highrisk3	0.0095
6	Pain_2Epidural	Highrisk4	<.0001
7	Pain_2Epidural	Highrisk6	0.1380
8	Pain_2Epidural	Highrisk7	0.3903
9	Pain_2Epidural	Highrisk5_sum	0.5175
10	Pain_2Epidural	Highrisk5_1Anaesthet	0.3975
11	Pain_2Epidural	Highrisk5_2Cardiolog	0.7745
12	Pain_2Epidural	Highrisk5_3Paediatri	0.9426
13	Pain_2Epidural	Highrisk9_1episiotom	0.0148
14	Pain_2Epidural	Highrisk9_2forceps	0.0403
15	Pain_2Epidural	Highrisk9_4No	0.4657
16	Pain_2Epidural	team_sum	0.0199
17	Pain_2Epidural	team_1Obstetrician	0.1893
18	Pain_2Epidural	team_2Midwife	0.5935
19	Pain_2Epidural	team_3Cardiologist	0.8569
20	Pain_2Epidural	team_4Physician	0.3768
21	Pain_2Epidural	team_5Anaesthetist	0.0002
22	Pain_2Epidural	team_6Intensivist	0.9066
24	Pain_2Epidural	team_8Other	.
25	Pain_2Epidural	Cardiac_consultation	0.2784
26	Pain_2Epidural	ANRQ_scoreRECORDED	0.5580

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
27	Pain_2Epidural	EPPSD_scoreRECORDED	0.6287
28	Pain_2Epidural	Age	0.8677
29	Pain_2Epidural	Weight	0.4961
31	Pain_2Epidural	BMI	0.2991
34	Pain_2Epidural	Live_baby_weight	0.8189
35	Pain_2Epidural	Babys_length_birth	0.6755
36	Pain_2Epidural	Babys_Head_circ_birth	0.5328
37	Pain_2Epidural	ANRQ_score	0.6272
38	Pain_2Epidural	EPPSD_score	0.1705
39	Pain_2Epidural	Gestational_age_admission	0.0415
40	Pain_2Epidural	Gravida	0.1104
41	Pain_2Epidural	Parity	0.1361
42	Pain_2Epidural	Gestational_age	0.2341
43	Pain_2Epidural	Apgar_1min	0.0006
44	Pain_2Epidural	Apgar_5min	0.0012
1	Pain_3Combined	Revised_Groups	0.9854
2	Pain_3Combined	Site	0.0501
3	Pain_3Combined	Highrisk1	0.5614
4	Pain_3Combined	Highrisk2	0.9640
5	Pain_3Combined	Highrisk3	0.0183
6	Pain_3Combined	Highrisk4	<.0001
7	Pain_3Combined	Highrisk6	0.1420
8	Pain_3Combined	Highrisk7	0.4533
9	Pain_3Combined	Highrisk5_sum	0.0413
10	Pain_3Combined	Highrisk5_1Anaesthet	0.2690
11	Pain_3Combined	Highrisk5_2Cardiolog	0.1024
12	Pain_3Combined	Highrisk5_3Paediatri	0.0274
13	Pain_3Combined	Highrisk9_1episiotom	.
14	Pain_3Combined	Highrisk9_2forceps	0.4581
15	Pain_3Combined	Highrisk9_4No	0.0175
16	Pain_3Combined	team_sum	<.0001
17	Pain_3Combined	team_1Obstetrician	<.0001
18	Pain_3Combined	team_2Midwife	0.6702
19	Pain_3Combined	team_3Cardiologist	0.8801
20	Pain_3Combined	team_4Physician	0.0013
21	Pain_3Combined	team_5Anaesthetist	0.0028
22	Pain_3Combined	team_6Intensivist	0.0770

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
24	Pain_3Combined	team_8Other	0.4806
25	Pain_3Combined	Cardiac_consultation	0.0365
26	Pain_3Combined	ANRQ_scoreRECORDED	0.2106
27	Pain_3Combined	EPPSD_scoreRECORDED	0.2882
28	Pain_3Combined	Age	0.3734
29	Pain_3Combined	Weight	0.3358
31	Pain_3Combined	BMI	0.3014
34	Pain_3Combined	Live_baby_weight	0.0940
35	Pain_3Combined	Babys_length_birth	0.0770
36	Pain_3Combined	Babys_Head_circ_birth	0.1409
37	Pain_3Combined	ANRQ_score	0.1839
38	Pain_3Combined	EPPSD_score	0.2854
39	Pain_3Combined	Gestational_age_admission	0.2992
40	Pain_3Combined	Gravida	0.6209
41	Pain_3Combined	Parity	0.9645
42	Pain_3Combined	Gestational_age	0.0123
43	Pain_3Combined	Apgar_1min	0.1659
44	Pain_3Combined	Apgar_5min	0.3378
1	Pain_4Other	Revised_Groups	0.0668
2	Pain_4Other	Site	0.9900
3	Pain_4Other	Highrisk1	0.0054
4	Pain_4Other	Highrisk2	0.8233
5	Pain_4Other	Highrisk3	0.9198
6	Pain_4Other	Highrisk4	<.0001
7	Pain_4Other	Highrisk6	0.8731
8	Pain_4Other	Highrisk7	0.8057
9	Pain_4Other	Highrisk5_sum	0.8733
10	Pain_4Other	Highrisk5_1Anaesthet	0.6690
11	Pain_4Other	Highrisk5_2Cardiolog	0.8039
12	Pain_4Other	Highrisk5_3Paediatri	0.6067
13	Pain_4Other	Highrisk9_1episiotom	0.1021
14	Pain_4Other	Highrisk9_2forceps	0.1163
15	Pain_4Other	Highrisk9_4No	0.3724
16	Pain_4Other	team_sum	0.7442
17	Pain_4Other	team_1Obstetrician	0.8440
18	Pain_4Other	team_2Midwife	0.4548
19	Pain_4Other	team_3Cardiologist	0.0567

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
20	Pain_4Other	team_4Physician	0.7860
21	Pain_4Other	team_5Anaesthetist	0.0333
22	Pain_4Other	team_6Intensivist	0.0980
24	Pain_4Other	team_8Other	0.3259
25	Pain_4Other	Cardiac_consultation	0.7419
26	Pain_4Other	ANRQ_scoreRECORDED	0.7609
27	Pain_4Other	EPPSD_scoreRECORDED	0.9222
28	Pain_4Other	Age	0.9811
29	Pain_4Other	Weight	0.0400
31	Pain_4Other	BMI	0.0293
34	Pain_4Other	Live_baby_weight	0.0018
35	Pain_4Other	Babys_length_birth	0.4127
36	Pain_4Other	Babys_Head_circ_birth	0.0226
37	Pain_4Other	ANRQ_score	0.6304
38	Pain_4Other	EPPSD_score	0.3249
39	Pain_4Other	Gestational_age_admission	0.0066
40	Pain_4Other	Gravida	0.2123
41	Pain_4Other	Parity	0.2182
42	Pain_4Other	Gestational_age	0.0225
43	Pain_4Other	Apgar_1min	0.1293
44	Pain_4Other	Apgar_5min	0.1426
1	Cardiac_consultation	Revised_Groups	0.6959
2	Cardiac_consultation	Site	0.4421
3	Cardiac_consultation	Highrisk1	<.0001
4	Cardiac_consultation	Highrisk2	0.0990
5	Cardiac_consultation	Highrisk3	<.0001
6	Cardiac_consultation	Highrisk4	<.0001
7	Cardiac_consultation	Highrisk6	0.0269
8	Cardiac_consultation	Highrisk7	<.0001
9	Cardiac_consultation	Highrisk5_sum	0.0007
10	Cardiac_consultation	Highrisk5_1Anaesthet	0.0063
11	Cardiac_consultation	Highrisk5_2Cardiolog	0.0015
12	Cardiac_consultation	Highrisk5_3Paediatri	0.0486
13	Cardiac_consultation	Highrisk9_1episiotom	0.8328
14	Cardiac_consultation	Highrisk9_2forceps	0.2877
15	Cardiac_consultation	Highrisk9_4No	0.8054
16	Cardiac_consultation	team_sum	0.0010

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
17	Cardiac_consultation	team_1Obstetrician	0.0043
18	Cardiac_consultation	team_2Midwife	.
19	Cardiac_consultation	team_3Cardiologist	.
20	Cardiac_consultation	team_4Physician	0.0166
21	Cardiac_consultation	team_5Anaesthetist	0.0010
22	Cardiac_consultation	team_6Intensivist	.
24	Cardiac_consultation	team_8Other	0.3405
25	Cardiac_consultation	Cardiac_consultation	1.0000
26	Cardiac_consultation	ANRQ_scoreRECORDED	0.4634
27	Cardiac_consultation	EPPSD_scoreRECORDED	0.0954
28	Cardiac_consultation	Age	0.1829
29	Cardiac_consultation	Weight	0.7380
31	Cardiac_consultation	BMI	0.7632
34	Cardiac_consultation	Live_baby_weight	0.0028
35	Cardiac_consultation	Babys_length_birth	0.0339
36	Cardiac_consultation	Babys_Head_circ_birth	0.1219
37	Cardiac_consultation	ANRQ_score	0.3482
38	Cardiac_consultation	EPPSD_score	0.5455
39	Cardiac_consultation	Gestational_age_admission	0.0027
40	Cardiac_consultation	Gravida	0.4077
41	Cardiac_consultation	Parity	0.2762
42	Cardiac_consultation	Gestational_age	0.0005
43	Cardiac_consultation	Apgar_1min	0.1541
44	Cardiac_consultation	Apgar_5min	0.0202
1	Paediatric_neonatal_staff	Revised_Groups	0.8214
2	Paediatric_neonatal_staff	Site	0.2391
3	Paediatric_neonatal_staff	Highrisk1	<.0001
4	Paediatric_neonatal_staff	Highrisk2	0.7159
5	Paediatric_neonatal_staff	Highrisk3	0.0037
6	Paediatric_neonatal_staff	Highrisk4	<.0001
7	Paediatric_neonatal_staff	Highrisk6	<.0001
8	Paediatric_neonatal_staff	Highrisk7	0.0220
9	Paediatric_neonatal_staff	Highrisk5_sum	<.0001
10	Paediatric_neonatal_staff	Highrisk5_1Anaesthet	0.0016
11	Paediatric_neonatal_staff	Highrisk5_2Cardiolog	0.0184
12	Paediatric_neonatal_staff	Highrisk5_3Paediatri	<.0001
13	Paediatric_neonatal_staff	Highrisk9_1episiotom	0.7720

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
14	Paediatric_neonatal_staff	Highrisk9_2forceps	0.0073
15	Paediatric_neonatal_staff	Highrisk9_4No	0.3528
16	Paediatric_neonatal_staff	team_sum	<.0001
17	Paediatric_neonatal_staff	team_1Obstetrician	<.0001
18	Paediatric_neonatal_staff	team_2Midwife	0.4819
19	Paediatric_neonatal_staff	team_3Cardiologist	0.0363
20	Paediatric_neonatal_staff	team_4Physician	<.0001
21	Paediatric_neonatal_staff	team_5Anaesthetist	<.0001
22	Paediatric_neonatal_staff	team_6Intensivist	0.0095
24	Paediatric_neonatal_staff	team_8Other	0.5347
25	Paediatric_neonatal_staff	Cardiac_consultation	0.0015
26	Paediatric_neonatal_staff	ANRQ_scoreRECORDED	0.0441
27	Paediatric_neonatal_staff	EPPSD_scoreRECORDED	0.0977
28	Paediatric_neonatal_staff	Age	0.3521
29	Paediatric_neonatal_staff	Weight	0.3284
31	Paediatric_neonatal_staff	BMI	0.1220
34	Paediatric_neonatal_staff	Live_baby_weight	<.0001
35	Paediatric_neonatal_staff	Babys_length_birth	0.0021
36	Paediatric_neonatal_staff	Babys_Head_circ_birth	0.0007
37	Paediatric_neonatal_staff	ANRQ_score	0.4680
38	Paediatric_neonatal_staff	EPPSD_score	0.4744
39	Paediatric_neonatal_staff	Gestational_age_admission	0.0547
40	Paediatric_neonatal_staff	Gravida	0.1933
41	Paediatric_neonatal_staff	Parity	0.0961
42	Paediatric_neonatal_staff	Gestational_age	0.0048
43	Paediatric_neonatal_staff	Apgar_1min	0.0016
44	Paediatric_neonatal_staff	Apgar_5min	0.0132

Table 3. Ordinal logistic regression results

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
1	ANC1	Revised_Groups	0.0694
2	ANC1	Site	<.0001
3	ANC1	Highrisk1	0.9275
4	ANC1	Highrisk2	<.0001
5	ANC1	Highrisk3	0.0033
6	ANC1	Highrisk4	0.0132
7	ANC1	Highrisk6	0.7307
8	ANC1	Highrisk7	0.4124
9	ANC1	Highrisk5_sum	0.8503
10	ANC1	Highrisk5_1Anaesthet	0.9976
11	ANC1	Highrisk5_2Cardiolog	0.3295
12	ANC1	Highrisk5_3Paediatri	0.0708
13	ANC1	Highrisk9_1episiotom	0.2829
14	ANC1	Highrisk9_2forceps	0.9791
15	ANC1	Highrisk9_4No	0.4770
16	ANC1	team_sum	0.8828
17	ANC1	team_1Obstetrician	0.2424
18	ANC1	team_2Midwife	0.0520
19	ANC1	team_3Cardiologist	0.9372
20	ANC1	team_4Physician	0.1045
21	ANC1	team_5Anaesthetist	0.9205
22	ANC1	team_6Intensivist	0.6762
24	ANC1	team_8Other	0.8838
25	ANC1	Cardiac_consultation	0.0950
26	ANC1	ANRQ_scoreRECORDED	<.0001
27	ANC1	EPPSD_scoreRECORDED	<.0001
28	ANC1	Age	0.6721
29	ANC1	Weight	0.4811
31	ANC1	BMI	0.6502
34	ANC1	Live_baby_weight	0.9540
35	ANC1	Babys_length_birth	0.6732
36	ANC1	Babys_Head_circ_birth	0.6426
37	ANC1	ANRQ_score	0.7858
38	ANC1	EPPSD_score	0.0389

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
39	ANC1	Gestational_age_admission	0.0316
40	ANC1	Gravida	0.8872
41	ANC1	Parity	0.6398
42	ANC1	Gestational_age	0.0457
43	ANC1	Apgar_1min	0.5391
44	ANC1	Apgar_5min	0.5334
1	ANC2	Revised_Groups	0.4112
2	ANC2	Site	0.0063
3	ANC2	Highrisk1	0.0021
4	ANC2	Highrisk2	0.0048
5	ANC2	Highrisk3	0.2270
6	ANC2	Highrisk4	0.2374
7	ANC2	Highrisk6	0.5490
8	ANC2	Highrisk7	0.5268
9	ANC2	Highrisk5_sum	0.0813
10	ANC2	Highrisk5_1Anaesthet	0.8809
11	ANC2	Highrisk5_2Cardiolog	0.1693
12	ANC2	Highrisk5_3Paediatri	0.4676
13	ANC2	Highrisk9_1episiotom	0.9552
14	ANC2	Highrisk9_2forceps	0.6666
15	ANC2	Highrisk9_4No	0.5635
16	ANC2	team_sum	0.2914
17	ANC2	team_1Obstetrician	0.9012
18	ANC2	team_2Midwife	0.2963
19	ANC2	team_3Cardiologist	0.9218
20	ANC2	team_4Physician	0.1329
21	ANC2	team_5Anaesthetist	0.0731
22	ANC2	team_6Intensivist	0.5904
24	ANC2	team_8Other	0.5521
25	ANC2	Cardiac_consultation	0.0366
26	ANC2	ANRQ_scoreRECORDED	0.9492
27	ANC2	EPPSD_scoreRECORDED	0.4947
28	ANC2	Age	0.9075
29	ANC2	Weight	0.9490
31	ANC2	BMI	0.9280

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
34	ANC2	Live_baby_weight	0.2280
35	ANC2	Babys_length_birth	0.0159
36	ANC2	Babys_Head_circ_birth	0.9225
37	ANC2	ANRQ_score	0.0261
38	ANC2	EPPSD_score	0.2693
39	ANC2	Gestational_age_admission	0.1497
40	ANC2	Gravida	0.8123
41	ANC2	Parity	0.5409
42	ANC2	Gestational_age	0.1768
43	ANC2	Apgar_1min	0.8066
44	ANC2	Apgar_5min	0.6593
1	ANC3	Revised_Groups	0.4757
2	ANC3	Site	0.6850
3	ANC3	Highrisk1	0.0023
4	ANC3	Highrisk2	0.7838
5	ANC3	Highrisk3	0.0278
6	ANC3	Highrisk4	0.0654
7	ANC3	Highrisk6	0.0283
8	ANC3	Highrisk7	0.4304
9	ANC3	Highrisk5_sum	0.2212
10	ANC3	Highrisk5_1Anaesthet	0.0468
11	ANC3	Highrisk5_2Cardiolog	0.0926
12	ANC3	Highrisk5_3Paediatri	0.7238
13	ANC3	Highrisk9_1episiotom	0.4438
14	ANC3	Highrisk9_2forceps	0.7231
15	ANC3	Highrisk9_4No	0.9794
16	ANC3	team_sum	0.4115
17	ANC3	team_1Obstetrician	0.8469
18	ANC3	team_2Midwife	0.4927
19	ANC3	team_3Cardiologist	0.3471
20	ANC3	team_4Physician	0.2058
21	ANC3	team_5Anaesthetist	0.0361
22	ANC3	team_6Intensivist	0.7128
24	ANC3	team_8Other	0.1267
25	ANC3	Cardiac_consultation	0.2401

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
26	ANC3	ANRQ_scoreRECORDED	0.6266
27	ANC3	EPPSD_scoreRECORDED	0.5476
28	ANC3	Age	0.7511
29	ANC3	Weight	0.6275
31	ANC3	BMI	0.4532
34	ANC3	Live_baby_weight	0.9453
35	ANC3	Babys_length_birth	0.3968
36	ANC3	Babys_Head_circ_birth	0.7454
37	ANC3	ANRQ_score	0.7666
38	ANC3	EPPSD_score	0.5026
39	ANC3	Gestational_age_admission	0.1605
40	ANC3	Gravida	0.6186
41	ANC3	Parity	0.2049
42	ANC3	Gestational_age	0.0653
43	ANC3	Apgar_1min	0.6651
44	ANC3	Apgar_5min	0.7050
1	FetalRisk1_sum	Revised_Groups	0.9762
2	FetalRisk1_sum	Site	0.2047
3	FetalRisk1_sum	Highrisk1	<.0001
4	FetalRisk1_sum	Highrisk2	0.0272
5	FetalRisk1_sum	Highrisk3	0.0001
6	FetalRisk1_sum	Highrisk4	<.0001
7	FetalRisk1_sum	Highrisk6	0.0038
8	FetalRisk1_sum	Highrisk7	<.0001
9	FetalRisk1_sum	Highrisk5_sum	0.0052
10	FetalRisk1_sum	Highrisk5_1Anaesthet	0.0046
11	FetalRisk1_sum	Highrisk5_2Cardiolog	0.2213
12	FetalRisk1_sum	Highrisk5_3Paediatri	0.0080
13	FetalRisk1_sum	Highrisk9_1episiotom	0.3344
14	FetalRisk1_sum	Highrisk9_2forceps	0.6538
15	FetalRisk1_sum	Highrisk9_4No	0.6343
16	FetalRisk1_sum	team_sum	0.0010
17	FetalRisk1_sum	team_1Obstetrician	0.0227
18	FetalRisk1_sum	team_2Midwife	0.6411
19	FetalRisk1_sum	team_3Cardiologist	0.0255

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
20	FetalRisk1_sum	team_4Physician	0.1047
21	FetalRisk1_sum	team_5Anaesthetist	0.0148
22	FetalRisk1_sum	team_6Intensivist	0.0590
24	FetalRisk1_sum	team_8Other	0.9661
25	FetalRisk1_sum	Cardiac_consultation	0.0003
26	FetalRisk1_sum	ANRQ_scoreRECORDED	0.4655
27	FetalRisk1_sum	EPPSD_scoreRECORDED	0.7011
28	FetalRisk1_sum	Age	0.9986
29	FetalRisk1_sum	Weight	0.0363
31	FetalRisk1_sum	BMI	0.0118
34	FetalRisk1_sum	Live_baby_weight	0.0094
35	FetalRisk1_sum	Babys_length_birth	0.3799
36	FetalRisk1_sum	Babys_Head_circ_birth	0.2796
99937	FetalRisk1_sum	ANRQ_score	0.7940
38	FetalRisk1_sum	EPPSD_score	0.1216
39	FetalRisk1_sum	Gestational_age_admission	0.1119
40	FetalRisk1_sum	Gravida	0.5456
941	FetalRisk1_sum	Parity	0.9936
42	FetalRisk1_sum	Gestational_age	0.0132
43	FetalRisk1_sum	Apgar_1min	0.1853
44	FetalRisk1_sum	Apgar_5min	0.0592
1	compromise_sum	Revised_Groups	0.7505
2	compromise_sum	Site	<.0001
3	compromise_sum	Highrisk1	0.9332
4	compromise_sum	Highrisk2	0.2695
5	compromise_sum	Highrisk3	0.0380
6	compromise_sum	Highrisk4	<.0001
7	compromise_sum	Highrisk6	0.7662
8	compromise_sum	Highrisk7	0.9547
9	compromise_sum	Highrisk5_sum	0.6450
10	compromise_sum	Highrisk5_1Anaesthet	0.4216
11	compromise_sum	Highrisk5_2Cardiolog	0.5342
12	compromise_sum	Highrisk5_3Paediatri	0.5314
13	compromise_sum	Highrisk9_1episiotom	0.0007
14	compromise_sum	Highrisk9_2forceps	0.9911

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
15	compromise_sum	Highrisk9_4No	0.3535
16	compromise_sum	team_sum	0.4647
17	compromise_sum	team_1Obstetrician	0.3437
18	compromise_sum	team_2Midwife	.
19	compromise_sum	team_3Cardiologist	0.7408
20	compromise_sum	team_4Physician	0.9869
21	compromise_sum	team_5Anaesthetist	0.6690
22	compromise_sum	team_6Intensivist	0.6964
24	compromise_sum	team_8Other	.
25	compromise_sum	Cardiac_consultation	0.8664
26	compromise_sum	ANRQ_scoreRECORDED	0.8393
27	compromise_sum	EPPSD_scoreRECORDED	0.1763
28	compromise_sum	Age	0.4599
29	compromise_sum	Weight	0.3818
31	compromise_sum	BMI	0.3277
34	compromise_sum	Live_baby_weight	0.6619
35	compromise_sum	Babys_length_birth	0.6864
36	compromise_sum	Babys_Head_circ_birth	0.2725
37	compromise_sum	ANRQ_score	0.4236
38	compromise_sum	EPPSD_score	0.0284
39	compromise_sum	Gestational_age_admission	0.2867
40	compromise_sum	Gravida	0.4873
41	compromise_sum	Parity	0.8665
42	compromise_sum	Gestational_age	0.2858
43	compromise_sum	Apgar_1min	0.7354
44	compromise_sum	Apgar_5min	0.1731
1	Pain_sum	Revised_Groups	0.0054
2	Pain_sum	Site	0.4158
3	Pain_sum	Highrisk1	0.0018
4	Pain_sum	Highrisk2	0.6872
5	Pain_sum	Highrisk3	0.0020
6	Pain_sum	Highrisk4	0.0895
7	Pain_sum	Highrisk6	0.0113
8	Pain_sum	Highrisk7	0.7848
9	Pain_sum	Highrisk5_sum	0.0693

Model number	*Outcome variable*	*Predictor variable*	*Global P value*
10	Pain_sum	Highrisk5_1Anaesthet	0.5523
11	Pain_sum	Highrisk5_2Cardiolog	0.2887
12	Pain_sum	Highrisk5_3Paediatri	0.0143
13	Pain_sum	Highrisk9_1episiotom	0.7469
14	Pain_sum	Highrisk9_2forceps	0.7488
15	Pain_sum	Highrisk9_4No	0.0740
16	Pain_sum	team_sum	<.0001
17	Pain_sum	team_1Obstetrician	<.0001
18	Pain_sum	team_2Midwife	0.1778
19	Pain_sum	team_3Cardiologist	0.0336
20	Pain_sum	team_4Physician	0.0318
21	Pain_sum	team_5Anaesthetist	<.0001
22	Pain_sum	team_6Intensivist	0.0128
24	Pain_sum	team_8Other	0.3237
25	Pain_sum	Cardiac_consultation	0.0586
26	Pain_sum	ANRQ_scoreRECORDED	0.0559
27	Pain_sum	EPPSD_scoreRECORDED	0.5899
28	Pain_sum	Age	0.4796
29	Pain_sum	Weight	0.3543
31	Pain_sum	BMI	0.5213
34	Pain_sum	Live_baby_weight	<.0001
35	Pain_sum	Babys_length_birth	0.0232
36	Pain_sum	Babys_Head_circ_birth	0.0046
37	Pain_sum	ANRQ_score	0.7901
38	Pain_sum	EPPSD_score	0.2746
39	Pain_sum	Gestational_age_admission	0.0328
40	Pain_sum	Gravida	0.2303
41	Pain_sum	Parity	0.2780
42	Pain_sum	Gestational_age	0.0014
43	Pain_sum	Apgar_1min	0.5088
44	Pain_sum	Apgar_5min	0.5174

B5. Supplementary descriptive statistics cardiac variables

All data: Frequency tables of cardiac variable

The FREQ Procedure

Previous_pregnancies_with_cardia	*Frequency*	*Percent*	*Cumulative Frequency*	*Cumulative Percent*
No	122	45.86	122	45.86
Yes	144	54.14	266	100.00
Frequency Missing = 5				

cardiac event in Pregnancy

Cardiac	*Frequency*	*Percent*	*Cumulative Frequency*	*Cumulative Percent*
HF	40	17.62	40	17.62
Arrhyth	74	32.60	114	50.22
IHD	20	8.81	134	59.03
CArrest	11	4.85	145	63.88
V& CHD	55	24.23	200	88.11
SBE	2	0.88	202	88.99
CVA	1	0.44	203	89.43
RHD	22	9.69	225	99.12
Cardiac PE	1	0.44	226	99.56
Aortic Dissect	1	0.44	227	100.00
Frequency Missing = 44				

AC data: Frequency tables of cardiac variable

The FREQ Procedure

Previous_pregnancies_with_cardia	*Frequency*	*Percent*	*Cumulative Frequency*	*Cumulative Percent*
No	82	66.67	82	66.67
Yes	41	33.33	123	100.00
Frequency Missing = 5				

Cardiac event in Pregnancy				
Cardiac	*Frequency*	*Percent*	*Cumulative Frequency*	*Cumulative Percent*
HF	28	25.69	28	25.69
Arrhythmia	49	44.95	77	70.64
IHD	18	16.51	95	87.16
CArrest	9	8.26	104	95.41
V&/CHD	2	1.83	106	97.25
SBE	1	0.92	107	98.17
CVA	1	0.92	108	99.08
Cardiac PE	1	0.92	109	100.00
Frequency Missing = 19				

PEC data: Frequency tables of cardiac variable

The FREQ Procedure

Previous_pregnancies_with_cardiac				
Previous_pregnancies_with_cardia	*Frequency*	*Percent*	*Cumulative Frequency*	*Cumulative Percent*
No	40	27.97	40	27.97
Yes	103	72.03	143	100.00

cardiac	*Frequency*	*Percent*	*Cumulative Frequency*	*Cumulative Percent*
HF	12	10.17	12	10.17
Arrhythmia	25	21.19	37	31.36
IHD	2	1.69	39	33.05
Card Arrest	2	1.69	41	34.75
VHD/CHD	53	44.92	94	79.66
SBE	1	0.85	95	80.51
RHD	22	18.64	117	99.15
Aortic Dissect	1	0.85	118	100.00

Frequency Missing = 25

Cardiac Characteristics	**Total -Frequency (%)**	**PEC - Frequency (%)**	**AC - Frequency (%)**
Cardiac event (prev preg)	144 (54)	103 (72)	∗41 (33)
Cardiac event (current preg)			
1 Heart failure HF	40 (18)	12 (10)	28 (26)
2 Arrhythmias	74 (33)	25 (21)	49 (45)
3 IHD	20 (9)	2 (2)	18 (17)
4 Cardiac Arrest	11 (5)	2 (2)	9 (8)
5 VHD / CHD	55 (24)	53 (45)	2 (2)
6 SBE	2 (1)	1 (1)	1 (1)
7 CVA	1 (0)	0	1 (1)
8 RHD	22 (10)	22 (19)	0
9 Cardiac PE	1 (0)	0	1 (1)
10 Aortic Dissection	1 (0)	1 (1)	0

Arrhythmias included: SVT/ VT/ Sinus bradycardia and complete heart block (CHB).
IHD: Ischaemic Heart Disease.
VHD/ CHD: included valvular heart disease and congenital heart disease
SBE: Subacute Bacterial Endocarditis.
CVA: Cerebrovascular accident.
RHD: rheumatic heart disease.
Cardiac PE: Cardiac pulmonary embolus.
Type B Aortic dissection.

Appendix C Chapter Four supplementary material

Supplementary materials for the third publication are presented

C1. Cardiac diagnosis

S1 Table Cardiac Diagnosis

ICD codes	Isolated cardiac arrhythmias
R00.0, R00.1, 144.1, 144.2, 144.30	Bradyarrhythmias and Atrioventricular (AV) heart blocks.
147.1, 147.0,	Supraventricular tachyarrhythmias (SVT), i.e., atrial tachycardia and atrioventricular nodal re-entry tachycardia (AVRNT).
148.0, 148.1, 148.4, 148.9	Atrial Fibrillation (AF), and Atrial Flutter.
147.2, !49	Ventricular tachyarrhythmias: Ventricular tachycardia and ventricular fibrillation (VT and VF).
145.6	Wolff-Parkinson-White (WPW) syndrome.
145.81, 149.8	Long QT syndrome and Brugada syndrome (BrS).
	Cardiomyopathies (CMP)
142, 142.9	Dilated cardiomyopathy (DCM) includes idiopathic cardiomyopathy.
125.5	Ischaemic cardiomyopathy (IC).
142.2, 090.3	Hypertrophic cardiomyopathy (HCM).
090.3,099.4, 142	Peripartum cardiomyopathy (PPCM).
142.9	Tachycardiomyopathy (TIC).
150.9, 075.4	Acute decompensated heart failure unspecified event.
142.3, 142.4	Spongiform Cardiomyopathy.

	High-risk cardiac lesions
124.9, 121.4	Acute coronary syndrome (ACS), i.e., coronary artery disease (CAD), ischaemic heart disease (IHD), acute myocardial infarction (AMI).
151.9	At least mild systemic ventricular systolic dysfunction.
D15.1	Atrial myxoma.
Q25.1, Q23.1	Coarctation + bicuspid aortic valve.
Q 20.8	High-risk left-sided valve disease/left ventricular outflow tract (LVOT) obstruction.
Q87.4	High-risk aortopathies, i.e., Marfans Syndrome, bicuspid aortic valve with aortic arch dilation.
Z 95.2	Mechanical heart valve.
127.0	Pulmonary hypertension.
142.8	Arrhythmogenic right ventricular dysplasia (ARVD).
	Type of Congenital heart disease (CHD)
	Complex CHD
Q25.6, Q23.0	Acyanotic congenital: Aortic/pulmonary stenosis with recent acute myocardial infarction, corrected as adult: ASD closure and pulmonary valvuloplasty for pulmonary valvular stenosis.
Q25.6	Anomalies of the pulmonary artery: multiple pulmonary artery stenosis with pulmonary hypertension.
Q21.3, Q22.3	Cyanotic CHD: Ventricular septal defect (VSD) corrected later, and Tetralogy of Fallot (TOF) corrected at one year, with pulmonary valve replacement 20 years later.
V13.65	Cyanotic CHD: Fontan procedure for double inlet left ventricle, VSD, ASD, PDA / Pulmonary stenosis/juxtaposition of the atrial appendage, corrected at three years of age.
Q 44.7, Q 20.8	CHD corrected (*Cardio hepatic dysplasia, portal hypertension and cirrhosis, with jejunal atresia corrected at birth)* Corrective adult surgery for closure of ASD with a pericardial patch, RVOT, PVR tissue, for severe pulmonary stenosis.
Q21.3, 745.1	Tetralogy of Fallot (TOF) Transvascular patch, right ventricular outflow tract (RVOT) corrected at 11 months (+surgery later).
Q21.3, Q23.2, 745.1	Tetralogy of Fallot (TOF) corrected with residual mild to moderate pulmonary hypertension (PH).
Q 25.6	Pulmonary stenosis**.**
	Non-Complex
Q21.1	Atrial septal defect (ASD).
Q21.1, Q21.0.	ASD and VSD non-surgical correction with Amplatzer device (ventricular septal aneurysm).
Q 89.3	Dextrocardia (situs inversus).
Q 25.0	Patent ductus arteriosus (PDA).
Q 21.1	Patent Foramen Ovale (PFO) discovered during pregnancy uncorrected.
Q25.0, V13.65	Patent Foramen Ovale corrected as an adult with an Amplatzer device 20 years later.
Q25.0, 745.9, 745.5	Patent Foramen Ovale corrected as an adult when found ASD as well.

Q 89.9,745.4	Ventricular septal defect (VSD).
	Valvular heart disease (VHD)
Q23.0, 106.2, 746.3, 746.4	Aortic Stenosis (AS) and Aortic insufficiency /incompetence.
Q 89.9.	Anomalies of great veins: Atresia of the aorta with patent foramen Ovale (PFO). Right-sided aortic arch with an anomalous left subclavian artery from a large-mouthed aortic diverticulum with compression of the trachea between the diverticulum and the ascending aorta- required urgent surgery during pregnancy.
127.22, Q23.2, 105.0, 134.2, 746.5,	Mitral valve stenosis (MS) and pulmonary hypertension (PH).
R11.10, Q23.3, 746.1,127.22	Mitral regurgitation (MR) accompanied by PH and Tricuspid regurgitation.
R11.10,105.2, 108.3,	Mitral insufficiency (Congenital, i.e., MR due to Mitral valve prolapse or mitral valve incompetence with increased LVOT velocity and width of ascending/descending aorta.
134.1	Mitral Valve Prolapse (MVP).
108, 135.0	Mixed Valve disease (MVD).
101.9, 105.9, 108.0,108.8	Rheumatic heart disease with MVD, MS, and AS and left ventricular hypertrophy (LVH).
107.0, 107.2.	Tricuspid valve disease: regurgitation or stenosis.
	Myocardial conditions with cardiac involvement
D 68.61	Antiphospholipid syndrome.
G71.09, G71.11	Maternal Myotonic Muscular Dystrophy (MMD).
Q87.19	Noonan syndrome.
171.0	Type B aortic dissection

ICD codes URL: https://www.cdc.gov/, https://www.who.int/classifications/icd/icdonlineversions/en/ accessed 25th August 2020.

C2. Neonatal diagnosis of congenital heart disease and abnormalities

Maternal cardiac status	ICD -10 code	Congenital abnormality diagnosis in neonates
Preexisting cardiac condition of uncorrected VSD	Q26.8	Diagnosed (*at birth*) with congenital heart disease (CHD), multiple issues: two ventricular septal defects (VSD), confirmed on echocardiogram. Congestive cardiac failure treated with diuretics. Patent ductus arteriosus (PDA), two VSDs: large perimembronous VSD, large atrial septal defects (ASD) and hemi anomalous pulmonary venous drainage. A variant of scimitar or pulmonary venolobar syndrome. The baby admitted to Neonatal Intensive Care Unit (NICU), where diuretics treated heart failure, but transferred to a paediatric facility under the care of a paediatric cardiologist.
Acquired cardiac condition unmasked during pregnancy	Q87.4	Marfans syndrome diagnosed in both mother and baby (*at birth*); therefore, genetic counselling and appropriate adult and paediatric cardiology follow-up implemented. The baby required NICU admission.
Preexisting Marfans syndrome family genetic history	Q87.4	Marfans syndrome also diagnosed in the baby. Therefore, paediatric cardiology follow-up implemented.
Preexisting cardiac condition of severe mitral stenosis, tricuspid and aortic regurgitation, pulmonary hypertension, underwent an elective mitral valvuloplasty antepartum.	Q87.0	Facio-Auricular-Vertebral Spectrum (Goldenhar syndrome) premature delivery with baby admission to NICU where the congenital condition was diagnosed, and ongoing paediatric follow-up was implemented.
Preexisting cardiac condition of bicuspid aortic valve and aortic incompetence with left ventricular dysfunction	Q79. 0	Diagnosis of cyanosis and CHD (*at birth*): Rapidly cyanosed within the first few minutes of birth when found to have a significant diaphragmatic hernia on chest transferred to a paediatric facility for surgery. Required intubation and mechanical ventilation on FiO2 80 % further investigations identified pulmonary hyperplasia. Ongoing paediatric cardiology follow-up
Preexisting Genetic Congenital Noonan syndrome with secondary hypertrophic cardiomyopathy	Q87.1	The baby diagnosed with genetic 'Noonan syndrome' while in Special Baby Care Unit (SBCU) post-birth. Medical genetic counselling antepartum post fetal echocardiogram and post-delivery. Long-term paediatric follow-up.
Preexisting cardiac condition of congenital peripheral pulmonary stenosis and pulmonary hypertension	128.8	Baby to NICU *at birth* diagnosed with pulmonary stenosis with paediatric cardiology follow-up

Legend. Scimitar or pulmonary venolobar syndrome is a rare but well known congenital cardiovascular defect accessed 12102020 via URL:

https://www.ahajournals.org/doi/full/10.1161/circulationaha.109.931857 ICD codes via URL: https://www.who.int/classifications/icd/icdonlineversions/en/.

C3. Coding of clinical interventions, complications and outcomes for SPSS Variables for obstetric neonatal and maternal cardiac

SPSS variable	Description
ID	STUDY ID
Gravida	Gravida
Parity	Parity
Gestational_age_admission	Gestational_age_admission
Maternal_age	Maternal age
Apgar_1min	Apgar_1min
Apgar_5min	Apgar_5min
POSTCODE	PC
SCORE	Total Adherence score
ACQUIREDGROUP	Acquired cardiac group
PREEXISTENTGROUP	Pre-existing cardiac group
Obstetric variables that include interventions, modes of delivery and complications	
EMERGENCYLSCSHYSTRECTOMY	Emergency lower segment caesarean section (LSCS) + Hysterectomy/Laparotomy
EMERGENCYLSCS	Emergency LSCS
DELIVERYMODELSCS	(Elective) LSCS
DELIVERYNVD	Normal vaginal delivery (NVD)
DELVERYASSISTED	Assisted vaginal delivery (AVD)
DEVIATIONDELIVERYMODE	Deviation from planned delivery mode
FTP	Delayed / Failure to progress in labour (FTP)
TPOL	Threatened premature onset of labour (TPOL)
PLACENTAACCRETTA	Placenta accreta (PA)
PLACENTAPREVIA	Placenta previa (PP)
APH	Antepartum haemorrhage (APH)
PPH	Postpartum haemorrhage (PPH)
HYPERTENSIONPIT	Pregnancy-induced hypertension (PIH)
PET	Preeclampsia (PET)
IUGR	Intrauterine growth restriction or small for dates (IUGR)

SEPSIS	Sepsis (maternal)
Neonatal variables that include interventions and complications	
BABYOUTCOME1	Alive and well
BABYOUTCOME2	Neonatal Death*
BABYOUTCOME3	Intrauterine Fetal Death (IUFD)
BABYOUTCOME4	Termination of pregnancy (TOP)
BABYOUTCOME5	Prematurity <37 weeks gestation
BABYOUTCOME6	Prematurity +†NICU/SBCU3 required to stay.
BABYOUYCOME7	Active resuscitation with ‡O2 / BMV/Intubated/ IPPV
BABYOUTCOME8	Retrieval/ §CPAP/ Ventilation
BABYOUTCOME9	Active resuscitation low invasive
BABYOUTCOME10	Septic workup/ Sepsis
BABYOUTCOME11	Respiratory Distress Syndrome (RDS)
BABYOUTCOME13	Respiratory Distress Syndrome required CPAP
BABYOUTCOME12	Clinical Diagnosis of IUGR/SFD small for dates
BABYOUTCOME14	Diagnosis of congenital heart disease (CHD)
BABYOUTCOME15	Diagnosis of Congenital Abnormalities
BABYOUTCOME17	Low Apgar Score<7 at 1 minute
BABYOUTCOME18	Low Apgar score <7 at 5minutes
NICUADMISSION	NICU/SBCU3 admission
SBCU3ADMISSION	SBCU3Admission
Maternal Cardiac variables that include required interventions, complications and outcomes	
MATERNALOUTCOME1	Maternal Cardiac Death
MATERNALOUTCOME2	Cardiac Arrest
MATERNALOUTCOME3	Decompensated Heart Failure (HF)
MATERNALOUTCOME4	Acute Myocardial Infarction AMI
MATERNALOUTCOME5	Valvular Heart Disease (VHD) or Congenital Heart Disease (CHD) Diagnosis during pregnancy.
MATERNALOUTCOME6	Sustained Arrhythmias requiring treatment
MATERNALOUTCOME7	Supraventricular Tachycardia (SVT)

MATERNALOUTCOME8	Bradyarrhythmias without syncope or heart failure (HF)
MATERNALOUTCOME9	Non-specific chest pain
MATERNALOUTCOME10	Cardiovascular Implantable Electronic Device (CIED) i.e., Defibrillator /Permanent Pacemaker
MATERNALOUTCOME11	Cardiac Surgery required
MATERNALOUTCOME12	Balloon Valvoplasty required.
MATERNALOUTCOME13	‖EP studies/Cardiac ablation required
MATERNALOUTCOME14	**CTPA+ Echocardiogram required
MATERNALOUTCOME15	Coronary angiogram with/without PCI required
MATERNALOUTCOME16	An episode of cardiogenic shock requiring Intra-aortic balloon pump (IABP)
MATERNALOUTCOME17	Other complications non-cardiac

Legend: *No neonatal deaths in the cohort, †NICU/SBCU3: neonatal intensive care unit / Special Baby Care Unit level 3, ‡ O2 / BMV/Intubated/ IPPV: oxygen therapy, bag-mask ventilation, Intermittent Positive Pressure Ventilation., §CPAP/ Ventilation: Continuous Positive Pressure Ventilation, ‖CTPA EP studies/cardiac ablation = electrophysiology (EP) study and cardiac ablation procedure, ** CTPA+ echocardiogram =Computed-Tomography Pulmonary Angiogram and cardiac Echocardiogram,*** PCI percutaneous coronary intervention.

C4. Baseline characteristics of cohort

Total (n=261)	**Overall cohort=261**	**Pre-existing cardiac (PEC) n=139**	**Acquired cardiac (AC) n=122**
Maternal Age (years)	30.4±5.8	29.7±5.6	31.2±6.0
Weight (kg)	76.4±19.5	73.7 ±17.6	79.6±21.1
Height (cm)	165±7.9	165.2±8.4	165.0±7.3
∗BMI (kg/m$^{2)}$	28±7.5	27±6.4	30.1±8.4
Born in Australia	211(80.8)	112 (80.6)	99 (81.1)
Born overseas	47 (18)	24 (17.3)	23 (18.9)
Ethnicity			
Aboriginal	32 (12.3)	21(15)	11 (9.0)
Asian	15 (5.7)	8 (5.8)	7 (5.7)
Caucasian	205 (78.5)	106(76)	99 (81.1)
Other	4 (3.2)		4 (3.2)
Metropolitan	201 (77)	100 (71.9)	101 (82.8)
Rural	45(17.2)	30 (21.6)	15 (12.3)
Remote	11 (4.2)	8 (5.8)	3 (2.5)
Marital status			
Married	160 (61.3)	78 (56)	82 (67)
De facto	54(20.7)	37 (26.6)	17 (13.9)
Divorced/ Separated	6(2.3)	2 (1.4)	4 (3.3)
Single	32(12.3)	18 (12.9)	14 (11.5)
Perinatal assessment (SD)			
Gestational age on admission	37.1±3.7	36.9± 4.45	36.9±3.5
†Gravida	3.1±2.08	3.0 ±1.9	3.1 ±2.2
‡Parity	1.5±1.7	1.4 ±1.6	1.5±1.8
Blood pressure **(SD)**			
○ Systolic	115±17.3	113±17.1	117±17.4
○ Diastolic	69.9±13.3	68.2±12.8	71.9±13.8
Mental Health Scores (SD)			
§Antenatal Risk Questionnaire, (ANRQ)	18.4±12.5	17.4±12.1	19.8±13.2
‖Edinburgh Postnatal Depression Scale (EPDS)	6.3±5.9	6.0±5.9	6.8±5
Overall Adherence score (SD) =/40	16.7±6.5	17.7±6.4	15.2±6.2

∗BMI=Body Mass Index Kg/m^{2,} † Gravida on admission: number of times a woman is or has been pregnant, regardless of the outcome. ‡Parity: number of pregnancies reaching viable gestation age (includes live births & stillbirths). §ANRQ: documented score for antenatal risk questionnaire – self-reported psychosocial assessment tool. ‖ EPDS: documented score for the Edinburgh postnatal depression scale for risk of perinatal depression high score indicates depression

C5. Univariate linear regression model results for the adherence score versus obstetric clinical variables

Clinical variables	Mean difference Adherence score (95% CI)	Standardised Coefficients Beta	P value	Adjusted R Square	R Square Change	n (%) N=261
Obstetric complications.						
Pregnancy-induced hypertension (PIH)	3.060 (0.861,5.259)	0.168	0.007	0.024	0.028	39 (14.9)
Preeclampsia (PET)	3.202 (0.528,5.875)	0.145	0.019	0.017	0.021	25 (9.6)
Threatened premature onset of labour (TPL)	2.857 (0.388,5.325)	0.140	0.023	0.016	0.020	30 (11.5)
Delayed / Failure to progress in labour (FTP).	0.931 (-1.636,3.497)	0.044	0.476	-.002	0.002	28 (10.7)
Placenta accreta (PA)	2.659 (-4.794,10.111)	0.044	0.483	-0.002	0.002	3 (1.1)
Placenta previa (PP)	4.818 (0.243,9.393)	0.128	0.039	0.013	0.016	8 (3.1)
Antepartum haemorrhage (APH)	-1.306 (-5.660,3.049)	-0.037	0.555	-0.003	0.001	9 (3.4)
Modes of delivery.						
Normal vaginal delivery	-5.358 (-6.850, -3.866)	-0.402	<0.001	0.159	0.162	104 (39.1)
Assisted vaginal delivery	-1.199 (-3.806,1.407)	-0.056	0.366	-0.001	0.003	27 (10.3)
Elective caesarean (†LSCS)	5.316 (3.676,6.956)	0.369	<0.001	0.133	0.136	74 (28.4
Clinical variables.	**Mean difference Adherence score (95% CI)**	**Standardised Coefficients Beta**	**P value**	**Adjusted R Square**	**R Square Change**	**N=261**
Emergency LSCS	1.726 (-0.225,3.6278)	0.108	0.083	0.008	0.012	54 (20.7)
Emergency LSCS+ Hysterectomy/Laparotomy	1.569 (-4.901, 8.039)	0.030	0.633	-0.003	0.001	4 (1.5)
***Deviated from planned delivery mode.**	2.000 (0.354,3.646)	0.147	0.017	0.018	0.022	92 (35.2)
Obstetric complications continued.						
Postpartum haemorrhage (PPH)	0.503 (-1.802,2.808)	0.027	0.668	-0.003	0.001	36 (13.8)
Abnormal Doppler	4.413 (-0.479,9.305)	0.110	0.077	0.008	0.012	7 (2.7)
Abnormal ‡ IUGR	5.610 (1.525,9.695)	0.166	0.007	0.024	0.027	10 (3.8)
Sepsis	-3.082 (-6.478,0.313)	-0.110	0.075	0.008	0.012	15 (5.7)

Legend: Significance p value <0.2. All covariates /predictors were yes vs no. * Deviated from planned delivery mode; those women with planned NVD who required alternate listed modes or Elective LSCS deviated to precipitous SVD or Emergency LSCS. †LSCS: Lower Segment Caesarean Section. ‡ IUGR: Intrauterine Growth Restriction

C6. Univariate linear regression model results for the total adherence score versus neonatal clinical variables

Clinical variables	Mean difference Adherence score (95% CI)	Standardised Coefficients Beta	P value	Adjusted R Square	R Square Change	n (%) N=261
⋆Baby Alive and well	-3.457 (-5.185, -1.729)	-0.238	<0.001	0.053	0.057	189 (72.4)
Intrauterine Fetal Death (IUFD)	2.304 (-10.564,15.171)	0.022	0.725	-0.003	0.000	1 (0.4)
Termination of pregnancy (TOP)	-6.731 (-19.575,6.114)	-0.064	0.303	0.000	0.004	1 (0.4)
Birth complications						
Prematurity	3.762 (1.727, 5.798)	0.221	0.001	0.045	0.049	46 (17.6)
†Prematurity+ NICU/SBCU3	3.927 (1.817,6.037)	0.222	<0.001	0.049	0.049	42 (16.1)
Active resuscitation with O2 / BMV/Intubated/ IPPV	4.093 (1.784,6.402)	0.212	<0.001	0.045	0.045	34 (13)
Retrieval/ †CPAP/ Ventilation	2.492 (-1.855,6.839)	0.070	0.260	0.001	0.005	9 (3.4)
Active resuscitation of baby (low invasive) at birth	1.698 (-0.996,4.391)	0.077	0.216	0.006	0.006	25 (9.6)
‡ Low Apgar Score<7 at 1 minute	3.092 (0.718,5.403)	0.162	0.009	0.023	0.026	35 (13.4)
Low Apgar Score<7 at 5 minutes	5.025 (1.942,8.108)	0.196	0.001	0.035	0.038	18 (6.9)
Respiratory Distress Syndrome (RDS)	4.658 (2.501,6.814)	0.256	<0.001	0.065	0.065	39 (14.9)
Respiratory Distress Syndrome (RDS) with CPAP ventilation	3.998 (1.116,6.880)	0.167	0.007	0.024	0.028	21 (8)
Clinical variables	**Mean difference Adherence score (95% CI)**	**Standardised Coefficients Beta**	**P value**	**Adjusted R Square**	**R Square Change**	**n (%) N=261**
§NICU Admission	5.240 (3.589,6.892)	0.362	<0.001	0.128	0.131	73 (28)
SBCU3 Admission	0.677 (-3.206,1.852)	-0.033	0.599	-0.003	0.001	29 (11.1)
‖Clinical Diagnosis of IUGR/SFD.	5.194 (1.101,9.287)	0.153	0.013	0.020	0.024	10 (3.8)
Diagnosis of congenital heart disease (CHD)	6.443 (1.196,11.690)	0.149	0.016	0.018	0.022	6 (2.3)
Diagnosis of Congenital Abnormalities (other)	7.010 (2.477,11.542)	0.186	0.003	0.31	0.035	8 (3.1)
Septic workup/ Sepsis	0.854 (-2.282,3.990)	0.033	0.592	-0.003	0.001	18 (6.9)

Legend: Significance p value <0.2. All covariates /predictors were yes vs no. ⋆Documented as 'Alive and Well' by clinicians at birth, †Prematurity required admission to neonatal intensive care unit (NICU) or special baby care unit (SBCU3). †Active Resus+ O_2/BMV/ intubate /IPPV: active resuscitation that required oxygen administration (O_2), bag-mask ventilation (BMV) but also required intubation (intubate) and mechanical ventilation mode of intermittent positive pressure ventilation (IPPV) CPAP: mode of ventilation Continuous Positive Pressure ventilation,‡ Missing data totals for Apgar score<7at 1 min = 2, and at 5 min =1, §NICU admission baby admitted for other reasons, i.e. flat at birth, required active resuscitation, RDS, hypothermia, for observations and as boarder due to maternal issues, ‖ IUGR/SFD intrauterine growth restriction/ small for dates.

C7. Univariate linear regression model results for the adherence score versus maternal cardiac clinical variables

Clinical variables	Mean difference Adherence score (95% CI)	Standardised Coefficients Beta	P value	Adjusted R Square	R Square Change	n (%) N=261
Acquired cardiac group	-2.278 (-3.847, -0.709)	-0.175	0.005	0.027	0.031	122 (46.7)
Pre-existing cardiac group	2.278 (0.709, 3.847)	0.175	0.005	0.027	0.031	139 (53.2)
Complications and clinical outcomes.						
Maternal Cardiac Death.	-9.742 (-22.558, 3.073)	-0.093	0.136	0.005	0.009	1 (0.4)
Cardiac Arrest.	2.016 (-1.933,5.966)	0.062	0.316	-0.000	0.004	11 (4.2)
Decompensated Heart failure.	4.353 (1.925,6.145)	0.246	<0.001	0.061	0.061	42 (16.1)
Acute Myocardial Infarction (AMI).	-4.185 (-9.963,1.593)	-0.088	0.155	0.004	0.008	5 (1.9)
Valvular Heart Disease (VHD) or Congenital Heart Disease (CHD) New Diagnosis.	0.410 (-1.448,2.267)	0.027	0.664	-0.001	0.001	63 (24.1)
Sustained Arrhythmias requiring treatment.	-0.055 (-1.792,1.682)	-0.004	0.951	-0.004	0.000	78 (29.9)
Supraventricular Tachycardia (SVT).	-0.256 (-2.027,1.515)	-0.018	0.776	-0.004	0.000	73 (28)
Bradyarrhythmias without syncope or heart failure (HF).	-1.001 (-4.796, 2.794)	-0.032	0.604	-0.003	0.001	12 (4.6)
Non-specific chest pain.	0.584 (-1.405,2.574)	0.036	0.563	-0.003	0.000	52 (19.9)
Clinical variables.	**Mean difference Adherence score (95% CI)**	**Standardised Coefficients Beta**	**P Value**	**Adjusted R Square**	**R Square Change**	**n (%) N=261**
Cardiac investigations during pregnancy included diagnostic and treatment.						
Coronary angiogram with and without *PCI.	-1.349(-4.874,2.177)	-0.047	0.452	-0.002	0.002	14 (5.4)
†CTPA+ Echocardiogram.	-2.064 (-4.707,0.578)	-0.095	0.125	0.009	0.009	26 (10)
‡EP studies/Cardiac ablation.	-1.766 (-6.118, 2.587)	-0.050	0.425	-0.002	0.002	9 (3.4)
Cardiovascular Implanted Electrical Device (CIED)	4.396 (-0.882,9.674)	0.101	0.102	0.006	0.010	6 (2.3)
Cardiac Surgery required.	8.149 (2.938,13.360)	0.188	0.002	0.032	0.035	6 (2.3)
Balloon Valvoplasty procedure during pregnancy.	9.403 (2.033,16.773)	0.154	0.013	0.020	0.024	3 (1.1)
Cardiogenic Shock with intra-aortic balloon pump (IABP).	1.300 (-11.570,14.170)	0.012	0.842	-0.004	0.000	1 (0.4)

Other non-cardiac complications						
‡Other non-cardiac complications	2.863 (-0.437,6.163)	0.106	0.089	0.007	0.011	16 (6.2)

Legend: Significance p value <0.2. All clinical variables were yes vs no. * PCI =percutaneous coronary intervention, CTPA+ Echocardiogram= Computed -Tomography Pulmonary Angiogram and cardiac echocardiogram ‡EP studies/Cardiac ablation = electrophysiology (EP) study and cardiac ablation procedure. §Other non-cardiac complications included ruptured splenic artery –laparotomy and splenectomy, hepatic encephalopathy and bleeding gastric varices, oesophageal sclerotherapy.

C8 Cardiac arrests cases, associated pathology and outcomes

Timing	Pathology	Outcomes
First trimester antepartum	Primigravida with no comorbidities. Out of hospital cardiac arrest of Ventricular Fibrillation (VF) with paramedics in attendance.	Resuscitation with hospital admission for intensive care therapy and cardiovascular implantable electronic device (CIED). Live baby at term.
Second trimester antepartum	Multigravida with comorbidities of Rheumatic heart Disease (RHD), Mitral regurgitation (MR). Cardiac arrest with current pregnancy complicated by pneumonia, severe preeclampsia and eclampsia seizure.	The mother was resuscitated, treated with hydralazine, magnesium sulphate with early emergency LSCS. Baby and mother survived and followed up by cardiology.
Second trimester antepartum	Multigravida presented to the hospital with evidence of intracranial bleed (unknown aetiology), cardiac arrest with sudden Acute Pulmonary Oedema (APO).	Intensivist referred to the cardiologist—multidisciplinary team discussion with retrieval to a higher care facility. Mother resuscitated with advanced life support in transit, required neurosurgery and emergency LSCS—diagnosis of ongoing left ventricular failure, provisional peripartum cardiomyopathy. Preterm newborn required active resuscitation and admission to the neonatal intensive care unit (NICU).
Second trimester antepartum	Multigravida with comorbidities of chronic hypertension and Gestational Diabetes (GD). Hospital admission for chest pain and dysponea rapidly deteriorated with APO and cardiopulmonary arrest.	She was resuscitated with advanced life support. Hypertension treated with IV hydralazine, esmolol, lignocaine 1% 80mg, and magnesium sulphate infusion preceded emergency LSCS and subsequent retrieval to a higher care facility for intensive care therapy diagnosis of preeclampsia with APO and diastolic heart failure. Medical follow-up for chronic hypertension. The baby required resuscitation at birth and admission to NICU for prematurity
Second trimester postpartum	Multigravida, with history of Rheumatic Fever (MR), Polycystic ovary syndrome, cholecystectomy. This pregnancy precipitous preterm delivery of the first baby of multiple births *at home,* subsequent deliveries in hospital complicated by unconscious maternal collapse postpartum.	The mother survived in the postnatal ward with the resuscitation team in attendance and followed up with cardiology. Triplets required admission to NICU for prematurity.

Second trimester Antepartum	Multigravida, with known mixed valve disease RHD, left brachial artery thrombosis. Recurrent tracheal papillomas and diagnosis of granuloma gravidarium of the trachea accompanied by severe mitral regurgitation, eccentric left ventricular hypertrophy. Respiratory followed by cardiac arrest.	Mother and baby survived with advanced life support measures by the retrieval team—emergency LSCS following retrieval to the higher obstetric care facility. The preterm baby required active resuscitation, respiratory support in NICU for 48 hours. Cardiothoracic surgery with cardiopulmonary support occurred 24 hours post-delivery for debulking of the tumour.
Third trimester antepartum	Primigravida. Pregnancy complications of gestational diabetes and chronic hypertension. Rapid deterioration while attending the blood pressure monitoring clinic with cardiac arrest, ECG: Ventricular Tachycardia (VT) Acute Pulmonary Oedema (APO), (*Post cardiac arrest undeclared congenital condition previous atrial switch procedure).*	Protracted resuscitation with advanced life support and emergency LSCS. Retrieval to a higher care facility for intensive care treatment for subsequent cardiogenic shock and long-term rehabilitation. Baby retrieved to NICU. Both mother and baby survived, with long-term cardiology follow-up.
Third trimester at delivery	Primigravida, a high risk pregnancy complicated by antepartum haemorrhage (APH) treated with blood transfusion. Hospitalised when placenta praevia grade IV and accreta were noted. Emergency LSCS for APH and hysterectomy. Cardiac arrest occurred during the anaesthetic preparation, with VT.	Resuscitation managed by an anaesthetic team with CPR and IV drugs while the surgeon closed the abdominal wound, having achieved haemostasis. Normalisation of the ECG (Sinus tachycardia with ST-segment depression) and Cardiac output. The woman required respiratory support and intensive care treatment for a further 24 hours.
Third trimester at delivery	Multigravida planned (repeat) LSCS for breech presentation (*no issues with spinal*). Cardiac arrest with Asystole on ECG during delivery.	She was resuscitated with CPR, IV drugs and urgent LSCS for fetal bradycardia. Mother and baby alive and well. Post cardiac arrest anaesthetic and cardiology follow-up.
Third trimester at delivery	Primigravida, comorbidities of familial hyperlipidaemia and an incidental finding of Wolf Parkinson White syndrome (WPW) on ECG following cardiology review. Pregnancy complications of preeclampsia and pulseless electrical activity (PEA) cardiopulmonary arrest, post epidural analgesia during labour.	Resuscitated with 20 minutes of CPR and IV drugs, until ECG, and cardiac output (CO) restored. The woman required invasive respiratory support, therapeutic hypothermia, and intensive care therapy for 48 hours—mother followed up by cardiology. Finally, the baby boarded in NICU.
Third trimester postpartum	Multigravida comorbidities of chronic hypertension, gestational diabetes, recent diagnosis of left bundle branch block (LBBB) on ECG. Unwitnessed VF cardiac arrest while an inpatient (unmonitored).	Resuscitation protracted with advanced life support and ongoing ICU management for respiratory support, further cardiac investigations, and CIED. Finally, the mother required residential care and long-term respiratory support following complication of global hypoxic encephalopathy.

C9. Cardiac, obstetric, and other indications for the Emergency /Elective lower segment caesarean sections.

Cardiac Indications ± Obstetric complications	**Frequency**	**Women=Deviation from plan**
Valve disease with preeclampsia.	n=2	n=2
Valve disease with decompensated heart failure.	n=3	n=3
Stable severe stenotic valve disease.	n=1	n=1
Dilated cardiomyopathy resulting in severe pulmonary hypertension and / or decompensated heart failure.	n=5	n=5
Worsening primary pulmonary hypertension with heart failure. \	n=1	n=1
Marfans Syndrome, with significant aortic root dilation.	n=3	n=2
Type B aortic dissection antepartum.	n=1	n=1
Complex Cardiovascular Anatomy with preeclampsia.	n=1	n=1
Cardiac arrests.	n=3	n=3
Acute pulmonary oedema of unclear cause.	n=1	n=1
Obstetric Indications		
Antepartum:		
Placental Abruption (n=1)/ Placenta Accreta /Placenta Previa, Grade III and IV /Antepartum haemorrhage.	n=16	n=1
Pregnancy-induced hypertension (23)/ Preeclampsia and eclampsia (25) with additional obstetric complications.	n=48	n=25

Obstetric Indications continued	**Frequency**	**Women= deviation from plan**
Delivery related:		
Repeat Lower Segment Caesarean Section **(**LSCS) +	n= 70	n=50
Failed to progress (FTP)/instrumental delivery or induction of labour + Cord prolapse (n=1).	n=27	n=27
Malpresentation: Breech / Brow + cholestasis of pregnancy.	n= 6	n=6
Threatened premature onset labour and /premature onset of labour, with MCDA twins and malpresentation.	n=19	n=19
Failed instrumental delivery or induction of labour (IOL).	n=5	n=5
Premature rupture of membranes <24 hours with additional obstetric complications, e.g., threatened premature labour (TPL) with a congenital cardiac condition.	n=6	n=5
Obstetric Baby related:		
Fetal distress, e.g., Fetal Tachycardia /bradycardia.	n=13	n=13
Abnormal Doppler (n= 5) /‡IUGR/(N=6) /Asymmetrical growth.	n= 11	n=11
IUGR + Polyhydramnios/ Oligohydramnios low liquor.	n=5	n=5
Multiple births, i.e., §MCDA/ DCDA twins with growth discrepancy, malpresentation or past LSCS.	n=3	n=3
Other indications		
Maternal Myotonic Muscular dystrophy (MMD) plus uterine dehiscence.	(n=1)	n=1
‖. IVF pregnancy + maternal request, history of pregnancy loss, FTP, repeat LSCS (n=2) + hypertensive heart disease.	(n=3)	n=1
Preexisting poorly controlled hypertension with decompensated heart failure.	(n=1)	n=1

Legend, ‡IUGR: intrauterine growth restriction, §MCDA: monochorionic diamniotic twins share the same chorionic sac but have two amniotic sacs, DCDA: dichorionic diamniotic twins each twin has its own chorionic and amniotic sac, ‖IVF: in vitro fertilisation. NB: There were women with multiple adverse clinical factors for obstetric indications for LSCS; therefore, overlapping of indications occurred.

Appendix D Additional Supplemental materials

1. SAPPGS Chapter 64 Cardiac Disease in pregnancy 2010.
2. South Australian Pregnancy Record 2004.
3. South Australian Pregnancy Record 2012

Included in this section is the South Australian Perinatal Guidelines for Cardiac Disease in pregnancy which are no longer available online at the SA health website for perinatal guidelines. These guidelines were used for the development of the data abstraction tool (DAT). Also, included ae two examples of the South Australian pregnancy used in clinical practice for 2004 and 2012 respectively. The KEMH cardiac guidelines have not been included here as they are still available online, and were used in the development of DAT.

South Australian Perinatal Practice Guidelines

Chapter 64 Cardiac disease in pregnancy

Maternity Care in SA

Government of South Australia
SA Health

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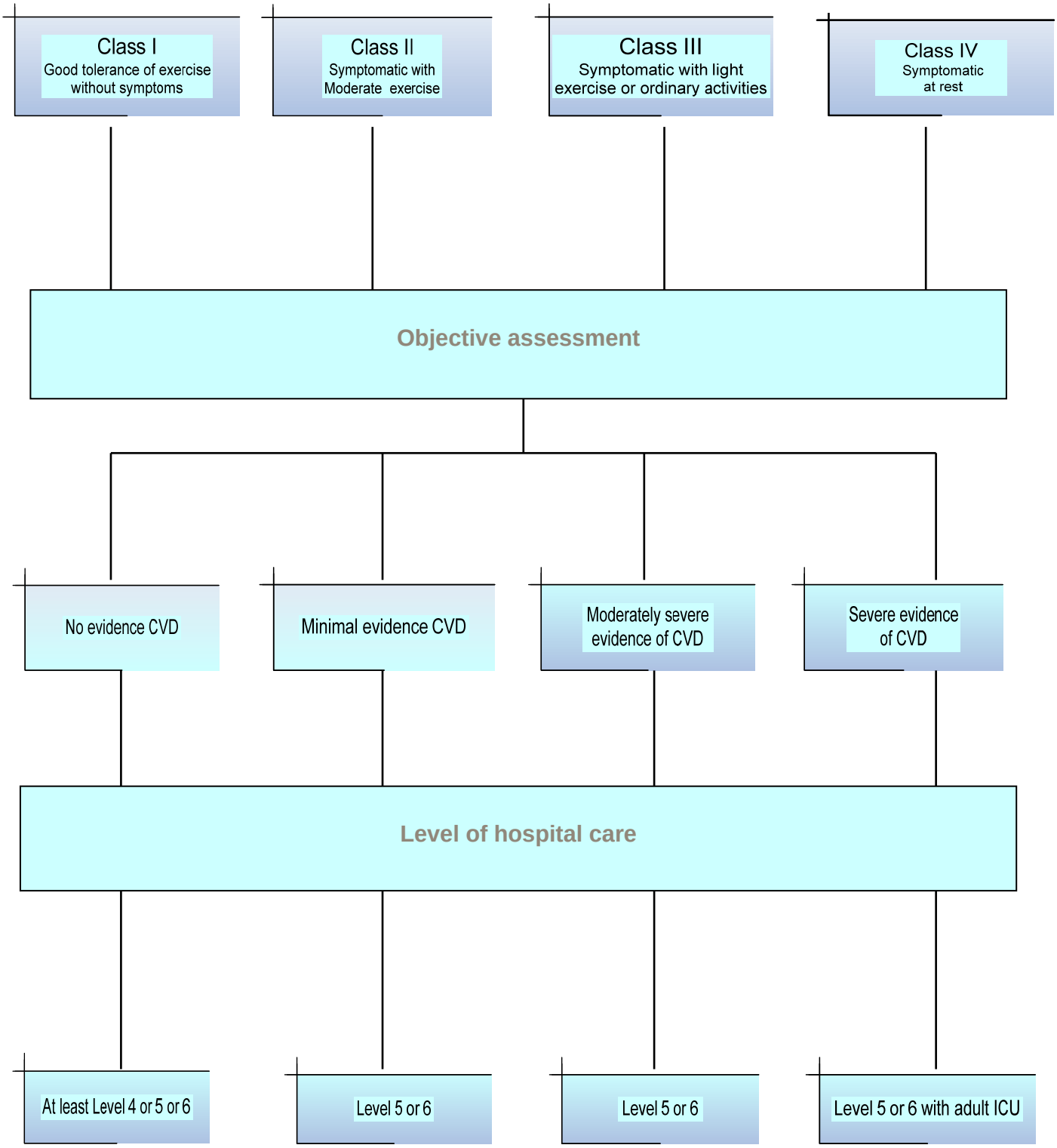
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Although the clinical material offered in this guideline provides a minimum standard it does not replace or remove clinical judgement or the professional care and duty necessary for each specific patient case. Where care deviates from that indicated in the guideline contemporaneous documentation with explanation should be provided.

This guideline does not address **all** the elements of guideline practice and assumes that the individual clinicians are responsible to:

- Discuss care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes the use of interpreter services where necessary
- Advise consumers of their choice and ensure informed consent is obtained
- Provide care within scope of practice, meet all legislative requirements and maintain standards of professional conduct
- Document all care in accordance with mandatory and local requirements

Level of hospital care according to NYHA functional classification



Abbreviations

NYHA	New York Heart Association
e.g.	For example
EDC	Estimated date of confinement
ECG	Electrocardiogram
AFI	Amniotic fluid index
TOP	Termination of pregnancy
SVT	Supraventricular tachycardia
AV	Atrio ventricular
RF	Radio frequency
ICD	Internal cardiac defibrillator
PA	Pulmonary artery
DC	Direct current
BSA	Body surface area
ACE	Angiotensin converting enzyme
TCPC	Total cavopulmonary connection
MI	Myocardial infarction
CEMCH	Confidential Enquiry into Maternal and Child Health
AHA	American Heart Association
UFH	Unfractionated heparin
LMWH	Low molecular weight heparin
INR	International normalised ratio
APTT	Activated Partial Thromboplastin Time
mL	Millilitre(s)
mg	Milligram(s)
AS	Atrial stenosis
AR	Atrial regurgitation
MS	Mitral stenosis
MR	Mitral regurgitation
BPM	Beats per minute
LV	Left ventricular
EF	Ejection fraction
RPM	Respirations per minute
IU	International unit(s)
ICU	Intensive care unit
IUCD	Intrauterine contraceptive device
g	Gram(s)
DVT	Deep venous thrombosis
ACC	American College of Cardiology
CCU	Coronary care unit
IUGR	Intrauterine growth restriction

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Table 64.1 Allocation of care according to severity of cardiac disease

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Table 64.3 CEMACH 2003-2005 Indirect maternal deaths

Table 64.4 Cardiovascular Drugs in Pregnancy

Introduction

- Between 1 % and 3 % of women will have a form of cardiac disease diagnosed before or during pregnancy
- Cardiac pathology may be:
    - Congenital or acquired
    - Functional or structural
    - Cyanotic or non-cyanotic
    - Or may include endocardial, myocardial or pericardial defects (Gei, Hankins 2001)
- Specific hazards for women with cardiac disease in pregnancy include:
    - The occurrence of pulmonary oedema (main cause of death)
    - Pulmonary hypertension
    - Infective endocarditis
    - Thromboembolism
    - Fulminating peripartum cardiomyopathy
    - Aortic dissection, arrhythmias
- The most frequent causes of cardiac disease in pregnancy are:
    - Rheumatic heart disease
    - Congenital heart disease
    - Arrhythmias
    - Ischemic heart disease
    - Heart failure
- Fetal risks
    - Congenital heart disease
    - Intrauterine growth restriction
    - Prematurity

New York Heart Association (NYHA) functional classification

- Classification of the severity of heart disease can aid in the prediction of maternal and neonatal outcomes and in the counselling of prospective parents (Davies, Herbert 2007a)

Class	Clinical Implications	Objective Assessment
I	Good tolerance of exercise without symptoms (chest pain, angina, dyspnoea, palpitations, fatigue)	No objective evidence of cardiovascular disease
II	Symptomatic with moderate exercise	Objective evidence of minimal cardiovascular disease
III	Symptomatic with light exercise or ordinary activities	Objective evidence of moderately severe cardiovascular disease
IV	Symptomatic at rest	Objective evidence of severe cardiovascular disease

Adapted from American Heart Association. In: Dobbenga-Rhodes YA, Privé AM. Assessment and evaluation of the woman with cardiac disease during pregnancy. J Perinat Neonat Nurs 2006; 20: 295-302.

Preconception care

- Assessment of the woman's general physical condition, medications and cardiac function
- Optimise management of hypertension / arrhythmias
- Assess lifestyle risk factors e.g. smoking and education to optimise exercise tolerance
- Ideally, discussions should occur between the woman, her family and a cardiologist,

physician, obstetrician and / or anaesthetist familiar with the management of cardiac diseases in pregnancy to agree and decide on the best timing for pregnancy

- Points to be discussed include:
    - The natural history of the woman's disease, including the possibility of a successful pregnancy through medical treatment and optimising the woman's cardiac function
    - Present clinical staging of cardiac disease as per New York Heart Association functional classification
    - Optimising the woman's clinical condition by changes in medications or surgical procedures before conception
    - Expected outcomes including chance of spontaneous miscarriage, live birth, death, proposed care plan of the pregnancy and implications of admissions, antenatal care, anaesthesia, medications and peripartum management
    - The risk of transmitting the cardiac condition or syndrome to offspring (Alfredo et al. 2001)

Antenatal management

- Routine booking visit around 10 to12 weeks
- Early ultrasound to establish estimated date of confinement (EDC)
- These women should be managed by a multi disciplinary team, which might include an obstetrician, cardiologist or obstetric physician, anaesthetist and intensivist. These clinicians should all be familiar with the management of cardiac problems in pregnancy
- The woman should be involved in a discussion about the management of the pregnancy. This should include:
    - Decision about the most appropriate facility to deliver the woman and criteria for changing the place of birth
    - Antenatal visits in high risk medical clinic every 2 weeks if required because of severity of disease
    - Regular review of functional cardiac status at each visit
    - Echo cardiograms with timely follow up by Obstetrician and Cardiologist
    - Avoid anaemia – iron supplementation, prenatal vitamins and dietary counselling and regular haemoglobin checks
    - Ongoing discussion regarding work schedules and levels of activity
    - Arrange anaesthetic review before 28 weeks

Clinical assessment

History

- Maternal age, gestational age, parity status, NYHA functional classification, comorbid conditions, previous cardiac events / surgery / interventions, cardiac lesions, cyanosis (oxygen saturation < 90 %), medications, use of cigarettes and / or alcohol

Investigations

- 12-lead electrocardiogram (ECG)
- Echocardiographic assessment to determine:
    - Systemic (left) and venous (right) ventricular systolic function,
    - Doppler quantification of inflow or outflow obstruction
    - Doppler quantification of valvular function
    - Right heart pressures and systolic if measurable (Siu et al. 2001)

Fetal wellbeing

- Women with cyanotic heart disease, NYHA III or IV, left heart obstruction, smokers, multiple gestation and anticoagulation are at high risk of having a fetus with growth restriction. These women should be offered regular ultrasound assessments of fetal

well being (growth, umbilical artery Doppler, AFI) and cardiotocography in the third trimester

Fetal risks

- Fetal cardiac assessment is necessary because there is a 2 to 16 % risk of congenital heart disease in the fetus in pregnant woman with congenital heart disease. The incidence of congenital heart disease in the offspring is more common in the fetus when the mother, rather than the father, is affected, particularly if the mother has a condition such as bicuspid aortic valve, which is more common in the male
- Early diagnosis of congenital heart defect in the fetus (before 24 weeks of gestation) allows the possibility of termination of the pregnancy (TOP)
- Affected fetuses benefit from delivery in a tertiary care centre with Paediatric Cardiac Support
- The two main determinants of fetal prognosis are maternal functional class and the degree of maternal cyanosis. When the mother is in functional class III to IV, or has a high risk disease such as severe aortic stenosis or Eisenmenger syndrome or is cyanosed, monitoring of fetal growth is very important
- Neonatal survival is low before 28 weeks (< 75 %) and the risk of cerebral palsy in the surviving neonates is high (10–14 %). Therefore, when cardiac function is reduced to critical levels, surgery or percutaneous procedures to improve maternal cardiac function should be undertaken, if feasible, in order to postpone delivery as long as possible
- The choice between corrective procedures and delivery may be difficult between 28 and 32 weeks, and decisions must be individualized. If the fetus is going to be delivered at < 34 weeks, lung maturation must be induced by betamethasone administration to the mother

Level of hospital care (see Table 64.1)

- Echocardiographic assessment results and the ongoing NYHA functional classification will determine if the level of hospital care required is:
    - Hospital of choice care (must be at least Level 4)
    - Tertiary centre care (Level 5 or 6)
    - Tertiary centre with onsite specialist adult cardiac service care and adult intensive care (available at some Level 5 or 6 hospitals)
- It may be possible for some women to have some antenatal visits with a geographically closer unit (“shared care”) if delivery at a higher level unit is required. This should be negotiated on a case by case basis
- Women with NYHA functional class I will usually require care in a tertiary centre (Level 4, 5 or 6)
- Women with NYHA functional class II, III, IV may be referred to a hospital with onsite specialist adult cardiac service care and adult intensive care (Level 5 or 6), particularly if there is a history of:
    - Severe cardiac condition (see specific cardiac conditions)
    - Valve replacement or other cardiac surgery
    - Any particular risk of endocarditis
- Referral to a hospital with specialist adult cardiac service (Level 5 or 6) may be required if condition worsens

Cardiac condition stable:

- Aim for vaginal birth at term (see individual cardiac diagnoses for specific contra indications for vaginal delivery)
- Consider caesarean section only for obstetric indications

- Inform the woman that decisions about her management may change at short notice
- Maintain ongoing communication within the high risk medical team
- Further investigations may be indicated, e.g. echo, chest X ray etc

Specific conditions

Benign arrhythmias

- Includes sinus tachycardia, premature atrial and ventricular contractions, paroxysmal supraventricular tachycardia (SVT), atrial fibrillation, atrial flutter
    - The majority of women with arrhythmias during pregnancy have a benign increased rate of atrial or ventricular premature beats (Davies, Herbert 2007e). Both ectopic beats and sustained arrhythmias become more frequent during pregnancy. They may even develop for the first time. In general they are treated in the same way as non pregnant patients, but as conservatively as possible. Definitive treatment is reserved for the post partum period if it is safe to do so. Women who are worried about ectopic beats can usually be reassured unless the frequency increases on exercise
    - Haemodynamically stable women do not usually require treatment
    - Advise woman to avoid precipitating factors such as caffeine, alcohol, tobacco, fatigue and anxiety

Other arrhythmias

- Women with more ominous atrial arrhythmias (supraventricular tachycardia, atrial fibrillation and flutter) should be managed in collaboration with a cardiologist, usually using the same agents that would be chosen in the non pregnant woman, including electrical cardioversion when necessary (Davies, Herbert 2007e)
- All commonly used anti-arrhythmic drugs cross the placenta. The pharmacokinetics of drugs are altered in pregnancy and require close clinical monitoring to ensure maximum efficacy and avoid toxicity
- Supraventricular tachycardias are corrected by vagal stimulation or, failing that, intravenous adenosine. If adenosine is unsuccessful at restoring sinus rhythm consider using β-blockers or verapamil. Electrical cardioversion is not contraindicated and should be used for any sustained tachycardia causing haemodynamic instability and therefore threatening fetal wellbeing. Beta blocking drugs with beta-1 selectivity are the first choice for prophylaxis. Verapamil is constipating but may be used if there is a contraindication to β-blocker use (such as asthma)
- Both β-blockers and the dihydropyridone calcium antagonists can cause fetal bradycardia. If the arrhythmia is uncontrolled and severely compromising the health of the mother and fetus, radio frequency ablation for atrio ventricular (AV) nodal re-entry or certain atrio ventricular re-entry tachycardias can, if necessary, be performed during pregnancy with suitable lead shielding and maximal use of echo rather than X-ray fluoroscopy
- Class I agents such as flecainide may be considered if the maternal left ventricle is normal. Information on its use in pregnancy is limited. Of the Class III agents, sotalol is much more preferable to amiodarone and has similar risks to β-blockers with the increased risk of torsdae de pointes due to QT prolongation. Amiodarone should be avoided unless the maternal arrhythmia is life-threatening to the mother or fetus, other agents have failed and the arrhythmia is not manageable with radiofrequency (RF) ablation. Long term use of amiodarone can cause neonatal hypothyroidism (9 % of newborns), hyperthyroidism, and goitre

- Potentially life threatening ventricular tachyarrhythmias are much less common and should be terminated by electrical cardioversion if causing maternal haemodynamic compromise. Management requires the opinion of a cardiologist and should be managed as in the non-pregnant woman. This includes the use of antiarrhythmic medication in the short- to long-term and / or the likely insertion of an automatic internal cardiac defibrillator (ICD)

Pacemakers and automatic internal cardiac defibrillators (ICD)

- The presence of a pacemaker or an ICD does not itself contraindicate pregnancy. The presence of any underlying structural heart disease determines the risk of pregnancy
- Pregnancy in patients with an ICD does not cause increased ICD–related complications or adverse events in the mother or fetus; neither does it increase the number of ICD discharges
- A pacemaker for the alleviation of symptomatic bradycardia, or ICD can be implanted at any stage of pregnancy using X-ray fluoroscopy with suitable lead shielding and echo guidance
- Any woman with an ICD should be advised to carry identification information about the ICD type, date implanted, and location of implantation in her South Australian pregnancy record. A plan for deactivation in case of an emergency should be documented in her South Australian pregnancy record.
- The presence of a pacemaker or ICD should not alter the mode of delivery. This is determined by obstetric indications
- If Caesarean section is required, the ICD should be temporarily inactivated (preferably by reprogramming or in an emergency by application of a magnet over the generator) until the procedure is finished. While inactivated, the patient should have continuous ECG monitoring and external defibrillation available at all times

Rheumatic heart disease and mitral stenosis

- The incidence of rheumatic heart disease is decreasing in developed countries. Mitral stenosis is the most common sequelae
- In women with rheumatic heart disease, the mitral valve is most commonly affected. Mitral stenosis occurs in 90 % of cases, mitral regurgitation in 7 %, aortic regurgitation 2.5 % and aortic stenosis in 1 % of cases of rheumatic heart disease (Davies, Herbert 2007c)

Mitral stenosis

- Women with mild (NYHA class I) mitral stenosis may be asymptomatic until pregnancy – the increase in left atrial pressure may lead to subsequent symptoms of dyspnoea, and eventually tachypnoea, orthopnoea, and paroxysmal nocturnal dyspnoea
- Manage according to symptoms and with the guidance of echocardiography, which is the key to the assessment of valvular severity. Mitral stenosis is considered severe and associated with significant increased maternal and fetal risk when the mitral valve area is estimated to be < 1.5 cm^2, the functional capacity is NYHA III or IV or the right heart pressures rise significantly (estimated PA systolic pressure > 50 mmHg or > 75 % of the systemic pressure)

Medical treatment

- Limitation of exercise, fluid and salt restriction should be used when the functional class is NHYA II or more

- In cases of poor functional tolerance, consider oral β-adrenergic blockers (decreases maternal tachycardia), and judicious use of diuretics, avoiding vigorous volume depletion to protect against uteroplacental hypoperfusion (caution in women with severe mitral stenosis – may need concurrent use of invasive haemodynamic monitoring) (Davies, Herbert 2007c)
- Aggressively cardiovert new onset atrial fibrillation back to sinus rhythm with β-blockers, verapamil and / or direct current (DC) cardioversion (see above)
- Consider digoxin to control the ventricular response to chronic atrial fibrillation.
- See anticoagulation prophylaxis for treatment recommendations

Intervention

- Women who fail medical treatment during pregnancy with repeated episodes or persistent heart failure should be considered for percutaneous mitral valvotomy if suitable anatomy is present. After successful mitral valvotomy, pregnancy can often continue successfully to term
- Surgical replacement of the mitral valve is used as a last resort with high fetal risk of peri-operative death. If possible, this should be delayed until the fetus is viable and can be delivered before the surgical intervention

Intrapartum

- The mode of delivery is determined by obstetric indications only.
- Care in tertiary centre for NYHA functional class I, II. These patients can be managed in the delivery suite without invasive monitoring. ECG monitoring to monitor maternal heart rate would be preferable.
- NYHA functional class III, IV: Refer to hospital with specialist adult cardiac service and invasive monitoring in labour. These patients should be managed in an intensive care setting with invasive monitoring, avoiding haemodynamic stress and having careful control of heart rate. Tachycardia can be prevented with intravenous esmolol as necessary
- Excellent pain control is important and choices should be planned in advance in consultation with the anaesthetist
- Close monitoring for the first 48 hours after birth

Mitral regurgitation

- Mitral valve prolapse is the most common cause of mitral regurgitation in women who are pregnant
- May also be associated with mitral stenosis if the aetiology is of rheumatic fever
- Pregnancy is generally well tolerated (It is theorised that mitral regurgitation may improve in pregnancy due to the physiologic reduction in systemic vascular resistance)

Medications

- Pharmacological treatment is not often needed. Diuretics and digoxin can be used for pulmonary congestion. Vasodilator therapy with hydralazine should be used with caution only in those with associated hypertension. ACE inhibitors are considered unsafe for the fetus and are therefore contradicted
- Previously asymptomatic women may worsen immediately after delivery because of sudden increases in systemic vascular resistance
- Increased risk of left atrial enlargement and subsequent atrial fibrillation

Aortic stenosis

- The most common cause is congenital aortic valve disease (e.g. Bicuspid aortic valve). There is an association with bicuspid aortic valve and aortic root dilatation and co-arctation
- May also be associated with mitral stenosis if the aetiology is rheumatic fever
- Maternal mortality associated with severe aortic stenosis is 17 % with a fetal mortality of 32 % (Davies, Herbert 2007c)
- Echocardiography is essential in determining the severity of the stenosis. In pregnancy an aortic valve area < 1.0 cm^2 (0.6 cm^2 / m^2 BSA) is associated with a significant increased maternal and foetal risk
- Decisions regarding anaesthesia and mode of delivery must be individualised on the basis of obstetric indications, severity of maternal symptoms and aortic valve area
- In severe or symptomatic aortic stenosis, the intrapartum management should be carried out in a hospital with adult cardiac services and an adult intensive care. Invasive monitoring, especially intra-arterial pressure monitoring is of utmost importance. Avoidance of hypotension and hypovolaemia is essential to avoid haemodynamic collapse

Aortic regurgitation

- May also be associated with mitral stenosis
- Clinical course is determined more by the extent of their mitral valve disease than by their aortic regurgitation
- When aortic regurgitation is the predominant lesion, pregnancy is usually well tolerated and may improve in pregnancy due to the decrease in systemic vascular resistance
- Also, the physiologic tachycardia of pregnancy may reduce regurgitant flow as diastolic filling times are shortened
- Murmurs normally associated with both aortic and mitral regurgitation may be reduced in pregnancy
- Women with severe aortic regurgitation and symptoms of left-sided heart failure should decrease their physical activity and bed rest may be required.
- Reduce sodium intake < 2 g per day
- Consider diuresis or vasodilators (e.g. hydralazine or nifedipine) and inotropic therapy in difficult cases
- Despite aggressive medical therapy, some women will require aortic valve replacement in pregnancy. Case reports suggest that pulsatile perfusion at bypass may help preserve placental haemodynamic function (Davies, Herbert 2007c)

Congenital heart disease

- May be organised into acyanotic and cyanotic types
- Acyanotic congenital heart lesions include:
    - Atrial / ventricular septal defects,
    - Patent ductus arteriosus, aortic coarctation,
    - Marfan syndrome,
    - Aortic / pulmonary stenosis
- Cyanotic congenital heart lesions include:
    - Cyanotic congenital heart disease,
    - Tetralogy of Fallot,
    - Post Fontan operation
- Usually require referral to a tertiary centre with specialist adult cardiac service care

- Fetal echocardiogram at 20 weeks of gestation
    - If on warfarin, look for echogenic foci in the heels and coccyx, profile to assess nasal bridge
    - Identified cardiac fetal anomaly carries a 4-5 % risk of associated chromosomal abnormality – recommend amniocentesis with antibiotic prophylaxis as above
- Most women present as NYHA class I or II lesions and remain largely asymptomatic
- The risk of a cardiac event in pregnancy is increased for women with:
    - A prior cardiac event or arrhythmia
    - NYHA functional class > II
    - Cyanosis
    - Left heart obstruction
    - Systemic ventricular dysfunction

Coarctation of the aorta

- Coarctation of the aorta should be repaired before pregnancy. It is rare during pregnancy (9 % of all congenital defects). The management of hypertension is difficult in the unoperated pregnant woman. Fetal growth is usually normal and in contrast to essential hypertension, there is not an increased incidence of preeclampsia. Over enthusiastic treatment may cause hypotension in the distal segment. This may result in abortion or fetal death even though pressure in the proximal segment continues to rise on effort
- Rupture of the aorta is the most common reported cause of death, and rupture of an aneurysm of the circle of Willis has also been reported during pregnancy. The increase in blood volume and cardiac output increases the risk of aortic dissection or rupture during pregnancy and a beta blocker should be prescribed
- Restriction of physical activity is the only way of minimising potentially dangerous surges in blood pressure
- Surgical correction is only very rarely indicated during pregnancy if systolic hypertension is uncontrolled or heart failure is present
- Balloon angioplasty is contraindicated because of the risk of dissection or rupture. Whether this risk is avoidable with stenting is not known

Marfan syndrome

- Rare - incidence is 5 in 100,000
- Mortality rate is high 50 %
- Women with a documented aortic root diameter of < 40 mm without an abnormal aortic valve have a mortality rate of < 5 %
- Risk of aortic dissection during pregnancy or shortly thereafter is approximately 17 %
- Aortic or mitral regurgitation is also seen in 60 % of women with Marfan syndrome and may complicate pregnancy
- Regular echocardiography before, during and after pregnancy
- Genetic testing through chorionic villus biopsy, amniocentesis cell culture or postnatal testing
- B-blockers are strongly recommended before and during pregnancy to decrease the risk of aortic dilatation
- Pregnancies complicated by Marfan syndrome are not associated with poor perinatal outcomes, though some suggest there is an increased risk of incompetent cervix
- Physical, echocardiographic, and ophthalmologic examination of newborns

- Counsel woman regarding the risk of autosomal dominant inheritance and need for follow-up for their offspring (Davies, Herbert 2007b)

Intraatrial repair for transposition of great arteries (TGA)

- Angiotensin-converting enzyme (ACE) inhibitors should be stopped before pregnancy or as soon as possible. Frequent review is recommended

Congenitally corrected transposition of the great arteries

- Women without significant other cardiac defects usually do well, but problems can develop through failure of the systemic right ventricle with increasing regurgitation through its tricuspid atrioventricular valve. Supraventricular arrhythmias, embolism, and atrioventricular block are other potential complications

Fontan procedure

- Careful patient selection is important. The successful Fontan Procedure with a small right atrium or total cavopulmonary connection (TCPC) in functional class I or II can probably complete pregnancy with a normal live birth. Fontan patients with a large right atrium and some venous congestion have to be monitored very carefully. They need anticoagulant treatment and conversion to total cavopulmonary connection before pregnancy is considered

Prosthetic heart valves

- The majority of women with bioprosthetic valves do not require anticoagulation during pregnancy (Davies, Herbert 2007e).
- Women with mechanical valves require anticoagulation prophylaxis and should receive a detailed discussion of the advantages and disadvantages of the three anticoagulant options (warfarin, unfractionated heparin and low molecular weight heparin) (see anticoagulation prophylaxis below)
- Despite valve replacement there remains a mild functional stenosis across these valves due to the prothesis itself
- Women with valve replacements are at high risk of bacterial endocarditis
- Perform blood cultures if any signs of bacterial endocarditis
- Observe for signs of cardiac failure e.g. dyspnoea (respirations > 24 per minute), tachycardia (> 130 beats per minute), fatigue, oedema, hypoxia / cyanosis

Warfarin

- Warfarin crosses the placenta, is teratogenic and may cause haemorrhage in the fetus
- The teratogenic effects appear to result from inhibition of vitamin K and / or arylsulphatase E activity during skeletal development
- The fetal warfarin syndrome comprises nasal hypoplasia, short fingers with hypoplastic nails, low birth weight, stippling of epiphyses on X-ray and intellectual disability
- Recent estimates indicate the risk of fetal warfarin syndrome in babies of women who require warfarin throughout pregnancy is around 5 %
- The period of greatest embryonic susceptibility is between 6 and 9 weeks of gestation. It is recommended that, wherever possible, the drug is avoided throughout the first trimester (Liebelt, Hotham 2002)

Pulmonary hypertension

Ischaemic heart disease

- Includes acute myocardial infarction (MI), unstable angina, stable angina
- Requires care in a tertiary centre or care in a tertiary centre with specialist adult cardiac service care depending on echocardiograph findings and symptoms according to NYHA functional classification
- Rare in pregnancy - ischaemic heart disease occurs on average in 1 in 10,000 deliveries
- Myocardial infarction (MI) in pregnancy occurs on average in 7.5 in 100,000 deliveries with mortality highest in the third trimester in women under 35 years of age (Davies, Herbert 2007d)
- CEMCH 2003-2005 noted an increase in maternal deaths from ischaemic heart disease. The following risk factors were identified:
    - Obesity
    - Older age
    - Higher parity
    - Smoking
    - Diabetes
    - Pre existing hypertension
    - Family history

Myocardial infarction management

- Similar to management of the non-pregnant woman with MI and includes:
    - Oxygen, nitrates, morphine, and most antiarrhythmics, calcium channel blockers, β-blockers, heparin, low-dose aspirin, and invasive hemodynamic monitoring if necessary
    - Case reports using percutaneous interventions and systemic and local thrombolytic therapy have also been successful (Davies, Herbert 2007d)
- MI is not an indication for immediate delivery (mortality is higher in women who deliver within 2 weeks of MI)
- Caesarean section only for obstetrical indications (does not protect women from the dramatic changes in stroke volume and cardiac output associated with the immediate postpartum period)
- Electrocardiographic monitoring in labour

Heart failure and cardiomyopathy

- Includes left sided, right heart failure and biventricular heart failure
- Common causes for heart failure in the puerperium include iatrogenic fluid therapy overload, pre-eclampsia, thyrotoxicosis, peri-partum cardiomyopathy, anaemia or previously undiagnosed rheumatic or congenital heart disease (Davies, Herbert 2007d)

Hypertrophic cardiomyopathy

Clinical assessment

- Echocardiography
- electrocardiography (ECG), including ambulatory ECG
- Exercise testing

Treatment

- Genetic counselling
- β-blockers
- Diuretics

- Anticoagulation in the presence of atrial fibrillation
- Amiodarone or implantation of an internal cardiac defibrillator for documented ventricular arrhythmias
- Dilated cardiomyopathy reversion
- Normal vaginal birth

Peripartum or dilated cardiomyopathy

- Several etiological factors but no specific cause
- Includes women with unrecognised pre-existing dilated cardiomyopathy and women with acute viral myocarditis during pregnancy
- Counsel women to avoid pregnancy / consider termination of pregnancy

Clinical assessment

- Echocardiography

Diagnosis criteria

- Development of cardiac failure in the last month of pregnancy or within five months postpartum
- Lack of another cause for the woman's cardiac failure
- Lack of cardiac disease preceding the month before delivery

Risk factors

- Older, multiparous women and women with preeclampsia or twins

Symptoms

- Shortness of breath, lung field crackles, oedema within the first 3 months postpartum

Investigations

- Complete blood count, electrolytes and renal function, electrocardiogram, chest X-ray, arterial blood gases, and an echocardiogram

Treatment

- Reduce preload and afterload and maximise ventricular contractility
- Hospitalisation to medically stabilise decompensated heart failure
- Reduce salt intake < 2 g per day
- Fluid restriction 1.5 – 2L per day

Medical treatment

- Diurese with frusemide
- In the prepartum period, reduce afterload by using hydralazine and nitrates
- β-blockers may improve left ventricular systolic function and should be used if not contraindicated once the heart failure is in a compensated state
- Angiotensin-converting enzyme inhibitors may be safely used to reduce afterload in the postpartum period
- Digoxin may improve the symptoms of heart failure
- Avoid or treat severe anaemia to prevent decompensated heart failure
- Prophylactic anticoagulation while dilation of the heart persists (see anticoagulation prophylaxis)
- Counsel regarding recurrence risk in future pregnancies. If the woman recovers fully and has normal ventricular function, future pregnancies may be considered

Heart transplant recipients

- After heart transplant, approximately 90 % of otherwise healthy young female recipients survive the first year and almost two-thirds will survive the next ten years with an excellent quality of life. These women may desire pregnancy and children (Subramaniam, Robson 2008)
- These women require high risk care by both transplant physicians and obstetric specialists in a tertiary centre with onsite specialist adult cardiac service care and adult intensive care
- Pregnancy risks for heart transplant recipients include:
    - Rejection
    - Hypertension, pre-eclampsia
    - Psychological stress
    - Fetal growth restriction (20 %)
    - Pre-term birth (up to 50 %)

Preconception counselling

- Ideally, preconception counselling should be introduced at the pre-transplant stage and continue throughout the post-transplant process
- Individual factors such as
    - History of rejection in the first year
    - Advanced maternal age
    - Comorbidities (see below)
    - Medical non-compliance should be considered when counselling women for or against pregnancy
- Comorbidities that may influence pregnancy outcome include
    - Risk of recurrent disease
    - Chronic allograft dysfunction
    - Cardiovascular or pulmonary disease
    - Diabetes mellitus
    - Hypertension
    - Inherited diseases-maternal or paternal (genetic versus chromosomal)
    - Hepatitis B, hepatitis C, cytomegalovirus
    - Obesity
- Include the woman and her partner in counselling
- Where possible, vaccinate pre-transplant or pre-pregnancy for influenza, hepatitis B, tetanus, pneumococcus
- Discuss possible consequences of preterm birth, intrauterine growth restriction with both parents

Timing of pregnancy

Before conception ensure:

- No rejection in the past year
- Adequate and stable graft function
- Try to defer pregnancy for at least one year after transplantation
- No acute infections that might impact the fetus
- Maintenance immunosuppression is at stable doses

Antenatal care

- Graft dysfunction during pregnancy warrants appropriate investigation (by biopsy if necessary)
- Immunosuppression must be maintained during pregnancy to avoid rejection

- Future studies need to address optimal selection and dosing of these agents
- Hyperemesis gravidarum may lead to decreased absorption or inadequate immunosuppression
- Caesarean section indicated only for obstetric reasons

Treatment goals:

- Ensure that patients maintain graft function using appropriate immunosuppressive dosing during gestation and immediately after delivery
- Optimise maternal health including graft function
- Maintain a normal metabolic environment
- Minimise complications associated with preterm birth
- Detect and manage hypertensive complications especially preeclampsia
- Ensure adequate fetal growth

Antibiotic prophylaxis

- Generally, routine antibiotic prophylaxis is not recommended for women with valvular heart disease undergoing uncomplicated vaginal birth or caesarean section unless infection is suspected (AHA 2007)
- Intrapartum antibiotic prophylaxis is recommended for vaginal birth complicated by amnionitis (suspected or proven) or prelabour rupture of membranes, and other suspected infections where one of the following cardiac conditions is present:
    - Prosthetic heart valves
    - Complex congenital heart disease
    - Past history of endocarditis
    - Surgically constructed systemic-pulmonary shunts, or conduits

Recommended intrapartum antibiotic treatment

- Gentamicin 2 mg / kg IV as a single intrapartum dose given at the commencement of labour

  and
- Ampicillin [or amoxycillin] 2 g IV as a stat dose as close as practical to the time of birth

Allergy to penicillin

- Gentamicin 2 mg / kg IV as a single intrapartum dose given at the commencement of labour

  and
- Vancomycin 1 g IV, administered slowly (over at least one hour) and repeat after 8 hours if birth has not occurred
- For further information, link to chapter 103 Peri partum prophylactic antibiotics

Anticoagulation prophylaxis

- Anticoagulation is indicated for women who have mechanical heart valves, atrial fibrillation or atrial flutter in the presence of structural heart disease, past documented cardiac embolic events, a past history of multiple pulmonary emboli, cyanotic congenital heart defects and Fontan circulation
- Women with mechanical heart valves are at very high risk of thromboembolism in pregnancy and require continued anticoagulation
- There are no definitive recommendations about optimal antithrombotic treatments for

women with mechanical heart valves in pregnancy

- Substantial concern remains about the fetal safety of warfarin, the efficacy of subcutaneous unfractionated heparin (UFH) and low molecular weight heparin (LMWH) in preventing thromboembolic complications, and the risk of maternal bleeding with the various regimens (Bates et al. 2004)

A clinically appropriate anticoagulation regimen would be:

- Warfarin should be avoided between 6 weeks and 12 weeks of gestation (to avoid embryopathy) and close to term (to avoid delivery of an anticoagulated fetus). The association of neuro-developmental problems with mid pregnancy use of warfarin should also be considered (Bates et al. 2004)
- Use of one of the following three regimens after explaining the associated risks with the woman:

1. Either LMWH or UFH between 6 weeks and 12 weeks and close to term only. Use vitamin K antagonists e.g. warfarin at other times (despite fetal risks)
    - If warfarin is used, adjust dose to attain a target INR of 3.0 (a lower therapeutic range of 2.0 to 3.0 can be used in women with mechanical bileaflet aortic valves
2. Dose-adjusted subcutaneous UFH throughout pregnancy
    - Initiate subcutaneous UFH in high doses (start at 17,500-20,000 units every 12 hours) and adjust to prolong a 6 hour post injection APTT into the therapeutic range (at least twice control) or to attain an anti-Xa heparin level of 0.35 to 0.70 U / mL
3. Dose-adjusted LMWH throughout pregnancy
    - Administer twice a day in dose to achieve anti-Xa levels of 1.0 to 1.2 U / mL 4 to 6 hours after subcutaneous injection or according to weight.

- Aspirin 100 to 150 mg / day may offer additional protection against thromboembolism

Cardiac conditions associated with high maternal and / or fetal risk during pregnancy

(See Table 64.1)

- Primary pulmonary hypertension
- Eisenmenger syndrome
- Uncorrected coarctation of the aorta
- Severe atrial stenosis (AS) (valve area < 1 cm^2) with or without symptoms
- Atrial regurgitation (AR) with NYHA functional class III-IV symptoms
- Mitral stenosis (MS) with NYHA functional class II-IV symptoms and / or valve area < 1.5 cm^2
- Mitral regurgitation (MR) with NYHA functional class III-IV symptoms
- Aortic and / or mitral valve disease resulting in severe pulmonary hypertension (pulmonary pressure > 75 % of systemic pressures)
- Aortic and / or mitral valve disease with severe LV dysfunction (EF < 0.40)
- Mechanical prosthetic valve requiring anticoagulation
- Marfan syndrome with aortic complications with or without AR
- History of peripartum cardiomyopathy with persistent left ventricular dysfunction and / or NYHA functional class IV

Management in labour

- Ensure that adult resuscitation equipment is available including the ability to perform a peri mortem Caesarean Section within 5 minutes of Cardiac Arrest

Management team includes:

- Obstetrician
- Midwife
- Cardiologist / physician
- Anaesthetist
- Intensive care specialist
- Other allied health professionals as required

Thromboembolism prophylaxis

- Follow link to regional anaesthesia / analgesia considerations after antenatal administration of intravenous unfractionated heparin or subcutaneous low molecular weight heparin
- Use anti-embolic stockings

Intrapartum antibiotic prophylaxis

- Follow link to antibiotic prophylaxis in cardiac disease

Preterm labour

- Notify cardiologist / physician if any cardiac advice is required quickly

Term Labour

- Most women with cardiac disease should be encouraged to labour spontaneously
- Syntocinon® infusion for induction or augmentation of labour or prostaglandin E_2 may be used if indicated
- In women with risk of fluid overload use low volume Syntocinon® infusion (Follow link to Syntocinon® regimen)
- In fixed cardiac output disorders / aortic aneurysm women may be offered elective caesarean section
- Ensure intravenous access
- Maintain continuous midwifery presence and care

Pain management and anaesthesia

- Nitrous oxide and other pain relief should be provided only after consultation with the anaesthetist
- An epidural block and assisted vaginal birth may be advised after discussion between the woman, anaesthetist, obstetrician and others
- Epidural anaesthesia may be hazardous in women with:
    - A fixed cardiac output
    - Aortic stenosis
    - Mitral stenosis
    - Hypertrophic cardiomyopathy
    - Fontan circulation
- Consider combined spinal-epidural anaesthesia (decreases the preload and afterload with a positive effect on most cardiac lesions) (Gei, Hankins 2001)
- Regional anaesthesia (epidural or spinal) is contraindicated during anticoagulation treatment (risk of spinal haematoma)

Fluid management

- Closely monitor fluid management in labour and maintain accurate fluid balance chart (increased risk of pulmonary oedema)

Oxygen treatment

- Oxygen saturation should be continuously monitored with pulse oximetry. Regulate oxygen flow (via mask or nasal specs) to maintain oxygen saturations > 95 %

Signs of cardiac failure:

- Observe for signs of cardiac failure e.g. dyspnoea (respirations > 24 per minute), tachycardia (> 130 beats per minute [bpm]), fatigue, oedema, cyanosis
- Position woman in a supported upright sitting position

Continuous electrocardiographic (ECG) monitoring

- Required in moderate to high risk women
- Maternal cardiac monitoring should occur throughout labour and after birth for 24 hours, according to the severity of maternal condition
- High risk women may require invasive cardiac monitoring in labour

Infection risks

- Limit vaginal examinations to reduce risk of infection and possible subacute bacterial endocarditis
- Bacterial endocarditis is a very rare, but serious risk in women with valvular abnormalities and valve replacements. Particular attention should be paid to preventing infection e.g. regular changing of intravenous lines in addition to bacterial endocarditis prophylaxis
- Report a pulse rate of > 130 bpm and respiratory rate of > 24 respirations per minute (rpm) to senior responsible clinician (physician or cardiologist)

Electronic fetal monitoring

- Continuous electronic fetal monitoring during labour

Observations

- Take and record the following observations every fifteen minutes:
    - Pulse
    - Respiration
- Take and record the following observations every hour:
    - Intake and output
    - Oedema
    - Colour
    - Blood pressure

High risk cardiac management in labour

- Women with severe or barely controlled heart failure present significant problems during labour and birth
- Labour and birth should occur in a hospital with an adult intensive care or cardiac unit

Timing of labour and birth

- Increased risk of preterm labour
- Before 30 weeks gestation, in partnership with the woman, the high risk management

team (obstetrician, physician, cardiologist and anaesthetist) should discuss and agree on the time and mode of birth

- Document plan in case notes
- The time and mode of the birth is ultimately the obstetrician's decision
- Aim to birth at term if cardiac state is well stabilised
- Inform the woman of possible management change at short notice if cardiac function and reserve alter rapidly

During labour

- Contact the cardiologist or physician, anaesthetist and paediatrician before birth
- Consider Endocarditis antibiotic prophylaxis
- Cardiac drugs during labour should be planned in consultation with microbiologist, obstetrician and cardiologist / physician

Birth

- To shorten second stage and avoid excessive maternal expulsive efforts:
    - Consider episiotomy
    - Consider forceps delivery
    - Do not use local anaesthetic with adrenaline
- To minimise cardiac compromise
    - Do not use stirrups without discussion between obstetrician, anaesthetist and cardiologist / physician
    - Report a pulse rate > 130 or < 40 bpm
    - Report respiratory rate > 24 or < 5 rpm
    - Report rapidly changing pulse or respiration rate (even if within threshold)

Postpartum

Management of the third stage, including complications

- Many of these women are intolerant of changes in vascular resistance and venous return. Therefore care is required to avoid vasodilatation from bolus doses of Syntocinon®, whilst avoiding excessive bleeding from uterine atony

Oxytocic for active management of the third stage

- Syntocinon® 10 IU diluted to 9 mL with sodium chloride 0.9 % in a 10 mL syringe
- Give 2 x 1 mL aliquots (i.e. Syntocinon® 1 IU) 30 seconds apart to produce uterine contraction following delivery of the anterior shoulder
- Await classic signs of separation of the placenta before attempting to deliver placenta
- if no signs of separation after 60 seconds give a third aliquot of 1 IU (1mL) of Syntocinon®

Syntocinon Infusion for prevention or control of PPH

- Syntocinon® 40 IU diluted in 100 mL bag of sodium chloride 0.9 % and run at 25 mL / hour
- The Syntocinon® is delivered at the normal dose but in 1/10th the volume

Management of PPH

- Prompt treatment important to avoid hypovolaemia and reduced preload

- Large boluses of Syntocinon® are contraindicated.
- Ergometrine and Prostaglandin F2 alpha are contra indicated
- Rub up a contraction manually and administer 1 mL of dilute Syntocinon® solution (10 IU in 10 mL)
- Administer misoprostol (Cytoctec®) 200 micrograms orally (1 tablet) and 800 micrograms rectally (4 tablets)
- Judicious resuscitation with assistance of intensive care unit and anaesthetic colleagues

Observations

- Observe woman very closely for 24 hours postpartum. This is a high risk period for the woman since blood volume increases from auto transfusion and after load increases as placental bed circulation ceases (Davies, Herbert 2007)
- Refer and report any signs of cardiac failure:
    - Dyspnoea
    - Cyanosis / pallor
    - Tachycardia
    - Cold clammy extremities
    - Haemoptysis
    - Oedema of the face and hands
- Take and record the woman's respiration when pulse is taken
- Continue to position the woman in a semi-upright position
- Encourage deep breathing and passive leg exercises
- The clinician should realise that maternal mortality associated with pulmonary hypertension and Eisenmenger syndrome may occur up to several weeks postpartum

Contraception

- Sterilization of the male partner carries the least risk in monogamous couples who have completed their family
- Oral contraceptives can be used with several exceptions:
    - Women with right to left shunts
    - Cardiac disease with associated hypertension
- Progestin-only oral contraceptives or medroxy-progesterone acetate (Depro-Provera®) may be used by these women, as the thromboembolic risk of oral contraceptives is thought to be due to the oestrogen component.
- The progestin-releasing intrauterine contraceptive device (IUCD) has a failure rate of < 1 % and in a monogamous couple the risk of endocarditis associated with the use of an IUCD is rare. Prophylaxis with oral amoxicillin (2 g taken one hour before insertion or removal) is recommended

Follow up

- Postnatal follow up should be at a high risk medical clinic and with the woman's cardiologist

Summary

Antenatal Care

Low risk

- Tertiary hospital

- Consultation with anaesthetists, cardiologist / obstetric physician in high risk clinic

Intermediate or high risk

- High risk obstetric centre with multidisciplinary care from obstetrician, anaesthetist, intensivist, neonatologist, midwifery and nursing

Antepartum Management

- Multidisciplinary approach
- Serial cardiac assessments to identify and act upon cardiac deterioration
- Fetal echo for mothers with congenital heart disease +/- genetic counselling
- Optimise medication for pregnancy
- Early admission for high risk women

Peripartum Management

Low and intermediate risk

- Epidural anaesthesia
- Cardiac telemetry and oximetry if required
- Deep venous thrombosis (DVT) prophylaxis

High Risk

- Multidisciplinary approach including decision on delivery in an intensive care unit (ICU) or not and level of invasive monitoring
- Planned delivery at term
- Aim for vaginal delivery except in specific instances (e.g. Marfan's, critical aortic stenosis)
- Care in labour and delivery unit, coronary or intensive care unit if indicated. Continued careful observation using special observation charts and possibly including systems such as 'Early warning scores' for signs of clinical deterioration in the 4th stage

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Table 64.1 Allocation of care according to severity of cardiac disease

Cardiac Condition	Tertiary centre	Tertiary centre with onsite CCU and ICU
Primary pulmonary hypertension		Yes
Eisenmenger syndrome		Yes
Uncorrected coarctation of the aorta		Yes
AS	Mild to moderate stenosis	Severe with or without symptoms Ao valve area < 1.0 cm^2
AR	NYHA functional class I-II	NYHA functional class III-IV
MS	NYHA functional class I	NYHA functional class II-IV Valve area < 1.5 cm^2 PA systolic pressure > 50 mm Hg or > 75 % systemic pressure
MR	Yes NYHA functional class I-II	Yes NYHA functional class III-IV
Aortic and / or mitral valve disease resulting in severe pulmonary hypertension		Yes (pulmonary pressure > 75 % of systemic pressures)
Aortic and / or mitral valve disease with severe LV dysfunction		Yes (EF < 0.40)
Mechanical prosthetic valve requiring anticoagulation		Yes
Marfan syndrome		Yes with aortic complications, with or without AR
History of peripartum cardiomyopathy		Yes with persistent left ventricular dysfunction and NYHA functional class IV
Pacemakers	yes	
Implanted Cardioverter Defibrillator management in pregnancy		yes
Management of ventricular arrhythmias		yes

Table 64.2 Maternal mortality CEMACH 2003-2005

Type and cause of death	Indirect	Late
Acquired		
Aortic Dissection	9	0
Myocardial Infarction	12	4
Ischaemic Heart disease		0
Sudden Adult Death Syndrome	4	9
Peripartum Cardiomyopathy	3	12
Cardiomyopathy	0	4
Myocarditis or myocardial fibrosis	1	0
Mitral valve disease	5	0
Infectious endocarditis	3	2
Right or left ventricular hypertrophy or hypertensive heart failure	2	1
Congenital		
Pulmonary hypertension	3	0
Congenital heart disease	3	2
Total	**47**	**34**

Table 64.3 CEMACH 2003-2005 Indirect maternal deaths

Triennium	Congenital	Acquired		Total	Rate	95 per cent CI	
		Ischaemic	Other				
	n (%)	n (%)	n (%)	n (%)			
1985-1987	10 (43)	9 (39)	4 (17)	23 (100)	1.01	0.68	1.52
1988-1990	9 (50)	5 (28)	4 (22)	18 (100)	0.76	0.48	1.21
1991-1993	9 (24)	8 (22)	20 (54)	37 (100)	1.60	1.16	2.20
1994-1996	10 (26)	6 (15)	23 (59)	39 (100)	1.77	1.30	2.43
1997-1999	10 (29)	5 (14)	20 (57)	35 (100)	1.65	1.19	2.29
2000-2002	9 (20)	8 (18)	27 (61)	44 (100)	2.20	1.64	2.96
2003-2005	4 (8)	16 (33)	28* (58)	48 (100)	2.27	1.67	2.96

Table 64.4 Cardiovascular Drugs in Pregnancy

Drug	Use in pregnancy	Potential side effects	Breast feeding	Risk factors
Adenosine	Maternal and fetal arrhythmias	No side effects reported; data on use during first trimester are limited	Data NA	C
Amiodarone	Maternal arrhythmias	IUGR, prematurity, congenital goiter, hypothyroidism and hyperthyroidism, transient bradycardia, and prolonged QT in the newborn	Not recommended	C
Angiotensin-converting enzyme inhibitors / Angiotensin receptor II antagonists	Hypertension, heart failure	Oligohydramnios, IUGR, prematurity, neonatal hypotension, renal failure, anemia, death, skull ossification defect, limb contractures, patent ductus arteriosus	Compatible	D
Beta blockers	Hypertension, maternal arrhythmias, myocardial ischemia, mitral stenosis, hypertrophic cardiomyopathy,	Fetal bradycardia, low placental weight, possible IUGR, hypoglycemia, no information on carvedilol	Compatible, monitoring of infant's heart rate recommended	Acebutolol: B Labetalol: C Metoprolol: C Propranolol: C Esmolol: C Atenolol: D

	hyperthyroidism, Marfan syndrome			
Digoxin	Maternal and fetal arrhythmias, heart failure	No evidence for unfavorable effects on the fetus	Compatible	C
Diltiazem	Myocardial ischemia, tocolysis	Limited data; increased incidence of major birth defects	Compatible	C
Diuretics	Hypertension, congestive heart failure	Hypovolemia leads to reduced uteroplacental perfusion, fetal hypoglycemia, thrombocytopenia, hyponatremia, hypokalemia; thiazide diuretics can inhibit labour and suppress lactation	Compatible	C
Flecainide	Maternal and fetal arrhythmias	Limited data; 2 cases of fetal death after successful treatment of fetal SVT reported, but relation to flecainide uncertain	Compatible	C
Heparin	Anticoagulation	None reported	Compatible	C
Hydralazine	Hypertension	None reported	Compatible	C
Lignocaine	Local anesthesia, maternal arrhythmias	No evidence for unfavorable fetal effects; high serum levels may cause central nervous depression at birth	Compatible	C
Nifedipine	Hypertension, tocolysis	Fetal distress related to maternal hypotension reported	Compatible	C
Nitrates	Myocardial infarction and ischemia, hypertension, pulmonary edema, tocolysis	Limited data; use is generally safe, few cases of fetal heart rate deceleration and bradycardia have been reported	Data NA	C
Procainamide	Maternal and fetal arrhythmias	Limited data; no fetal side effects reported	Compatible	C
Sodium nitroprusside	Hypertension, aortic dissection	Limited data; potential thiocyanate fetal toxicity, fetal mortality reported in animals	Data NA	C
Sotalol	Maternal arrhythmias, hypertension, fetal tachycardia	Limited data; 2 cases of fetal death and 2 cases of significant neurological morbidity in newborns reported, as well as bradycardia in newborns	Compatible, monitoring of infant's heart rate recommended	B
Verapamil	Maternal and fetal arrhythmias, hypertension, tocolysis	Limited data; other than a single case of fetal death of uncertain cause, no adverse fetal or newborn effects have been reported	Compatible	C
Warfarin	Anticoagulation	Crosses placental barrier; fetal hemorrhage in utero, embryopathy, central nervous system abnormalities	Compatible	X

IUGR indicates intrauterine growth restriction, NA - not available; and SVT - supraventricular tachycardia.

FDA classification:

Category B:

Either animal reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women, or animal reproduction studies have shown an adverse effect that was not confirmed in controlled studies in women.

Category C:

Either studies in animals have revealed adverse effects on the fetus and there are no controlled studies in women, or studies in women and animals are not available. Drugs should be given only if potential benefits justify the potential risk to the fetus.

Category D:

There is positive evidence of human fetal risk, but the benefits from use in pregnant woman may be acceptable despite the risk.

Category X:

Studies in animals or human beings have demonstrated fetal abnormalities. The risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.

Source: Drug Information for the Health Care Professional (USDPI Vol 1); Micromedex; 23rd ed (January 1, 2003). Adapted fom Elkayam U. Pregnancy and cardiovascular disease. In: Zipes DP, Libby P, Bonow RO, Braunwald E, editors. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine. 7th ed. Philadelphia, PA: Elsevier, 2005: 1965 (763).

Adapted from: Bonow RO, Carabello BA, Chatterjee K, de Leon AC Jr., Faxon DP, Freed MD, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology /American Heart Association Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Valvular Heart Disease).

Government of South Australia
Department of Health

South Australian

PREGNANCY RECORD

Surname *UR*

Given names *Date of birth*

Address

(complete or preferably affix label)

Please take care of this Record as it is the only official record of your pregnancy.

You should bring this Record with you when you visit any health care professional

If you find this Record call the contact numbers below or return it to the nearest hospital/maternity unit.

CONTACT DETAILS

Hospital/maternity unit _____ ***Phone*** _____

Obstetrician _____ ***Phone*** _____

Midwife _____ ***Phone*** _____

General Practitioner _____ ***Phone*** _____

This Record will be filed in the hospital case record or returned to your maternity care provider at the end of your pregnancy.

A copy is required for: Please tick (✓)
☐ Private Obstetrician ☐ Midwife ☐ GP

APPOINTMENTS

You should bring this Record with you when visiting any health care professional

For example: obstetrician, midwife, general practitioner, clinic, ultrasounds and procedures

Date	Time	What/Who	Where

SA PREGNANCY RECORD MR31

NOT FOR USE

ADVICE & INFORMATION

Surname *UR*

Given names *Date of birth*

Address

(complete or preferably affix label)

Call your hospital, midwife or doctor on the numbers provided on the front page if you have concerns or experience any of the following:

- Persistent headache
- Visual changes such as flashing lights
- Persistent abdominal pain
- Bleeding from your vagina
- Reduced baby movements
- Regular contractions or breaking of your waters

General information:

- **You will need to bring this Record with you whenever you see your health care provider and when you go to hospital at any time, including for the birth of your baby.**
- When you book into hospital, it is suggested you ask for a list of what you will need to bring with you, for example nappies, clothing etc.
- In South Australia, the average stay in hospital after an uncomplicated birth is 2 to 3 days. Some women may stay longer or shorter depending on their needs.
- You can receive a photocopy of this Record on request at the end of your pregnancy. The original will be filed in the hospital case record or returned to your maternity care provider.
- South Australian law states that when travelling in a car with a child, the child must be secured in a restraint. Please arrange to have a baby capsule fitted in your car before taking your baby home.
- During your hospital stay, you will be offered a home visit from a Child and Youth Health Nurse. This visit will provide your baby's first health check and answer any questions you may have. This home visit will usually occur within a few weeks of leaving hospital.

Use this space to write any questions you may have for your doctor or midwife.

NOT FOR USE

BIRTH PLAN

Surname	*UR*
Given names	*Date of birth*
Address	

(complete or preferably affix label)

Support person(s) for the birth

(Name/s) _____

Birth

Describe the kind of labour and birth you wish to experience (e.g. position, cutting the cord, pain relief).

Cultural or religious needs

How you would like to feed your baby

You are encouraged to breast feed your baby as breast feeding provides long term health benefits for both you and your baby and helps protect your baby against infections.

Previous pregnancy experiences

Any other information

Please note: Your plan will be used as the guide for your care but your doctor or midwife will discuss with you the need for any changes as a result of your clinical needs at the time.

NOT FOR USE

PERSONAL HISTORY

Name and designation of maternity care provider taking this history (please print):

_____

Date: _____

Surname *UR*

Given names *Date of birth*

Address

(complete or preferably affix label)

Woman

Preferred name: _____

Occupation: _____

Phone: (H)_____ (W)_____

(M):_____

Ethnicity/Cultural background: _____

Language preferred: _____

Interpreter required: Yes / No

Partner

Name: _____

Occupation: _____

Phone: (H)_____ (W)_____

(M):_____

Ethnicity/Cultural background: _____

Other contact person

Name: _____

Relationship: _____

Phone: (H)_____ (W)_____

(M):_____

Social history - *all items should be reviewed as pregnancy progresses.*

Use * to indicate sensitive information not recorded here.

If there is a concern about social issues, health providers should consider referral to an appropriate agency.

Smoking (number per day)
Alcohol (drinks per week)
Recreational drug use
Major stressors, life changes or losses
Relationship issues
Family and social supports
Children (e.g. contact with FAYS)
Accommodation issues
Financial issues
Other

Medical history

Deep venous thrombosis
Diabetes
Epilepsy
Gynaecological problems
Heart disease
High blood pressure
Pre pregnancy blood pressure (record BP)
Kidney disease
Thyroid disorders
Other

Mental health history

Anxiety/depression
Postnatal depression
Other psychiatric disorders
Family history of mental health problems (including partner)
Emotional issues

Family history and prenatal diagnostic issues

Diabetes
Heart disease
High blood pressure
Genetic disorders/congenital abnormalities
Other

NOT FOR USE

PERSONAL HISTORY
continued

Surname *UR*
Given names *Date of birth*
Address
(complete or preferably affix label)

Surgical history

Anaesthetic history Anaesthetic consultation may be required

Previous anaesthetic problems
Dental health and jaw problems
Back problems
Blood transfusion
Other:

Medications Include 'over the counter' drugs & alternative therapies.

	Dose	Frequency	Cessation

Allergies Detail all allergies including reactions to medication.

Past pregnancy information Use * to indicate sensitive information not recorded here.

Gravida _____ **Parity** _____

*	*Date*	*Place*	*Gestation (in weeks)*	*Labour, birth and postnatal details*	*Birth weight*	*Gender*	*Feeding type and duration*	*Baby's name*

Physical examination Date: / /

Weight _____ Height _____ BMI _____

Last Pap smear (should be performed if due) / /

Result of Pap smear: _____

Other examinations

Cardiac, respiratory and breast examinations if indicated

_____

_____

Guidelines for calculation of final due date

Step 1 **LMP** certain/uncertain normal/abnormal spontaneous/pill withdrawal
Date _____ (please circle) (please circle) (please circle)

Step 2 **Menstrual cycle**
Length _____ regular/irregular (please circle)

Step 3
Due date based on period and cycle _____ Consistent with first ultrasound scan? Yes / No (please circle)

Step 4 **FINAL DUE DATE** _____
Name and designation of person who calculated
_____
(please print)

NOT FOR USE

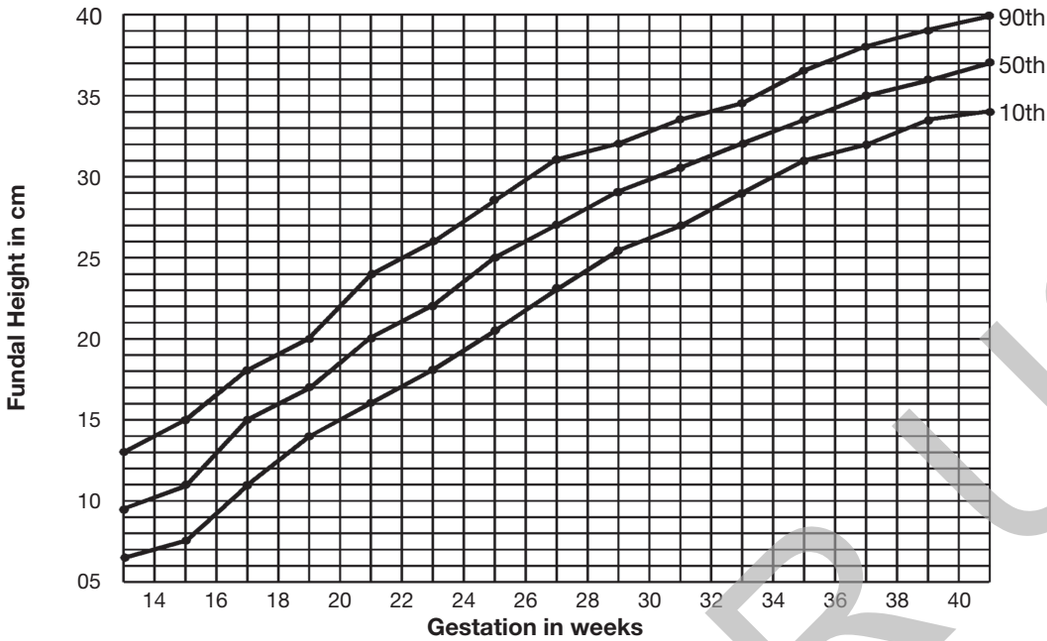
SYMPHYSIO-FUNDAL CHART

Surname *UR*

Given names *Date of birth*

Address

(complete or preferably affix label)



Taylor P, Coulthard AC, Robinson JS. Symphsio-fundal height from 12 weeks' gestation. Aust NZ J Obstet Gynaecol 1984; 24 (3):189-91

Guidelines

The woman should be lying in the supine position with her head supported on a single pillow. The couch should be flat.

Measure from the highest point of the fundus to the top of the symphysis pubis. Begin measuring from the fundus since this is the more variable end point.

Measure with the tape scale facing downwards so that you are less influenced by previous results. Measurements should be recorded to the nearest 0.5 centimetre.

NOT FOR USE

RECOMMENDED ROUTINE INVESTIGATIONS & SCHEDULE OF VISITS

All investigations must be preceded by appropriate discussion and counselling. To reduce duplication, please tick each test/activity when ordered/performed. Frequency of visits should be governed by clinical need.

The health professional who orders investigations is responsible for the follow up of results.

	Activity	Investigations
First visit Preferably before 12 weeks	☐ Discuss routine investigations undertaken during pregnancy ☐ Offer screening for Down syndrome between 11-13^{+6} weeks by ultrasound & serum screening or 14-20 weeks by serum screening ☐ Pap smear if due ☐ Discuss choice of care ☐ Book place of birth Note: Some Medical Defence Associations require that women are seen before 20 and at 36 weeks by a GP Obstetrician/Obstetrician.	☐ Complete blood examination ☐ Blood group and antibody screen ☐ Rubella titre ☐ Syphilis screen ☐ Hepatitis B screen ☐ Hepatitis C screen ☐ HIV screen ☐ MSSU for culture and sensitivity
Subsequent visits Every 4-6 weeks until 28 weeks	☐ Discuss breast feeding ☐ Book antenatal classes	☐ Morphology ultrasound (18-20 weeks)
28 weeks Every 2-4 weeks until 36 weeks	☐ If the woman is Rh negative, administer Anti-D prophylaxis at **28 and 34 weeks** after discussion/ informed consent. For more information, refer to the Statewide Anti-D Protocol.	☐ Complete blood examination ☐ Oral Glucose Challenge Test ☐ Rh antibodies (Rh negative women)
36 weeks Every 1-2 weeks until 41 weeks	☐ Develop birth plan ☐ Discuss infant vaccinations ☐ Discuss postnatal visits including Child and Youth Health, GP and domiciliary midwife ☐ Discuss when to call the hospital/midwife	☐ GBS Swab
40 weeks	☐ Plan induction of labour at 41 to 41^{+3} weeks	

Progress notes

• Plot the fundal height on the Symphysio-fundal chart.

Date	Weeks	• Fundal height (cms)	BP (seated)	Urine (if required)	Presentation	Fifths above brim	Fetal movements	Fetal heart	Next visit	Name & designation (maternity care provider)

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NOT FOR USE

Progress notes

• Plot the fundal height on the Symphysio-fundal chart.

Date	Weeks	• Fundal height (cms)	BP (seated)	Urine (if required)	Presentation	Fifths above brim	Fetal movements	Fetal heart	Next visit	Name & designation (maternity care provider)
NOTES										
NOTES										
NOTES										
NOTES										

NOT FOR USE

Progress notes

• Plot the fundal height on the Symphysio-fundal chart.

Date	Weeks	• Fundal height (cms)	BP (seated)	Urine (if required)	Presentation	Fifths above brim	Fetal movements	Fetal heart	Next visit	Name & designation (maternity care provider)

NOTES

NOTES

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NOTES

NOT FOR USE

Progress notes

• Plot the fundal height on the Symphysio-fundal chart.

Date	Weeks	• Fundal height (cms)	BP (seated)	Urine (if required)	Presentation	Fifths above brim	Fetal movements	Fetal heart	Next visit	Name & designation (maternity care provider)
NOTES										
NOTES										
NOTES										
NOTES										

NOT FOR USE

Progress notes

• Plot the fundal height on the Symphysio-fundal chart.

Date	Weeks	• Fundal height (cms)	BP (seated)	Urine (if required)	Presentation	Fifths above brim	Fetal movements	Fetal heart	Next visit	Name & designation (maternity care provider)

NOTES

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NOT FOR USE

Progress notes

• Plot the fundal height on the Symphysio-fundal chart.

Date	Weeks	• Fundal height (cms)	BP (seated)	Urine (if required)	Presentation	Fifths above brim	Fetal movements	Fetal heart	Next visit	Name & designation (maternity care provider)
NOTES										
NOTES										
NOTES										
NOTES										

NOT FOR USE

FINAL DUE DATE:

Surname *UR*

Given names *Date of birth*

Address

(complete or preferably affix label)

Blood group: _____

PREGNANCY ISSUES AND MANAGEMENT PLANS

Pregnancy issues

Management plans for pregnancy, birth and postnatal care

NOT FOR USE

INVESTIGATIONS

Surname *UR*

Given names *Date of birth*

Address

(complete or preferably affix label)

The original results of all pathology and other investigation results are to be attached here.
It is recommended that results are requested on A5 sized paper when ordering investigations.

NOT FOR USE

If hardcopies cannot be obtained, please write results here.

Investigations	Date	Result		Date	Result
Haemoglobin			28 weeks Hb		
Blood group			28 weeks Ab (if Rh-)		
Antibodies			28 weeks OGCT		
Rubella titre			36 weeks GBS		
Syphilis					
Hepatitis B					
Hepatitis C					
HIV					
MSSU					
Pap smear					
Down syndrome risk					

ULTRASOUND

Surname	*UR*
Given names	*Date of birth*
Address	

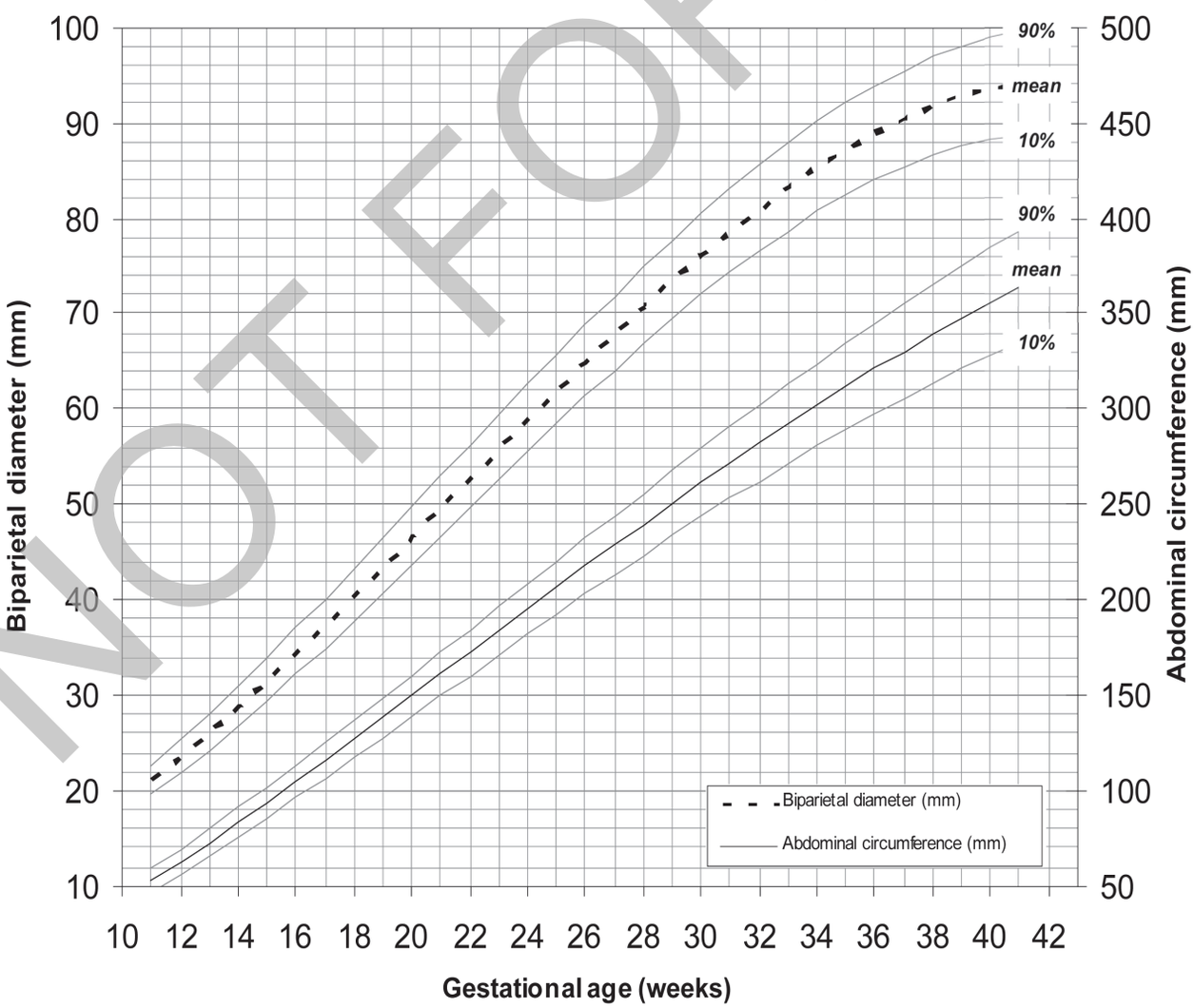
(complete or preferably affix label)

All ultrasound results are to be attached here.

If hardcopies cannot be obtained, please write results here

Date	Comments

Ultrasound chart (Plot by final due date)



Schluter PJ, Pritchard G and Gill MA. Ultrasonic fetal size measurements in Brisbane, Australia. Australasian Radiology (2004); 48: 480-456

NOT FOR USE

HEALTH INFORMATION FOR YOUR PREGNANCY

More information is available at www.health.sa.gov.au/pregnancy

Taking care with medicines
Some medicines can harm your developing baby. Only take those medicines that have been prescribed by your doctor. Always check with your doctor or pharmacist before taking anything else including 'over the counter' drugs and alternative therapies.

Smoking
Smoking during pregnancy affects the baby's growth and will mean more likelihood of health problems for you and your baby. Smokers have:

- higher risk of miscarriage or of having a preterm or stillborn baby
- higher risk of a low birthweight baby who is more vulnerable to infections and other health problems
- a greater chance of having complications during birth
- an increased risk of their baby dying at or shortly after birth, or due to SIDS ("cot death")

If you are pregnant and still smoke, your baby will benefit greatly if you and your partner can quit smoking now.
Call the Pregnancy Quitline on 1300 889 010 or for more information: www.quitsa.org.au.

Alcohol
Pregnancy and alcohol don't mix. Alcohol can harm your baby for life. There is no safe time to drink alcohol during pregnancy, nor is there a safe amount of alcohol that can be drunk. Every time you drink alcohol when you are pregnant it is carried by your bloodstream through the placenta to your baby. Drinking alcohol during pregnancy can cause brain damage to your baby and can cause a greater risk of miscarriage, preterm birth and stillbirth. If you drank small amounts of alcohol before you knew you were pregnant, the risk to your baby is low.
No alcohol is the best and safest choice during pregnancy.
More information is available under the health topics category of the parenting and child health section at: www.cyh.com

Cannabis and/or other recreational drugs
Using cannabis and/or other recreational drugs when you are pregnant can affect the development of your baby, possibly causing preterm birth or a low birth weight. **Avoid using these drugs.**

Infections during pregnancy
Some infections during pregnancy can cause serious illness to you and may harm your baby. Ask your doctor or midwife what you should do if you have been in contact with someone who has an infectious illness. These illnesses include Rubella (German Measles), Chicken Pox, Parvovirus (Slapped Cheek Syndrome), Hepatitis B, Hepatitis C and Herpes.

You may also want to ask your doctor or midwife about other infections which may cause harm to you and your baby. For example urinary tract infections, Group B Streptococcus (GBS), sexually transmitted infections (e.g. HIV, chlamydia or gonorrhoea), Toxoplasmosis or CMV. Listeriosis is another infectious disease which can be avoided during pregnancy by not eating foods such as unpasteurised cheeses (brie, camembert or ricotta), pate, oysters, smoked salmon, take-away cold meats or prepared salads. Food that is reheated or bought hot and ready-to-eat should be served steaming hot.
More information is available at: www.dh.sa.gov.au/pehs/food-index.htm or www.foodstandards.gov.au

Immunisation
Immunisation provides protection against infections that can cause serious illness in a pregnant woman, the unborn child and/or the new baby. Immunisation is recommended **before** pregnancy for the following and **you should wait a month after these immunisations before getting pregnant:**

- measles, mumps, rubella (booster vaccination may be needed)
- whooping cough (both parents can be immunized to prevent passing this on to their baby)
- chicken pox (a blood test can tell if you have protection against chicken pox infection).

You can be immunised against influenza before or during pregnancy.
More information is available at: www.dh.sa.gov.au/pehs/immunisation-index.htm

Glossary

Further terms are available at: www.health.sa.gov.au/pregnancy

Antenatal	During pregnancy, before the birth	**Gravida**	Number of times pregnant
BP	Blood pressure	**Haemoglobin (Hb)**	Amount of iron in the blood
Fetal heart	Unborn baby's heart rate	**MSSU**	Mid stream specimen urine
Fetal movement	Unborn baby's movements	**Parity**	Number of pregnancies that resulted in birth
Fifths above brim	Amount of baby's head that can be felt	**Postnatal**	After the birth
Fundal height	Size of uterus (womb)	**Presentation**	The part of the baby which is coming first, e.g. head, bottom.

NOT FOR USE

Government of South Australia
SA Health

South Australian

PREGNANCY RECORD

Version 5, January 2012

Affix patient identification label in this box

U.R. No.: .....
Surname: .....
Given Name: .....
Second Given Name: .....
D.O.B.: .....

Please take care of this Record as it is the only official record of your pregnancy.

You should bring this Record with you when you visit any health care professional

If you find this Record call the contact numbers below or return it to the nearest hospital/maternity unit.

SA PREGNANCY INFOLINE 1300 368 820

CONTACT DETAILS

Hospital/maternity unit _____ ***Phone*** _____

Obstetrician _____ ***Phone*** _____

Midwife _____ ***Phone*** _____

General Practitioner _____ ***Phone*** _____

This Record will be filed in the hospital case record or returned to your maternity care provider at the end of your pregnancy.

A copy is required for: Please tick (✓)
☐ Private Obstetrician ☐ Midwife ☐ GP

APPOINTMENTS

You should bring this Record with you when visiting any health care professional

For example: obstetrician, midwife, general practitioner, clinic, ultrasounds and procedures

Date	Time	What/Who	Where

NOT FOR USE

SA PREGNANCY RECORD MR31

PERSONAL HISTORY

Name and designation of maternity care provider taking this history (please print):

_____

Date: _____

Affix patient identification label in this box

U.R. No.: .....

Surname: .....

Given Name: .....

Second Given Name: .....

D.O.B.: .....

Woman

Preferred name: _____

Occupation: _____

Phone: (H)_____ (W)_____

(M)_____

Ethnicity/Cultural background: _____

Language preferred: _____

Interpreter required: Yes / No

Partner

Name: _____

Occupation: _____

Phone: (H)_____ (W)_____

(M)_____

Ethnicity/Cultural background: _____

Other contact person

Name: _____

Relationship: _____

Phone: (H)_____ (W)_____

(M)_____

Guidelines for calculation of final due date (please circle where appropriate)

Step 1 **LMP** certain/uncertain normal/abnormal spontaneous/pill withdrawal

Date _____

Menstrual cycle

Length _____ regular/irregular

Step 2

Due date based on period and cycle

Step 3 **1st ultrasound**

Date _____ Gestation _____ Consistent with LMP? Yes / No

Step 4 **FINAL DUE DATE** _____

_____

Name and designation of person who calculated (please print)

Past pregnancy information Use * to indicate sensitive information not recorded here. **Age** _____ **Gravidity** _____ **Parity** _____

*	*Date*	*Place*	*Gestation (in weeks)*	*Labour, birth and postnatal details*	*Birth weight*	*Gender*	*Feeding type and duration*	*Baby's name*

Medication history (over the counter drugs & alternative therapies)

Medications	Dose	Frequency	Cessation

Allergies Detail all allergies including reactions to medication

NOT FOR USE

PERSONAL HISTORY
continued

Affix patient identification label in this box

U.R. No.: .....
Surname: .....
Given Name: .....
Second Given Name: .....
D.O.B.: .....

Medical history

Deep venous thrombosis
Diabetes
Epilepsy
Gynaecological problems
Heart disease
High blood pressure
Kidney disease
Asthma/respiratory disease
Thyroid disorders
Alcohol (drinks per week)
Smoking (number per day)
Illicit drug use

Psycho - Social history - all items should be reviewed as pregnancy progresses.
Use * to indicate sensitive information not recorded here.
Health providers should refer to an appropriate agency as deemed necessary.

EPDS

ANRQ

Anxiety/depression
Postnatal depression
Other psychiatric disorders
Emotional issues
Major stressors, life changes or losses
Mental health problems (including partner)
Relationship issues
Contact with Families SA
Accommodation issues
Financial issues
Other

Surgical history

Anaesthetic history
Anaesthetic consultation may be required

Previous anaesthetic problems
Dental health and jaw problems
Back problems
Blood transfusion
Other

Family history and prenatal diagnostic issues

Diabetes
Heart disease
High blood pressure
Genetic disorders/congenital abnormalities
Other

Physical examination
Date: / /

Height _____ Weight _____ BMI _____

Last Pap smear (should be performed if due) / /

Results Pap Smear _____

Other examinations

Oral, cardiac, respiratory and breast examinations if indicated

_____

_____

NOT FOR USE

ANTENATAL SCHEDULE AND INVESTIGATIONS

Affix patient identification label in this box

U.R. No.: .....

Surname: .....

Given Name: .....

Second Given Name: .....

D.O.B.: .....

SCHEDULED VISIT	OUTLINE OF ASSESSMENT/TASKS REQUIRED
1st visit may be with GP and assessment may be completed at 2nd antenatal visit usually at 10-12 weeks	☐ Diagnose pregnancy ☐ **Calculate** EDC by dates and cycle. If uncertain, order dating ultrasound ☐ Commence SA Pregnancy Record ☐ **Order** routine blood and urine tests ☐ Complete blood picture ☐ Blood group and antibody screen ☐ Rubella titre ☐ Syphilis serology ☐ Hepatitis B screen ☐ Hepatitis C screen ☐ HIV ☐ MSSU ☐ **Screen** for perinatal mental health as per the National Perinatal Mental Health Initiative ☐ Commence Iodine supplement ☐ Commence Vitamin D regime for at risk women ☐ **Book** woman for birth ☐ Discuss breastfeeding and antenatal education ☐ **If woman 11 – 13[6]** weeks offer first or second trimester Down Syndrome screening ☐ Discuss options of CVS or amniocentesis to women at increased risk ☐ **If woman 14 – 20[6]** weeks offer second trimester Down Syndrome and NTD screening if indicated ☐ **Book** morphology ultrasound for 19-20 weeks. Consider delaying ultrasound to 22 weeks if woman's BMI > 35 kg/m²
22 weeks	☐ Discuss prophylactic Anti-D with Rh (-) women ☐ Discuss maternal blood screening, morphology & ultrasound results
28 weeks	☐ **Order** (copy to the hospital) ☐ Complete blood picture ☐ Oral glucose challenge test ☐ Blood group antibodies ☐ **Administer** prophylactic Anti-D to Rh (-) women without antibodies ☐ **EPDS Score** – to be repeated if previous score >13
32 weeks	☐ Check-up
34 weeks	☐ **Administer** prophylactic Anti-D as per protocol for Rh (-) women ☐ Discuss breastfeeding
36 weeks	☐ Discuss birthing plan ☐ **Undertake** Group B strep screening (copy to GP if GP Shared Care)
38 weeks	☐ Check-up
40 weeks	☐ Discuss induction of labour

All investigation must be preceded by appropriate discussion and counselling
The health professional who orders the investigation has the responsibility to follow up the results
To reduce duplication, please record each test/activity when ordered/performed
If a hard copy cannot be obtained, please record results here

Investigations	Date	Results	When	Date	Results
Haemoglobin			28 weeks Hb		
Blood group			28 weeks Ab if Rh (-)		
Antibodies			28 weeks OGCT		
Vitamin D screening			28 weeks Vit D (if indicated)		
Rubella titre			36 weeks GBS		
Syphilis					
Hepatitis B					
Hepatitis C					
HIV					
MSSU					
Pap smear					
Maternal serum screening					

NOT FOR USE

ULTRASOUND

Affix patient identification label in this box

U.R. No.: .....

Surname: .....

Given Name: .....

Second Given Name: .....

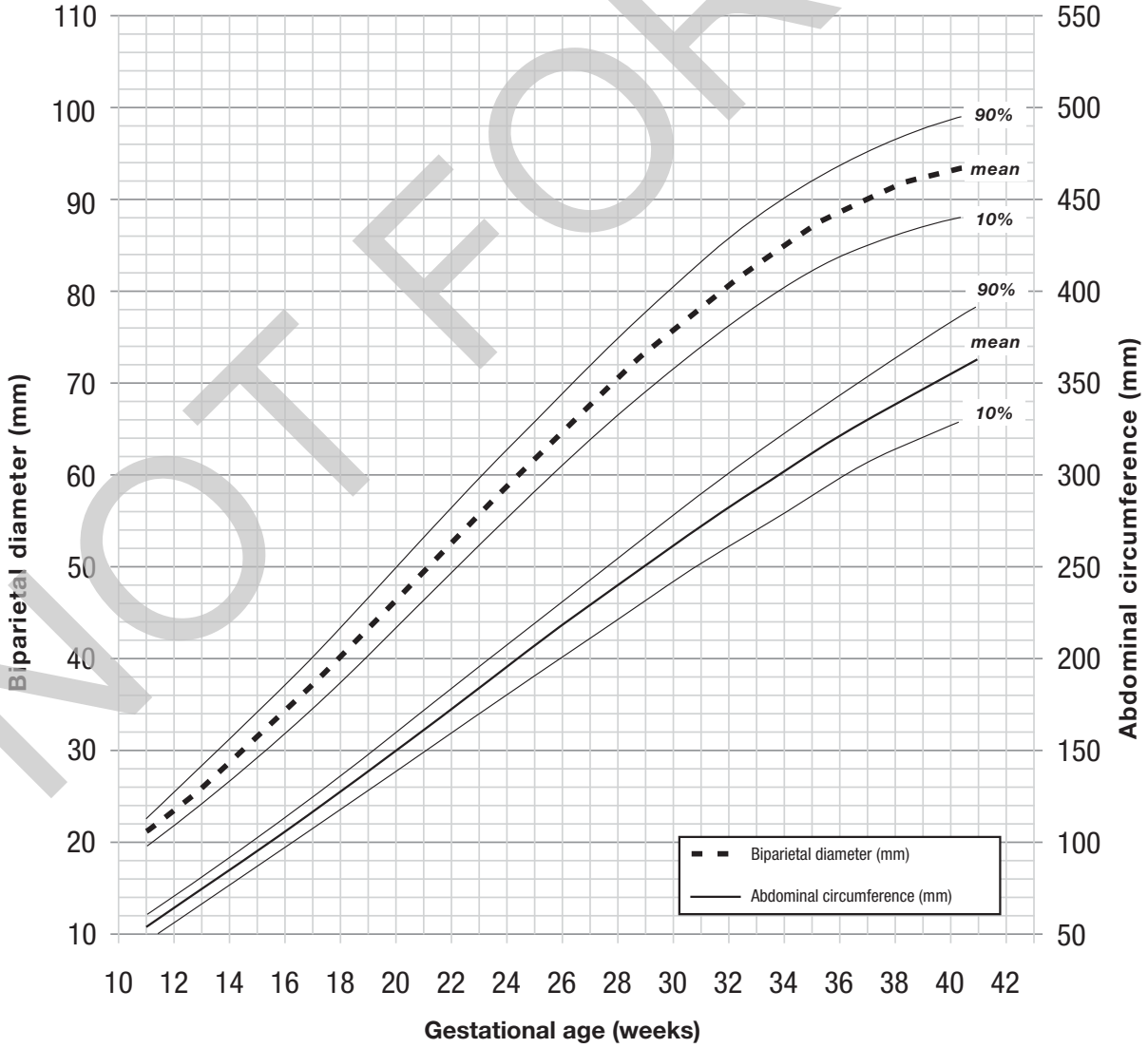
D.O.B.: .....

All ultrasound results are to be attached here

If hardcopies cannot be obtained, please write results here

Date	Comments

Ultrasound chart (Plot by final due date)



Schluter PJ, Pritchard G and Gill MA. Ultrasonic fetal size measurements in Brisbane, Australia. Australasian Radiology (2004); 48: 480-456

NOT FOR USE

SYMPHYSIO-FUNDAL CHART

Affix patient identification label in this box

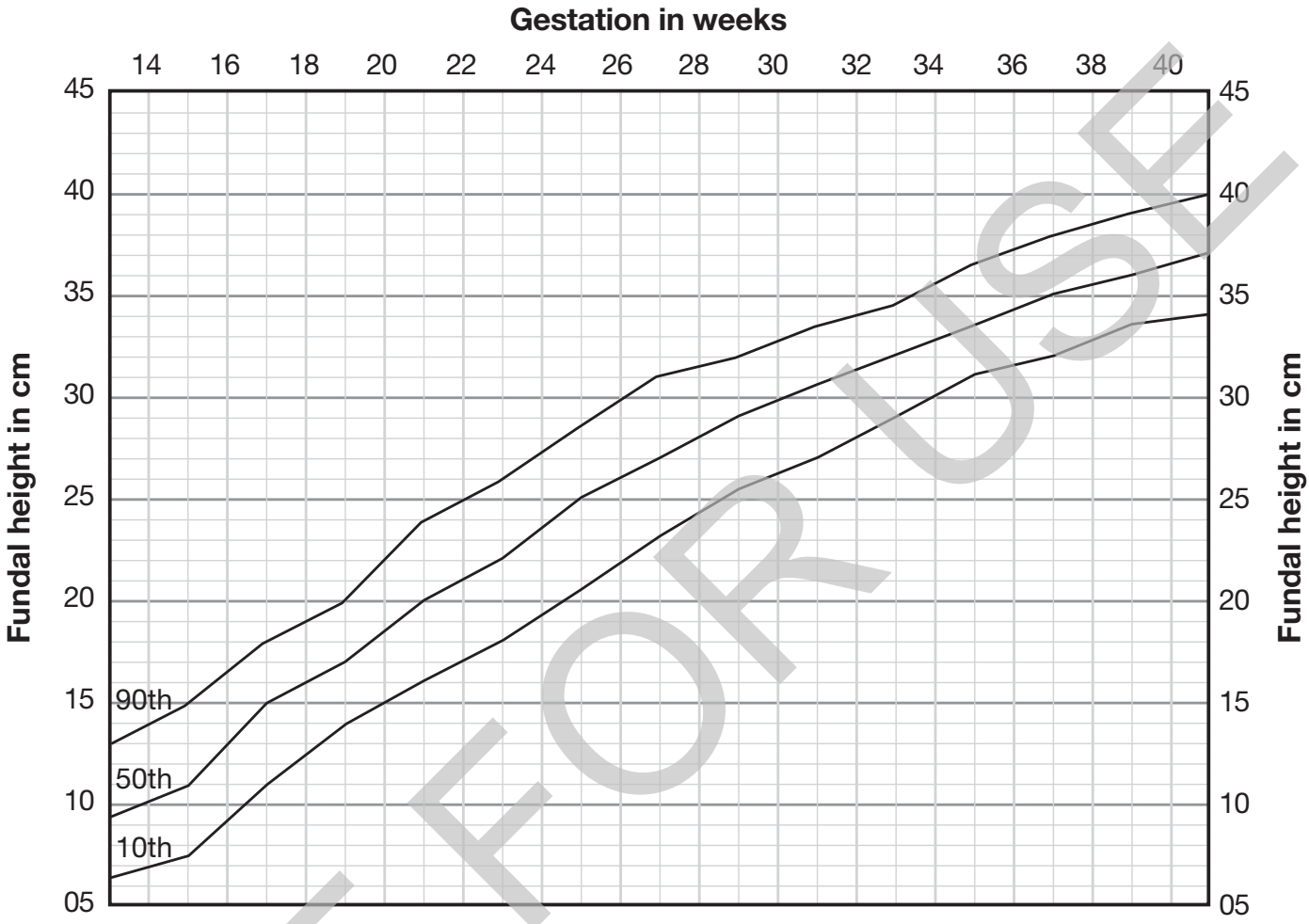
U.R. No.: .....

Surname: .....

Given Name: .....

Second Given Name: .....

D.O.B.: .....



Taylor P, Coulthard AC, Robinson JS. Symphsio-fundal height from 12 weeks' gestation. Aust NZ J Obstet Gynaecol 1984; 24 (3):189-91

NOT FOR USE

Guidelines

The woman should be lying in the supine position with her head supported on a single pillow. The couch should be flat.

Measure from the highest point of the fundus to the top of the symphysis pubis. Begin measuring from the fundus since this is the more variable end point.

Measure with the tape scale facing downwards so that you are less influenced by previous results. Measurements should be recorded to the nearest 0.5 centimetre.

Progress notes • Plot the fundal height on the Symphysio-fundal chart.

Date	Weeks	Weight kg	• Fundal height (cms)	BP (seated)	Urine (if required)	Presentation	Fifths above brim	Fetal movements	Fetal heart	Next visit	Name & designation (maternity care provider)

NOTES

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SMOKING ASSESSMENT *(Please complete the following EVERY 3rd visit for smokers and recent quitters)* Pregnancy Quitline 1300 889 010

Cigarettes per day	Advice offered (✓)	Quitting stage *(please circle)*					Referral faxed to Quitline 08 8291 4280 Circle: YES NO
		Recently quit	Preparing to quit	Thinking about quitting	Not interested in quitting	Relapse/Slip up	

NOT FOR USE

Progress notes • Plot the fundal height on the Symphysio-fundal chart.

Date	Weeks	Weight kg	• Fundal height (cms)	BP (seated)	Urine (if required)	Presentation	Fifths above brim	Fetal movements	Fetal heart	Next visit	Name & designation (maternity care provider)

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SMOKING ASSESSMENT *(Please complete the following EVERY 3rd visit for smokers and recent quitters)* Pregnancy Quitline 1300 889 010

Cigarettes per day	Advice offered (✓)	Quitting stage *(please circle)*					Referral faxed to Quitline 08 8291 4280 Circle: YES NO
		Recently quit	Preparing to quit	Thinking about quitting	Not interested in quitting	Relapse/Slip up	

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NOT FOR USE

Affix patient identification label in this box

U.R. No.: .....

Surname: .....

Given Name: .....

Second Given Name: .....

D.O.B.: .....

FINAL DUE DATE:

Blood group: _____

Anti-D:

28 weeks: Date Given _____ Batch no.: _____ 34 weeks: Date Given _____ Batch no.: _____

PREGNANCY ISSUES

MANAGEMENT PLANS FOR PREGNANCY, BIRTH & POSTNATAL CARE

NOT FOR USE

ADVICE, INFORMATION AND BIRTH PLAN

Affix patient identification label in this box

U.R. No.: .....

Surname: .....

Given Name: .....

Second Given Name: .....

D.O.B.: .....

Call your hospital, midwife or doctor on the telephone numbers provided on the front page of this Record if you have any concerns or experience any of the following:

- Persistent headache
- Visual changes such as flashing lights
- Persistent abdominal pain
- Bleeding from your vagina
- Reduce baby movements
- Regular contractions or breaking of your waters

If you experience mood changes, anxiety or feelings of being overwhelmed please contact Beyond Blue for more information. www.beyondblue.org.au

General information

You will need to bring this Record with you whenever you see your health care provider and when you go to the hospital at any time, including for the birth of your baby

- After an uncomplicated vaginal birth the expected length of stay in hospital is 1-2 days. In the event of a caesarean section, the expected length of stay in hospital is 3-5 days.
- On the day of discharge you will be expected to vacate the hospital by 11am.
- During your stay in hospital you will be offered a home visit from a Child and Family Health Nurse. This visit will provide your baby's first health check and answer any questions you may have. This home visit will usually occur within a few weeks of leaving hospital.
- At your request, a photocopy of this Record can be provided to you at the end of pregnancy. The original will be filed in your hospital record or returned to your maternity care provider.

Birth Plan

Support persons(s) for the labour and birth

Name(s) _____

Birth

Describe the kind of labour and birth you wish to experience.

Cultural or religious needs

How would like to feed your baby?

Breastfeeding your baby will provide long term benefits for you and your baby and will help protect your baby against infections

Previous pregnancy experiences

Any other information or questions

Please note: Your birth plan will be used as a guide for your care but your doctor or midwife will discuss with you the need for any changes as a result of your clinical needs at the time

NOT FOR USE

GLOSSARY OF TERMS AND HEALTH INFORMATION FOR YOU DURING YOUR PREGANCY

Glossary of abbreviations and terms

Anaemia	Is a lack of red blood cells and haemoglobin in the blood
ANRQ	Antenatal Risk Questionnaire
Antenatal	The time during pregnancy, before the birth
Antibodies	Vital element of the unborn body's immune system. Are secreted by the white blood cells
Biparietal	Measurement of the unborn baby's skull used to assess growth of the baby
BP	Blood pressure
CVS	Chorionic Villus Sampling
EDC	Expected date of confinement
EPDS	Edinburgh Perinatal Depression Score
Fetal heart	Unborn baby's heart beat
Fifths above brim	Amount of unborn baby's head that can be felt above the pelvis
Fundal height	Size of the uterus
GBS	Group B streptococcus
Gestation	Length of time from conception Usually recorded in weeks and days
Gravidity	Number of pregnancies
Haemoglobin (Hb)	Is a protein in red blood cells that carries oxygen
HIV	Human immunodeficiency virus
MSSU	Mid stream specimen of urine
NTD	Neural Tube Defect
Pap smear	A sample of cells from the cervix to check for early changes that may lead to cancer
Parity	Number of pregnancies that resulted in a birth
Postnatal	The time after the birth
OGCT	Oral Glucose Challenge Test
Presentation	The part of the unborn baby that is positioned to come first ie head, bottom
Rubella	A mild contagious disease caused by a virus and capable of producing congenital defects in babies born to infected mothers
Rh	Substance found on red blood cells that is used to determine a person's blood group

Health information

The following web sites may be useful sources of information during your pregnancy

- www.pregnancy.sa.gov.au
- www.quitsa.org.au
- www.foodstandards.gov.au
- www.beyondblue.org.au
- www.dh.sa.gov.au/pehs/immunisation-index.htm

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