Postmarketing Vaccine Safety Surveillance Using Data Linkage: The Issue Of Consent

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Contents

Abstract

Background: Linked electronic administrative health care databases are a valuable resource that can be used for postmarketing safety surveillance of medicines and vaccines. Australian legislation mandates that individual consent is required for the collection, use and dissemination of health information. However, the requirement for consent is not absolute; a waiver of consent may be granted by an appropriately constituted human research ethics committee, provided certain qualifying criteria are met and the research (or other activity) is deemed to be substantially in the public interest. In Australia, data linkage research projects are recommended to abide by a best practice protocol, whereby individual privacy is preserved as researchers only receive files of pre-linked data with no personal identifiers. Ethical approval of a waiver of consent is required for the disclosure of identifiable demographic information to an authorised data linkage unit for the purpose of creating a master linkage key. However, some ethics committees and data custodians still require informed consent.

Objective: The overall objective of this thesis was to examine the issue of consent in the context of postmarketing surveillance of vaccine safety using data linkage. A randomised controlled trial (RCT) was used for the primary aim of determining which method of obtaining parental consent (opt-in or opt-out) provided the highest participation rate. The secondary aims of the RCT were to examine reasons for participation and non-participation, socio-demographic factors, consent preferences and attitudes towards a data linkage study of vaccine safety. For this, a follow-up telephone interview of a parent from each family enrolled in the RCT was conducted. The generalisability of findings from the

follow-up telephone interview was examined by repeating selected questions in a population-based survey sample of South Australians.

Method: A total of 1129 families of children born at a South Australian hospital in 2009 were enrolled in a single-blind parallel group RCT of opt-in and opt-out consent at six weeks post-partum, with four weeks to respond by reply form, telephone or email. Interviews were conducted at 10 weeks post-partum (response rate 91%, *n*=1026). Computer-assisted telephone interviewing (CATI) of rural and metropolitan South Australian residents was conducted in 2010 (response rate 56%, *n*=2002).

Results: The participation rate was 21% (*n*=120/564) in the opt-in arm and 96% (*n*=540/565) in the opt-out arm [χ^2 (1df) = 567.7, *P*<0.001]. Participants in the opt-in arm were more likely than non-participants to be older, married or in a de facto relationship, university educated and of higher socioeconomic status. Participants in the opt-out arm were similar to non-participants, except men were more likely to opt out.

Substantial proportions did not receive, understand or properly consider study invitations, and opting in or opting out behaviour was often at odds with parents' stated underlying intentions. Three-fifths of the parents in the opt-in and opt-out arms reported reading the information (63% *vs* 67%, *P*=0.11), but only two-fifths correctly identified the health records to be linked (43% *vs* 39%, *P*=0.21). Parents who actively consented (opted in) were more likely than those who passively consented (did not opt out) to correctly identify the data sources (60% *vs* 39%, *P*<0.001).

Data linkage for postmarketing surveillance of vaccines was widely supported by parents enrolled in the RCT and by the wider community (96% and 94% respectively) and there was trust in its privacy protections (84% and 75%). The majority also preferred minimal or no direct involvement: either opt-out consent (40% and 40%) or no consent (30% and 31%). Only a quarter preferred opt-in consent (24% and 25%). Over half gave higher

priority to rapid vaccine safety surveillance (61% and 56%) rather than first seeking parental consent (21% and 27%), while one in seven was undecided (15% and 15%). Despite generally vaccinating their children (91% and 96%) and trusting vaccines as safe (90% and 92%), many were concerned that vaccines may be ineffective (42% and 40%) and may cause serious reactions (62% and 53%).

Conclusions: The opt-in approach resulted in low participation and a biased sample that would render any subsequent data linkage to be not feasible, whereas the opt-out approach achieved high participation and a representative sample.

Neither the opt-in nor opt-out approach was effective in achieving informed consent. The study's purpose was poorly understood, although comprehension was moderately better when parents actively rather than passively consented. Nonetheless, most parents and the general public supported data linkage for vaccine safety surveillance. A system utilising opt-out consent or no consent was preferred to one using opt-in consent.

These findings should inform public health policy and practice; the waiver of consent afforded under current privacy regulations for data linkage studies meeting all appropriate criteria should be granted by ethics committees, and supported by data custodians.

Declaration

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university or other institution and affirms that to the best of my knowledge, the thesis contains no material previously published or written by another person, except where due reference is made in the text of thesis.

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Date .....

Publications during candidature

- Berry JG, Ryan P, Braunack-Mayer AJ, Duszynski KM, Xafis V, Gold MS, the Vaccine Assessment using Linked Data (VALiD) Working Group. A randomised controlled trial to compare opt-in and opt-out parental consent for childhood vaccine safety surveillance using data linkage: study protocol. *Trials* 2011;12:1, doi: 10.1186/1745-6215-12-1.
- Berry JG, Ryan P, Gold MS, Braunack-Mayer AJ, Duszynski KM, the Vaccine Assessment using Linked Data (VALiD) Working Group. A randomised controlled trial to compare opt-in and opt-out parental consent for childhood vaccine safety surveillance using data linkage. *J Med Ethics* 2012;38(10):619-25.
- Berry JG, Ryan P, Duszynski KM, Braunack-Mayer AJ, Carlson J, Xafis V, Gold MS, the Vaccine Assessment using Linked Data (VALiD) Working Group. Parent perspectives on consent for the linkage of data to evaluate vaccine safety: a randomised trial of opt-in and opt-out consent. *Clinical Trials* (accepted 1/2/13).
- Berry JG, Gold MS, Ryan P, Duszynski KM, Braunack-Mayer AJ, the Vaccine Assessment using Linked Data (VALiD) Working Group. Public perspectives on consent for the linkage of data to evaluate vaccine safety. *Vaccine* 2012;30(28):4167-74.

Conference presentations during candidature

- Berry JG, Ryan P, Gold MS, Duszynski KM, Braunack-Mayer AJ, Carlson J, Xafis V. *Parent and public perspectives on consent for the linkage of data to evaluate vaccine safety.* International Data Linkage Conference 2012; 2012 May 2-4; Perth.
- Berry JG, Ryan P, Gold MS, Braunack-Mayer AJ, Duszynski KM, Xafis V, White J. *A randomised controlled trial to compare opt-in and opt-out parental consent for childhood vaccine safety surveillance using data linkage.* Australasian Epidemiological Association (AEA) of Australia Conference 'Combining Tradition and Innovation'; 2011 Sep 19-21; Perth.
- Berry JG. *A study of opt-in and opt-out consent for checking the safety of vaccines using data linkage.* Expert presentation for the 'Vaccine Safety Data Linkage Community Forum' Citizens' Jury; 2011 Mar 26; Adelaide.
- Berry JG, Ryan P, Gold MS, Braunack-Mayer AJ, Duszynski KM, Xafis V, Carlson-White J. *A randomised trial of consent options in data linkage for vaccine surveillance.* Public Health Association of Australia (PHAA) 12th National Immunisation Conference; 2010 Aug 17-19; Adelaide.
- Berry JG. *Using multiple imputation to fill in missing data for a randomised controlled trial of opt-in and opt-out consent to data linkage.* University of Adelaide, School of Population Health Seminar Series; 2011 Apr 7; Adelaide.
- Berry JG. *A randomised trial of consent options in data linkage for vaccine safety surveillance.* University of Adelaide, School of Population Health, Higher Degree by Research Symposium; 2010 Oct 1; Adelaide.

- Berry JG. *The feasibility of data linkage using routine administrative datasets for vaccine safety surveillance in Australia*. University of Adelaide, School of Population Health Seminar Series; 2009 Apr 24; Adelaide.

Poster presentations:

- Berry JG, Ryan P, Gold MS, Braunack-Mayer AJ, Duszynski KM, for the VALiD Working Group. *Is it feasible to obtain consent for data linkage studies of vaccine safety?* PHAA (SA branch) Conference 'Population Health: Working across sectors, settings and ages'; 2011 Oct 29; Adelaide. (Also presented at the University of Adelaide, Faculty of Health Sciences Postgraduate Research Conference; 2011 Aug 25; Adelaide.)

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'There's more to life than books, you know. But not much more.'

Morrissey

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Abbreviations

ABS	Australian Bureau of Statistics
ACIR	Australian Childhood Immunisation Register
ACSOM	Advisory Committee on the Safety of Medicines
ACT	Australian Capital Territory
ACTRN	Australian New Zealand Clinical Trials Registry
AEA	Australasian Epidemiological Association
AEFI	Adverse Event(s) Following Immunisation
AIHW	Australian Institute of Health and Welfare
APSU	Australian Paediatric Surveillance Unit
ARC	Australian Research Council
ASGC	Australian Standard Geographical Classification
CATI	Computer-Assisted Telephone Interviewing
CDC	Centers for Disease Control and Prevention
CDL	Centre for Data Linkage
CEO	Chief Executive Officer
CHeReL	Centre for Health Record Linkage
CI	Confidence Interval
CONSORT	Consolidated Standards of Reporting Trials
CYWHS	Children, Youth and Women's Health Service
DAEN	Database of Adverse Event Notifications
DEC	Departmental Ethics Committee
DLU	Data Linkage Unit
DTP	Diphtheria-tetanus-pertussis

ED	Emergency Department
EMR	Electronic Medical Record
FCS	Fully conditional specification
GP	General Practitioner
H1N1	Pandemic influenza A
Hep B	Hepatitis B
Hib	Haemophilus influenzae type B
HIPAA	Health Insurance Portability and Accountability Act Privacy Rule
HIPPO	Health Informatics, Policy and Performance Outcomes Unit
HMO	Health Maintenance Organization
HPV	Human papillomavirus
HREC	Human Research Ethics Committee
ICD	International Classification of Diseases
ID	Identification
IHDLN	International Health Data Linkage Network
IPV	Inactivated poliovirus vaccine
IQR	Interquartile range
IRR	Incidence rate ratio
IRSD	Index of Relative Socio-economic Disadvantage
MACSS	Multipurpose Australian Comorbidity Scoring System
MAR	Missing at random
MCV4	Meningococcal conjugate vaccine
MenCCV	Meningococcal C conjugate vaccine
MMR(V)	Measles-mumps-rubella(-varicella)
MNAR	Missing not at random
MVNI	Multivariate normal distribution

NCIRS	National Centre for Immunisation Research and Surveillance
NCRIS	National Collaborative Research Infrastructure Strategy
NHMRC	National Health and Medical Research Council
NHS	National Health Service
NICU	Neonatal Intensive Care Unit
NIP	National Immunisation Program
NSW	New South Wales
NT	Northern Territory
OPR	Office of Product Review
OPV	Oral poliovirus vaccine
7vPCV	Seven-valent pneumococcal conjugate vaccine
13vPCV	Thirteen-valent pneumococcal conjugate vaccine
PAEDS	Paediatric Active Enhanced Disease Surveillance
PHAA	Public Health Association of Australia
PHRN	Population Health Research Network
PIAG	Patient Information Advisory Group
PRISM	Post-licensure Rapid Immunization Safety Monitoring system
RCT	Randomised controlled trial
RR	Relative Risk
SA	South Australia
SAEFVic	Surveillance of Adverse Events Following Vaccination in Victoria
SAVeS	South Australian Vaccine Safety Data Linkage Pilot Project
SCCS	Self-controlled case series
SCR	Summary care record
SEIFA	Socio-Economic Indexes For Areas
SURE	Secure Unified Research Environment

TdaP	Tetanus-diphtheria-acellular pertussis
TGA	Therapeutic Goods Administration
TIV	Trivalent influenza vaccination
TP	Thrombocytopenic purpura
UK	United Kingdom of Great Britain and Northern Ireland
US	United States of America
VAESCO	Vaccine Adverse Event Surveillance and Communication
VALiD	Vaccine Assessment using Linked Data study
Vic	Victoria
VSD	Vaccine Safety Datalink
WA	Western Australia
WADLS	Western Australia Data Linkage System
WCH	Women's and Children's Hospital

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