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

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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 \( \chi^2 (1 \text{df}) = 567.7, P<0.001 \). 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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Signed............................................................................
Jesia Berry (Candidate)
Date ............................................................................
Publications during candidature


Conference presentations during candidature


• 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. *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.

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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
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ED</td>
<td>Emergency Department</td>
</tr>
<tr>
<td>EMR</td>
<td>Electronic Medical Record</td>
</tr>
<tr>
<td>FCS</td>
<td>Fully conditional specification</td>
</tr>
<tr>
<td>GP</td>
<td>General Practitioner</td>
</tr>
<tr>
<td>H1N1</td>
<td>Pandemic influenza A</td>
</tr>
<tr>
<td>Hep B</td>
<td>Hepatitis B</td>
</tr>
<tr>
<td>Hib</td>
<td>Haemophilus influenzae type B</td>
</tr>
<tr>
<td>HIPAA</td>
<td>Health Insurance Portability and Accountability Act Privacy Rule</td>
</tr>
<tr>
<td>HIPPO</td>
<td>Health Informatics, Policy and Performance Outcomes Unit</td>
</tr>
<tr>
<td>HMO</td>
<td>Health Maintenance Organization</td>
</tr>
<tr>
<td>HPV</td>
<td>Human papillomavirus</td>
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<tr>
<td>HREC</td>
<td>Human Research Ethics Committee</td>
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<tr>
<td>ICD</td>
<td>International Classification of Diseases</td>
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<tr>
<td>ID</td>
<td>Identification</td>
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<tr>
<td>IHDLN</td>
<td>International Health Data Linkage Network</td>
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<tr>
<td>IPV</td>
<td>Inactivated poliovirus vaccine</td>
</tr>
<tr>
<td>IQR</td>
<td>Interquartile range</td>
</tr>
<tr>
<td>IRR</td>
<td>Incidence rate ratio</td>
</tr>
<tr>
<td>IRSD</td>
<td>Index of Relative Socio-economic Disadvantage</td>
</tr>
<tr>
<td>MACSS</td>
<td>Multipurpose Australian Comorbidity Scoring System</td>
</tr>
<tr>
<td>MAR</td>
<td>Missing at random</td>
</tr>
<tr>
<td>MCV4</td>
<td>Meningococcal conjugate vaccine</td>
</tr>
<tr>
<td>MenCCV</td>
<td>Meningococcal C conjugate vaccine</td>
</tr>
<tr>
<td>MMR(V)</td>
<td>Measles-mumps-rubella(-varicella)</td>
</tr>
<tr>
<td>MNAR</td>
<td>Missing not at random</td>
</tr>
<tr>
<td>MVNI</td>
<td>Multivariate normal distribution</td>
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<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<tr>
<td>NCIRS</td>
<td>National Centre for Immunisation Research and Surveillance</td>
</tr>
<tr>
<td>NCRIS</td>
<td>National Collaborative Research Infrastructure Strategy</td>
</tr>
<tr>
<td>NHMRC</td>
<td>National Health and Medical Research Council</td>
</tr>
<tr>
<td>NHS</td>
<td>National Health Service</td>
</tr>
<tr>
<td>NICU</td>
<td>Neonatal Intensive Care Unit</td>
</tr>
<tr>
<td>NIP</td>
<td>National Immunisation Program</td>
</tr>
<tr>
<td>NSW</td>
<td>New South Wales</td>
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<tr>
<td>NT</td>
<td>Northern Territory</td>
</tr>
<tr>
<td>OPR</td>
<td>Office of Product Review</td>
</tr>
<tr>
<td>OPV</td>
<td>Oral poliovirus vaccine</td>
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<tr>
<td>7vPCV</td>
<td>Seven-valent pneumococcal conjugate vaccine</td>
</tr>
<tr>
<td>13vPCV</td>
<td>Thirteen-valent pneumococcal conjugate vaccine</td>
</tr>
<tr>
<td>PAEDS</td>
<td>Paediatric Active Enhanced Disease Surveillance</td>
</tr>
<tr>
<td>PHAA</td>
<td>Public Health Association of Australia</td>
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<tr>
<td>PHRN</td>
<td>Population Health Research Network</td>
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<tr>
<td>PIAG</td>
<td>Patient Information Advisory Group</td>
</tr>
<tr>
<td>PRISM</td>
<td>Post-licensure Rapid Immunization Safety Monitoring system</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
</tr>
<tr>
<td>RR</td>
<td>Relative Risk</td>
</tr>
<tr>
<td>SA</td>
<td>South Australia</td>
</tr>
<tr>
<td>SAEFVic</td>
<td>Surveillance of Adverse Events Following Vaccination in Victoria</td>
</tr>
<tr>
<td>SAVeS</td>
<td>South Australian Vaccine Safety Data Linkage Pilot Project</td>
</tr>
<tr>
<td>SCCS</td>
<td>Self-controlled case series</td>
</tr>
<tr>
<td>SCR</td>
<td>Summary care record</td>
</tr>
<tr>
<td>SEIFA</td>
<td>Socio-Economic Indexes For Areas</td>
</tr>
<tr>
<td>SURE</td>
<td>Secure Unified Research Environment</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
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<td>--------------</td>
<td>--------------------------------------------</td>
</tr>
<tr>
<td>TdaP</td>
<td>Tetanus-diphtheria-acellular pertussis</td>
</tr>
<tr>
<td>TGA</td>
<td>Therapeutic Goods Administration</td>
</tr>
<tr>
<td>TIV</td>
<td>Trivalent influenza vaccination</td>
</tr>
<tr>
<td>TP</td>
<td>Thrombocytopenic purpura</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom of Great Britain and Northern Ireland</td>
</tr>
<tr>
<td>US</td>
<td>United States of America</td>
</tr>
<tr>
<td>VAESCO</td>
<td>Vaccine Adverse Event Surveillance and Communication</td>
</tr>
<tr>
<td>VALiD</td>
<td>Vaccine Assessment using Linked Data study</td>
</tr>
<tr>
<td>Vic</td>
<td>Victoria</td>
</tr>
<tr>
<td>VSD</td>
<td>Vaccine Safety Datalink</td>
</tr>
<tr>
<td>WA</td>
<td>Western Australia</td>
</tr>
<tr>
<td>WADLS</td>
<td>Western Australia Data Linkage System</td>
</tr>
<tr>
<td>WCH</td>
<td>Women’s and Children’s Hospital</td>
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