Influenza Vaccination in Children with Special Risk Medical Conditions

Thesis presented for the degree of

Doctor of Philosophy (Medicine)

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The best vaccine imaginable is only valuable to the extent we get it to everyone who needs it.

Seth Berkley.
TED Talk. HIV and flu – the vaccine strategy, 2010.

CONTENTS

ABSTRACT

A considerable number of Australian children are at increased risk of disease or complications from influenza due to a medical condition. Focusing on the health of these children is a public health priority. Vaccination against influenza has been recommended in Australia for people with special risk medical conditions (SRMC) since 1991 (funded 2010). Despite this, vaccination coverage has not been routinely or uniformly measured. The primary aim of this thesis was to identify barriers to coverage in children identified at increased risk of influenza and translate this into interventions that could address low coverage.

This PhD thesis comprises five peer-reviewed published papers and one manuscript that present results from a systematic review and three observational studies. The systematic review assessed the current evidence of disease severity, complications and resource use experienced by children with SRMC who were hospitalised with influenza infection compared to healthy children. The first observational study was conducted with parents of children with a confirmed SRMC and examined confirmed influenza vaccination and reporting to Australian Immunisation Register (AIR). The second observational study used data from the 2016 South Australian Health Monitor survey to examine parental awareness of influenza vaccine recommendations. The third utilised a cross-sectional survey and qualitative interviews with the general practitioners (GP) and paediatric specialists, who were identified by parents as the children's (from observational study 1) treating doctors. Additionally, an intervention to address barriers identified in this thesis was designed.

Compared to healthy peers, children with SRMC hospitalised with influenza infection had higher odds of ICU admission [pooled odds ratio (OR) 1.66 (95% confidence

interval (CI): 1.25–2.21)], mechanical ventilation [pooled OR 1.53 (95% CI: 0.93–2.52)], death [pooled OR 1.34 (95% CI: 0.74–2.41)] suspected bacterial pneumonia (crude OR 1.7; 95% CI: 1.1–2.6) and experienced prolonged hospital length of stay [adjusted rate ratio 1.75 (95% CI: 1.44–2.11)].

In children with SRMC (n=410) confirmed influenza vaccine receipt at least once in the last two years was 50%. Characteristics associated with uptake included: receiving a specialist (adjusted OR [aOR] 15.80, CI 6.69–37.29) or GP recommendation (aOR 6.76, CI 2.99–15.29) or annual parental receipt (aOR 11.12, CI 5.36–23.06). Sensitivity of the AIR to reflect a child's influenza immunisation status was low (32.6%) and 78% of parent reported vaccinations were able to be substantiated by a provider with good (κ = 0.677) to very good agreement (κ = 0.814) for 2014 and 2015 respectively.

Overall, 33% of parents in the community were aware that all children (<5 years) were recommended influenza vaccine annually, with this knowledge associated with an awareness of the recommendation for children with a SRMC (aOR 9.72, CI 4.14-22.82), living in a metropolitan area (aOR 2.67, CI 1.15-6.22) and being born in Australia (aOR 3.11, CI 1.12-8.65). Overall 51.9% of parents were aware of the recommendation that children with SRMCs should receive the vaccine annually, with this awareness associated with knowledge of the influenza recommendation for children <5 years (aOR 10.22, CI 4.39-23.77) or not being born in Australia [UK/ Ireland (aOR 7.63, CI 1.86-31.31). The most influential cue to future receipt was a GP recommendation.

Only 38.4% of medical practitioners reported they 'always' recommended influenza vaccine and less (19.5%) were very confident in understanding all SRMCs.

Provision of a recommendation ‘always or mostly’, was associated with perceived responsibility to provide the recommendation (aOR 7.55, CI 1.71-33.30), confidence in understanding all SRMC (aOR 1.77, CI 0.96-3.24) and annual influenza vaccination receipt themselves (aOR 4.13, CI 1.09-15.69). Those practising in a regional location were less likely to provide a recommendation (aOR 0.25 CI 0.09-0.70).

The qualitative semi structured one-to-one interviews identified several themes, grouped using the COM-B model including: Capability - communication and knowledge and Motivation - clinical prioritisation and responsibility. However, much discussion was focused on barriers and potential drivers that fall under Opportunity - such as communication resources, social acceptance and normalisation and consistent messaging, with systems to identify children, prompt clinicians and remind parents reported as the most urgently required.

Influenza vaccination coverage in children with SRMC is suboptimal. The major driver to influenza vaccine receipt is a recommendation from a medical practitioner, with a preference for this to be delivered in the context of their child’s specialist care. GPs and specialists voiced low confidence in understanding the SRMC groups in the recommendation, and preferred in addition to education, strategies utilising systems approaches to address this. Forging a new paradigm of care in which GPs, specialists and families collaborate in providing better protection for this at-risk group is required with established roles and responsibilities. Improving influenza recommendation awareness and providing multimodal approaches that address other barriers is likely to positively effect vaccine uptake in children identified at increased risk.

THESIS DECLARATION

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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I acknowledge the support I have received for my research through the provision of an Australian Government Research Training Program Scholarship.

Name: Jane Tuckerman

Signed: Date: 20th December 2019

ACKNOWLEDGEMENTS

Firstly, I would like to extend thanks to the parents who generously participated in the work presented in this thesis. Some of you I saw many times around the hospital. Thank you for sharing your stories. Your narratives truly helped me appreciate and grasp the impact of influenza for children with ongoing medical conditions, as well as the experience of caring for a child with an ongoing medical condition. I would also like to thank the general practitioners and paediatric specialists who also gave up their time, in otherwise extremely busy schedules.

To my three supervisors, Prof Helen Marshall, Prof John Lynch and A/Prof Nigel Crawford who allowed these papers and this thesis to be my own but steered me in the right the direction whenever they thought I needed it. Thank you. I am especially indebted to Prof Helen Marshall, who has long been supportive of my career goals and patiently waited for me to undertake this PhD. I am thankful for her academic support and for helping me define the path of this research. For this, I am extremely grateful. I would also like to thank A/Prof Nigel Crawford for all things policy and clinical and Prof John Lynch, for his guidance with epidemiology concepts.

I also extend thanks to my other co-authors, Dr Siobhan Misan, Dr Salma Salih, Dr Bridget Joseph Xavier, A/Prof Margie Danchin and Dr Jessica Kaufman. I thank the Vaccinology and Immunology Research Trials Unit and Women's and Children's Hospital staff who have helped in some way with this project, Chris Heath, Kathryn Riley, Bing Wang, Manasa Krishna and Iann Homer, as well as fellow PhD students, Michelle Clarke and Mark McMillan. To my early mentors, Profs Fiona Wood and Judith

Finn, for encouraging me to embark on a research career path and for providing me with opportunities.

Most importantly, I thank my husband Steve, for his constant faith in my abilities, for listening about the write up of yet another paper, for the photocopying, Malbec, coffee and chocolate. No words will thank you enough. To my gorgeous children, Liam, Mabel and Isla who I don’t think ever really understood what Mummy was working on. I hope I inspire you to believe anything is possible, to contribute to the world around you, no matter how small.

PUBLICATIONS

MANUSCRIPTS ARISING FROM THIS THESIS

Published

Tuckerman J, Misan S, Salih S, Joseph Xavier B, Crawford NW, Lynch J, Marshall HS. Influenza vaccination: Uptake and associations in a cross-sectional study of children with special risk medical conditions. *Vaccine*. 2018 Dec 18;36(52):8138-8147.

Cited twice (Scopus 2 December 2019). Journal 5-year Impact Factor 3.293 (ISI web of knowledge InCites Journal Citation Reports Edition 2018).

Tuckerman J, Crawford NW, Lynch J, Marshall HS. Are children with special risk medical conditions receiving influenza vaccination? Validity of parental and provider report, and to a National Immunisation Register. *Hum Vaccin Immunother*. 2019;15(4):951-958.

Cited once (Scopus 2 December 2019). Journal 5-year Impact Factor 2.551 (ISI web of knowledge InCites Journal Citation Reports Edition 2018).

Tuckerman J, Misan S, Crawford NW, Marshall HS. Influenza in Children with Special Risk Medical Conditions: A Systematic Review and Meta-Analysis. *Pediatric Infectious Disease Journal*. 2019 38(9):912-919.

Journal 5-year Impact Factor 2.397 (ISI web of knowledge InCites Journal Citation Reports Edition 2018).

Tuckerman J, Crawford NW, Marshall HS. Disparities in parental awareness of children's seasonal influenza vaccination recommendations and influencers of vaccination. *PLoS One 2020;15(4): e0230425.*

Journal 5-year Impact Factor 3.337 (ISI web of knowledge InCites Journal Citation Reports Edition 2018).

Tuckerman J, Crawford NW, Marshall HS. Seasonal influenza vaccination for children with special risk medical conditions: does policy meet practice? *Journal of Paediatrics and Child Health 2020 01 June 2020*

Journal 5-year Impact Factor 1.742 (ISI web of knowledge InCites Journal Citation Reports Edition 2018).

Submitted for Publication

Tuckerman J, Kaufman J, Danchin M, Marshall HS. Influenza vaccination: a qualitative study of practice level barriers from medical practitioners caring for children with special risk medical conditions. Journal: *Vaccine*

OTHER MANUSCRIPTS ARISING DURING CANDIDATURE

The following manuscripts were published during my candidature but were outside the scope of this thesis.

Tuckerman JL, Shrestha L, Collins JE, Marshall HS. (2016). Understanding motivators and barriers of hospital-based obstetric and pediatric health care worker influenza vaccination programs in Australia. *Hum Vaccin Immunother*, 12(7), 1749-1756.

Tuckerman J, Thomas N, Marshall HS. (2016). Should professionals caring for children be vaccinated? Community perspectives on health care and child care worker immunisation. *Vaccine*, 34(14), 1726-1732.

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Wong CY, Thomas NJ, Clarke M, Boros C, **Tuckerman J,** Marshall HS. Maternal uptake of pertussis cocooning strategy and other pregnancy related recommended immunisations. *Hum Vaccin Immunother* 2015;11(5):1165-72

CONFLICT OF INTEREST

Professor Helen Marshall is an investigator on clinical trials of investigational vaccines sponsored by Industry. Her institution receives funding from Industry (GSK, Pfizer, Novavax) for Investigator led research. She does not receive any personal payments from Industry. There are no other conflicts of interest to declare.

LIST OF ABBREVIATIONS

AIR	Australian Immunisation Register
aOR	adjusted Odds Ratio
CI	Confidence Interval
GP	General practitioner
HCP	Healthcare Provider
ICU	Intensive care unit
LOS	Length of stay
MOOSE	Meta-analysis of Observational Studies in Epidemiology
NIP	National Immunisation Program
NPV	Negative predictive value
NSIVP	National Seasonal Influenza Vaccination Program
OR	Odds Ratio
PPV	Positive predictive value
QUIPS	Quality in Prognosis Studies
RoB	Risk of bias
SA	South Australia
SRMC	Special risk medical condition
USA	United States of America
VPD	Vaccine preventable disease
WCH	Women's and Children's Hospital

CHAPTER 1 THESIS OVERVIEW

1.1 BACKGROUND AND RATIONALE FOR RESEARCH

In Australia, influenza takes more children's and adolescent's lives than any other vaccine preventable disease (VPD) and is the most common VPD requiring hospitalisation. (1) Direct hospital costs for children aged <9 years are estimated in excess of 5 (AU$) million per annum (2, 3), with an estimated 1,500 Australian children aged <5 years hospitalised with influenza each year.(3)

Increasingly, it is recognised that children and adolescents with medical conditions, as defined in the Australian Immunisation Handbook (AIH) (4) (hereafter referred to as children with special risk medical conditions (SRMC)) are overrepresented in hospitalisations and deaths from influenza compared to healthy children of the same age. (5) These conditions include those with chronic cardiac, respiratory, neurological, metabolic, liver or kidney diseases; cancer; diabetes; Trisomy 21 and underlying immunosuppression.(4) This immunosuppression can be due to both the underlying disease and/or medications required to treat the condition.

Children and adolescents aged less than 19 years account for close to 25% of Australia's population (6) and a significant number will have at least one condition that places them in the SRMC group. It is difficult to estimate precisely the number of children affected by SRMCs as there is no one database or registry that collects this information in Australia, unlike national registries for chronic disease that exist in European countries such as the Netherlands and Sweden. (7) The single most prevalent SRMC is asthma, affecting 9.3% of children aged <14 years or approximately 400,000 Australian children. (8) There are also significant numbers of Australian

children (aged <18 years) with cardiac and respiratory conditions including chronic obstructive pulmonary disease and cystic fibrosis; neurological conditions such as seizure disorders or spinal cord injuries, traumatic or neural tube defects such as spina bifida; immunocompromising conditions; chronic diseases such as diabetes and inherited metabolic disorders. (9) In addition to this, some conditions, such as bronchiectasis have a higher prevalence in Aboriginal and Torres Strait Islander children (14.7 per 1,000 Indigenous children). (10) Studies from the United States of America (USA) estimate the prevalence of children with SRMC to be around 10%. (11-13) Numbers of children and adolescents with SRMC are increasing. This is likely the result of a combination of improvements in life expectancy, (e.g. cystic fibrosis and spina bifida) and increasing prevalence of chronic disease (e.g. diabetes). It is widely argued that numbers of children and adolescents with SRMCs will continue to increase for some time to come. (7, 14-16)

Focusing on the health of children with SRMCs is important. Inadequately managed ongoing disease can seriously affect the social, psychological and physical development of children, resulting in limited education and participation opportunities as well as having the potential for these conditions to worsen. (9) The potential for additional health complications can also impact on school performance and social interactions with peers. These children and adolescents may have social difficulties keeping up with their friends. There are also the additional indirect costs of parents needing time off work to care for their sick child. Prior research from the USA has found that children (aged <18 years) with chronic conditions (similar in profile to that of the AIH) experience more than two bed days and three lost school days per year in addition to that resulting from acute infections such as influenza or colds. (17) While a prospective study, also from the USA, of children (aged 6-15 years) showed that for

every 100 children followed-up over an influenza season, influenza resulted in 63 missed school days and 20 missed work days for children and parents, respectively.(18)

Globally, immunisation is a highly cost-effective public health intervention. (4) Australia has a comprehensive National Immunisation Program (NIP) and National Seasonal Influenza Vaccination Program. In Australia, children ≥ 6 months of age who are deemed at increased risk, are strongly recommended and funded to receive the seasonal influenza vaccine.

In recent times, changes to recommendations, funding, the 2009/2010 pandemic and a cluster of serious adverse events with use of the BioCSL Fluvax vaccine have contributed to the changing landscape of children's influenza vaccination in Australia. Individuals from 6 months of age and older at increased risk due to a special risk medical condition (SRMC) have been recommended the seasonal influenza vaccination through the National Immunisation Program (NIP) since 1991 (funded since 2010). (4, 19, 20) It has also been recommended, but not funded for all children (aged ≥6 months to <5 years) since 2013. The vaccine remained unfunded on the NIP, although one jurisdiction, the Western Australian Government funded the vaccine in 2008, following several deaths in young children due to influenza. Almost all other states[1] followed in 2018, after heightened influenza activity across Australia in 2017 (19) and for the 2019 season, all states and territories funded a children's influenza vaccination program with the NT funding a non-Indigenous program this year.

Beginning 2020, a nationally funded program for all children < 5 years will be introduced in Australia following these various individual state-based programs. National influenza

[1] Australian Capital Territory, New South Wales, Queensland, South Australia, Tasmania and Victoria only.

immunisation policies differ significantly between countries. (21) Australia contrasts with other countries such as the United States, where the vaccine has been recommended to children of all ages since 2008, with funding supported under the Affordable Care Act (since 2010) whereby health insurers are required to cover all federally recommended vaccines at no charge to patients and additionally, government programs that pay for low-income children. (22, 23)

Yet despite an effective vaccine being available, currently, minimal data about seasonal influenza vaccine uptake in Australian children exists, as influenza vaccination is not routinely recorded on the Australian Immunisation Register, as are routine vaccines. There is a scarcity of information on the vaccination status of children with SRMCs for seasonal influenza. The majority of studies that examine influenza uptake have all been conducted in New South Wales and Western Australia and were too limited by sample size to explore associated characteristics.(24-28) No studies have captured the beliefs and attitudes of parents of these children in depth nor elicited the community's attitudes and views for influenza immunisation. Studies examining characteristics associated with influenza vaccine uptake have been conducted elsewhere in the USA, and Europe. Explanations often provided for the poor uptake of the influenza vaccine, from parents of children with high risk medical conditions comprise: lack of awareness about recommendations, lack of information, not identifying children as being at risk, fear of the vaccine/side effects, inconvenience, lack of perceived severity of influenza, advised against receiving it, negative social influences, need for a priming dose in children <9-10 years and perceived low efficacy of the vaccine. (29-36)

The introduction of the Australian Childhood Immunisation Register (ACIR) coincided with a National Strategy towards Immunisation including a National Childhood

Immunisation Agreement between the Commonwealth and the states/territories in 1996, just prior to Australia's 'Seven Point Plan'. (37, 38) It came at a time of several policy changes across Australia's three levels of government supporting a stronger immunisation plan. Enrolment is based on Australia's universal health care coverage system, Medicare, which as an opt-out scheme, enables capture of 99% of the population.(39, 40) ACIR enabled detailed geographical tracking of coverage, reminders for overdue immunisation and consolidated immunisation histories for parents and providers. Until 2016, the Register, captured only vaccinations given to children aged < 7 years, however more recently ACIR has expanded to now capture vaccinations given to people of all ages, with a subsequent name change to the Australian Immunisation Register (AIR).(39)

Only recognised vaccination providers can provide immunisation information to AIR including medical practitioners, midwives and nurse practitioners with a Medicare provider number, although other eligible health professionals and organisations can apply to be providers. Immunisation encounter details can be reported and recorded to AIR in several ways. Either directly, through the AIR website after identifying the individual (using the Medicare card and reference number), using practice management software that interfaces with the AIR, or in some cases, providers can send immunisation details to their state or territory health department. If an individual is unable to be located on AIR a record can be created using their name, date of birth, gender and address that can later be linked to their Medicare record if they enrol later.

Prior research (both Australian and international) strongly points to medical practitioner recommendation as being influential to uptake. Children with SRMCs often see several medical professionals, placing medical professionals in a key position concerning

vaccine recommendation and addressing any queries that may be raised regarding the vaccine, which is unique because it is required annually. Therefore, understanding the vaccination delivery practices of these medical professionals is important. Whist the vaccination of children with SRMC in Australia is supported and strongly recommended in the AIH, it is likely that there is a significant gap from recommendation to practice. There is a deficiency of information and data on the vaccination delivery practices from the perspective of medical practitioners who care for children with SRMCs and an understanding of current working practice remains crucial in order to develop strategies to increase uptake.

Understanding vaccine coverage and how influenza vaccine recommendations are implemented for children identified at increased risk of influenza should be a priority area. However, the implementation and evaluation of a vaccination policy is rarely straightforward. Other factors, such as knowledge and environmental constraints interact with parents' values and beliefs to moderate their vaccination behaviours; accurate coverage is required for program planning and the engagement and education of medical practitioners involved is critical for a recommendation to occur in the first instance. Without such understanding, vaccination programs and interventions cannot be designed that best address the needs of the target group. This research project was undertaken using cross-sectional quantitative and qualitative methodology to investigate vaccination in children with SRMC in Australia to address identified current knowledge gaps.

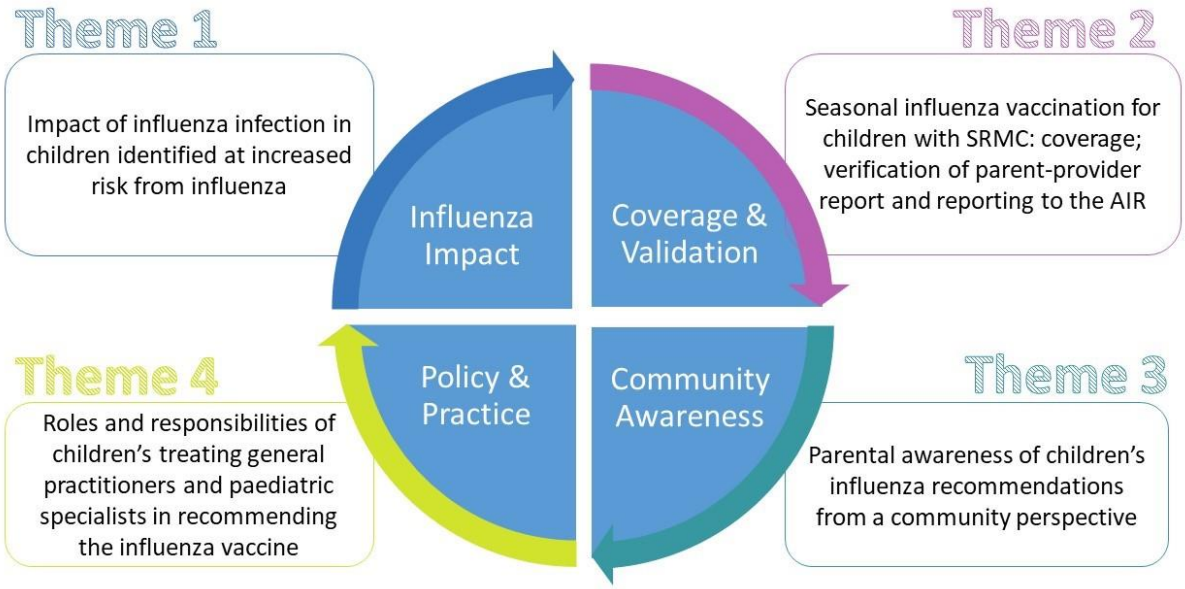
Several important changes have occurred since commencing my candidature. The most noteworthy is the provision of free influenza vaccines for children aged ≥ 6 months to <5 years almost universally across all Australian jurisdictions under state funded programs

(since 2018) except for the Northern Territory (2019) and noting that previously this was only Western Australia. As of 2020 the influenza vaccine will be funded in the NIP for all children aged ≥6 months to < 5 years. The Australian Childhood Immunisation Register also expanded to include vaccinations given to people of all ages, with a subsequent name change to the Australian Immunisation Register (AIR). Additionally, several influenza seasons have yielded high media coverage, as a result of significantly increased influenza activity in 2017 and 2019, with higher than anticipated notifications, hospitalisations and several deaths in children.

1.2 RESEARCH QUESTIONS

The ultimate aim of this thesis was to identify ways to improve influenza vaccination uptake in children identified at increased risk of influenza and translate this into interventions that could address low coverage and improve uptake and protection. The overall objective of this thesis is to examine influenza vaccine coverage and determine reasons for suboptimal vaccine uptake in children with SRMC from the perspective of their parents, treating general practitioners and paediatric specialists, as well as parents in the community. This PhD project aims to address the following research questions grouped by four themes (Figure 1).

Figure 1: Themes covered in this thesis



Research Themes and Questions

Theme 1: Impact

To determine the impact of influenza infection in children identified at increased risk from influenza complications compared to healthy children (Project 1).

i) Do children with special risk medical conditions hospitalised with influenza experience higher rates of complications compared to healthy counterparts? (Paper 1 in Section 3.2)

Theme 2: Coverage and Validation

To determine seasonal influenza vaccination coverage of children identified at increased risk and to verify parent reported influenza vaccination compared to provider report and the Australian Immunisation Registry (Project 2).

ii) What is the uptake of the influenza vaccine in children with SRMCs and what characteristics are associated with receipt? (Paper 2 in Section 4.2)

iii) How valid is parent reported receipt of influenza vaccination in children with SRMC and what is the level of reporting to the AIR? (Paper 3 in Section 1)

Theme 3: Parental Awareness

To explore parental awareness of children's influenza recommendations from a community perspective (Project 3).

iv) Amongst parents in the community, what is the level of awareness towards influenza vaccination in children; what characteristics are associated with awareness; and what influences future receipt of the influenza vaccine? (Paper 4 in Section 5.2)

Theme 4: Policy and Practice

To examine the role of children's treating general practitioners and paediatric specialists in recommending the influenza vaccine (Project 4).

v) What is known about the influenza vaccine recommendation practices among the treating general practitioners and paediatric specialists of children with

SRMCs and what are the most important influencers driving adherence to recommendations? (Paper 5 in Section 6.2)

vi) What are the experiences and challenges of general practitioners and paediatric specialists when delivering the influenza vaccine recommendation to parents of children with SRMC? and

vii) What practice improvements could be implemented to overcome these? (Paper 6 in Section 1.1)

1.3 THESIS OUTLINE

Chapter one is the thesis overview, Chapter 2 details the methodology for individual projects in this thesis. Chapter 3 covers the background to the broad areas covered by my thesis. A literature review highlights and documents the prevalence of SMRC in Australian children, the significance of SRMC in children, influenza disease and vaccination as well as, the delivery of vaccination and provider barriers to vaccination, thereby identifying current gaps in the literature.

As part of Chapter 3 a systematic review is presented which comprehensively assessed the severity, complications and resource use experienced by children with SRMC compared to healthy children hospitalised with influenza infection. Meta-analyses were undertaken to investigate the effect of SRMC on intensive care admission, mechanical ventilation and death, with results presented in Paper 1. Evidence of the considerable burden of influenza can assist medical professionals to directly address influenza vaccination hesitancy in parents in addition to, informing government funding of interventions to increase coverage.

Chapter 4 focuses on research gaps surrounding influenza vaccination for children with SRMC from a parental perspective. Results including vaccination coverage, parental

validity and reporting to AIR were obtained from a face-to-face survey conducted with parents (of children with SRMC) with subsequent follow-up with immunisation providers, general practitioners (GP) and current healthcare providers as well as medical case note and AIR vaccination review (Papers 2 and 3).

There was much lower annual uptake than reported awareness of the recommendation. Parents held in high regard a recommendation received from medical practitioner, particularly when delivered in the context of tertiary care (paediatric specialist). A child's vaccination uptake was also influenced by whether their parent received the influenza vaccine. Parent reported validity and reporting to AIR was also explored. Overall, there was good to very good agreement between parent reported vaccinations and those substantiated by a provider. The length of time since vaccination affected this agreement. The sensitivity of the AIR to reflect a child's influenza immunisation status was low. These results can be used to establish vaccine coverage estimates, educate providers on the importance of AIR and potentially provide impetus for providers to report influenza vaccinations to AIR.

Chapter 5 (Paper 4) describes results from a survey with a sample of parents from the South Australian community. Survey results indicated lower parental awareness of the influenza vaccine recommendations for children with SRMC and much lower parental awareness of the recommendation for children in general. Parents reported GP recommendation as the most important influence of future receipt. It also identified a disparity in awareness of recommendations based on place of residence. Understanding factors influencing influenza vaccination and their importance to parents can help to establish and support strategies to address vaccine uptake.

As vaccine recommendations are rarely delivered in isolation from a person's overall care requirements or a medical practitioner's previous knowledge and experience, it provided an opportunity to evaluate the context of how influenza vaccination messages are delivered and what, if any challenges are faced. In chapter 6, we obtained information from the treating medical practitioners (Project 4) who were directly linked to a cohort of children with known SRMC (Project 2). Results including the delivery practices and attitudes towards influenza vaccination were obtained from two studies, a cross-sectional survey, followed by qualitative one-to-one in-depth interviews with a subgroup of participants (Papers 5 and 6). The survey described the frequency with which MPs recommended the influenza vaccine to children, along with provider responsibility, confidence in understanding the conditions 'medically at risk' and beliefs towards influenza vaccination. Despite high awareness, medical practitioners reported considerable hesitation in recommending the vaccine to parents of children with SRMC, due to low capability to interpret and apply the recommendation for individual children with clinical practice. Confidence in understanding all of the conditions considered medically at risk' and perceived ownership of the responsibility to provide the recommendation were critical to the recommendation pathway. There was differential provision of the recommendation, based on practising location. Challenges and vaccination practice were further explored in qualitative one-to-one in-depth interviews with GPs and paediatric specialists.

General practitioners and paediatric specialists expressed challenges with divergent expectations towards the responsibility to provide a recommendation, lack of systems to support the identification of these children. Structural supports that could prompt providers and remind parents were lacking and there is uncoordinated collaboration, which critically affects expectations for delivery of the recommendation in conjunction

with opportunity. Additionally, substantial variability exists in the routine disease management and engagement with health services for these children and there were varied methods of communication styles when discussing influenza, dictated by personal practitioner style; with both groups identifying a need for additional, well defined resources to support discussions.

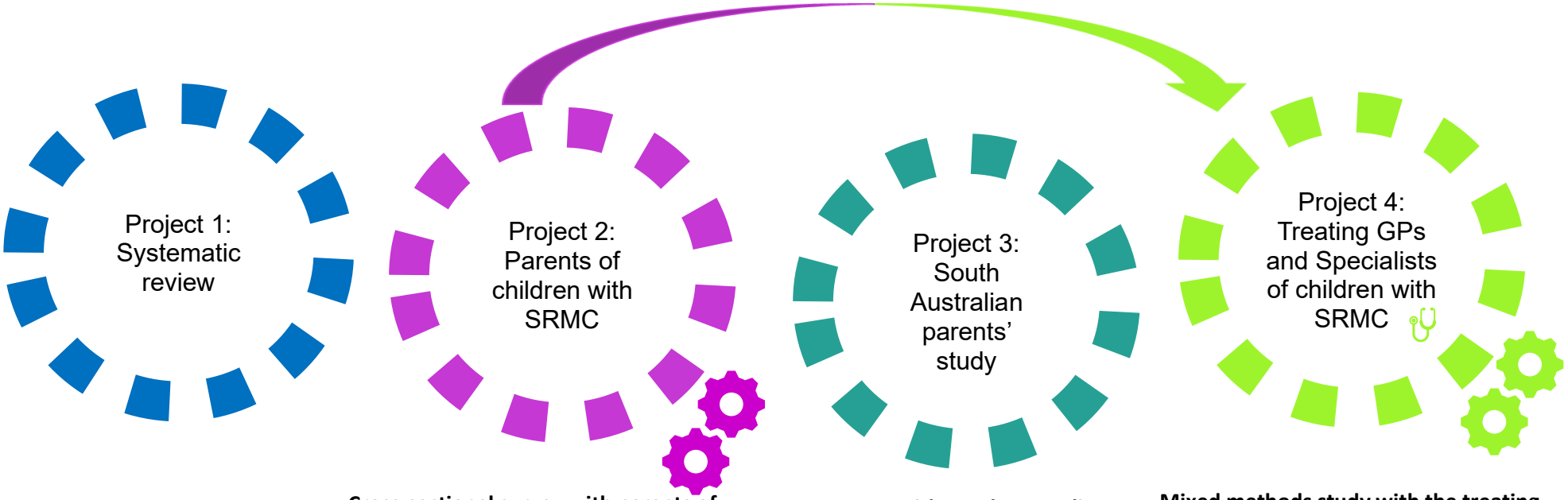
Chapter 7 discusses the possible contribution to the scientific literature, potential implications and translation of study results, and the directions of future research. Chapter 8 details the development of an intervention based on findings from this thesis and Chapter 9 summarises the main findings of this PhD thesis.

CHAPTER 2 METHODS

2.1 CHAPTER OUTLINE

Three observational studies and a systematic review form the body of this PhD thesis. The studies use quantitative, qualitative and systematic review methodology. The aim of this chapter is to provide a background to the study methods used, as well as an overview of how the research was conceptualised and the choice to use a pragmatic approach to address the research questions. The methods for each of the four projects are outlined, along with the unique link between project 2 and 4, which was the key part of the overall design of this PhD. Although the systematic review (Project 1) and community study (Project 3) stand-alone they are also central to the landscape of influenza vaccination for children with SRMC. As illustrated in Figure 2, Project 2 and Project 4 were interlinked, although data were collected independently. The main reason linking the parental and provider projects, was to be certain the challenges and barriers to influenza vaccination in children with SRMC were the focus. Directing questions to GPs who did not routinely care for children with SRMC or who specialised solely in another aspect of general practice for example, would not have enabled the problem of under immunisation of children with SRMC to be explored in depth. Chapters 3-6 therefore each represent 1 of 4 projects. For each, a literature review is presented at the beginning of each chapter.

Figure 2: Thesis projects including the link between Projects 2 and 4 and subsequent papers from all projects



A systematic review of complications and severity in children with SRMC hospitalised with influenza

Paper 1:

Influenza in Children with Special Risk Medical Conditions: A Systematic Review and Meta-Analysis. (published)

Cross-sectional survey with parents of children with SRMC

Paper 2:

Influenza vaccination: Uptake and associations in a cross-sectional study of children with special risk medical conditions. (published)

Paper 3:

Are children with special risk medical conditions receiving influenza vaccination? Validity of parental and provider report, and to a National Immunisation Register. (published)

CATI survey with South Australian parents on awareness of children's influenza vaccination recommendations

Paper 4:

Disparities in parental awareness of children's seasonal influenza vaccination recommendations and influencers of vaccination (published)

Mixed methods study with the treating medical practitioners of children with SRMC

Paper 5:

Seasonal influenza vaccination for children with special risk medical conditions: does policy meet practice? (published)

Qualitative study with a subgroup of the treating medical practitioners of children with SRMC

Paper 6:

Influenza vaccination: a qualitative study of practice level barriers from medical practitioners caring for children with special risk medical conditions (submitted)

Parents of children in Project 2 identified their child's paediatric specialist/s and general practitioner.

2.2 RATIONALE FOR RESEARCH APPROACH

This thesis sought to interweave both quantitative and qualitative research methods to better understand the perspective and influenza vaccination behaviours of parents of children with SRMC and their primary and tertiary care providers.

On the basis that this thesis focused on understanding the phenomenon of influenza vaccine recommendation and delivery for children with SRMC with the overarching aim of exploring potential solutions to improve uptake, a mixed methods research design informed by the pragmatic theoretical position was considered the most appropriate. (41-43) The rationale for using a mixed methods approach follows that neither quantitative nor qualitative methods alone would speak to the research questions proposed by this thesis and address possible solutions.(44) Although based on differing epistemological foundations, when used in combination these qualitative and quantitative approaches are widely argued to be complimentary. As such, a utilitarian and real-world rather than theoretical approach spoke to the practical nature and the outcomes sought by this thesis.

A mixed methods approach, now widely argued to represent the third research paradigm , emerged following the so called ‘paradigm wars’ (41, 45) offering an alternative to the either-or quantitative-qualitative dichotomy. (46, 47) Mixed methods research involves analysis of quantitative and qualitative data in a single study or series of studies that investigate the same underlying phenomenon and is defined by Tashakkori et al. as,

> *“an eclectic, pragmatic approach to employing combinations of research tools in answering multifaceted questions by seeking multiple, multilayered answers”.* (48)

A mixed methods research design is particularly useful for exploring the perspective of vaccination of children with SRMC for several reasons. Limited data are available in the literature and gaining such broad perspective is critical to advancing improvements to behaviour change in this area, as would be achieved through a typical survey or qualitative designs alone. Essentially, I wanted to focus the research on the insights afforded by both methods, in order to offer the best opportunities for answering the research questions, a so-called pragmatist approach.(49, 50) Rather than the piecemeal approach afforded by using either quantitative or qualitative methods in isolation. This more practical and pragmatic approach enabled me to be flexible in which methods were selected in order to best address the research question. Indeed, following a mono-method would have limited the breath of findings from this thesis, and is argued to be one of the greatest threats to advancing social science research.(50)

Evidence on this issue can be generated in a way that is not unattainable through independently conducted qualitative and quantitative studies alone. (43, 51) Quantitative methods can be used to explore characteristics associated with the core behaviours of vaccination (parents) and providing a recommendation and/or administration (providers) as well as the landscape and resources in which these phenomenon take place. Qualitative research can be used to conceptualize how medical practitioners recommended and administer the influenza vaccine and how strategies can influence that performance through targeted interventions.

The methodological components of the studies in this thesis primarily arose following discussions with my primary supervisor and co-supervisors. Whilst the research questions identified in theme 1 were addressed using quantitative methods (using systematic review methodology) I considered more broadly the aspects of the

subsequent studies. When planning the studies included in this thesis and undertaking the literature review, I considered that the first two research questions in theme 2 would require a quantitative approach as they sought data that would enable me to compare characteristics associated with coverage or reporting to the AIR (demographic details, receipt of provider recommendation). Addressing these questions using a qualitative approach would not have sufficiently illustrated the scale of the issue, nor enabled me to compare with any other published literature. The use of quantitative methods was extended when addressing the research questions under theme 3 and the first of theme 4. In contrast, the second and third research questions in theme 4 required a qualitative approach, as they sought to explore and understand medical practitioners' experiences, rather than report their behaviour. As such a qualitative line of inquiry was most appropriate to conceptualise provider patterns of vaccination behaviour (i.e., provision of recommendation, vaccine delivery).

Adding to this, the published literature in this field when I started (and indeed even now) was scarce. This was particularly so for understanding the barriers to recommendation for medical professionals who provide tertiary or primary care for children with SRMC. Limited published studies demonstrated low levels of providing a recommendation that was hindered by confusion over provider responsibility between the GPs and subspecialists. It therefore made sense to adopt a qualitative approach to examine and understand medical professionals' experiences of implementing influenza vaccine policy recommendations for children with SRMC, ultimately aiming to understand why coverage in these children is suboptimal. The decision to take a pragmatic approach and integrate the studies to address the research questions and selecting methodology accordingly, was taken in conjunction with my supervisor panel. The value of undertaking the thesis in this way, to position myself closely to the research, enabled a

detailed exploration of the barriers and drivers to influenza vaccination for children with SRMC that is rich in detail. It highlights the core elements contributing to the successful provision of a recommendation and delivery that could be addressed through simple yet practical measures.

2.3 STUDY SETTING AND POPULATION

Besides the systematic review, all other projects were undertaken in South Australia, which is the southern central part of Australia and shares borders with all other mainland states (Figure 3). It is the fifth largest of Australia's states with a total population of 1.7 million people; of whom 23.5% are aged <19 years.(52) Its population is the second most highly centralised in Australia, behind Western Australia, with more than 77 percent of South Australians living in the capital, Adelaide. (53) The southern part of the state has a Mediterranean climate, while the rest of the state has either an arid or semi-arid climate.

At the 2016 census, the most commonly nominated ancestries were: English (28.5%), Australian (25.0%), Scottish (6.3%), Irish (6.0%) and German (5.8%) with 78.2% of the population speaking only English at home. (52)

Figure 3: Relative size and geographic location of South Australia

Source: Australian Bureau of Statistics (54)

Australia has a public health system, with responsibility for management and funding shared by the Australian federal, state, territory, and local government councils. Medicare has been Australia's universal health care scheme since 1984. Primary care services are delivered by GPs in the community and tertiary level medical care is provided by specialists. Medicare and the public hospital system provide free or low-cost access for all Australians to most of these health care services; however, people also have the option to take out private health insurance. Vaccinations on the National Immunisation Program are federally funded and provided free to all people based on eligibility for Medicare benefits.

In Australia, immunisation providers deliver vaccines in several settings and while general practices predominately administer vaccinations, vaccines are also available through local council or community health clinics, Aboriginal Health Services, and school-based immunisation programs. To a lesser extent and dependent on the situation, vaccinations may also be given at: travel medicine clinics, public hospitals, staff occupational health clinics, aged care facilities and pharmacies. It is worth noting however that not all immunisation providers are able to provide free vaccines under the NIP and in some cases immunisation providers are limited in the vaccines and age group to whom they can administer vaccines. Additionally, some vaccines are only able to be administered by selected accredited providers, as is the case with Yellow Fever and Q Fever vaccines. While some hospitals deliver vaccines as part of inpatient care, not all hospitals provide this service for outpatients, although this is changing. Particularly, in terms of provision of the influenza vaccine, the ability to offer the vaccine is closely related to whether an immunisation clinic is located onsite and while many Australian tertiary paediatric hospitals now have dedicated immunisation clinics, not all offer a 'drop-in service'. Further detail on paediatric influenza vaccine delivery is provided in Chapter 5.

There are eight public hospitals across metropolitan Adelaide, with four providing care to children and adolescents aged < 18 years. In South Australia, the Women's and Children's Health Network (WCHN) is the leading provider of specialty care and health services for babies, young people and women in South Australia. The WCHN comprises the Women's and Children's Hospital (WCH) and a range of metropolitan, rural and remote community-based services for babies, children, young people and women across SA and interstate. The WCH is the state's leading provider of specialist care for children with acute and chronic conditions and SA's largest maternity and obstetric

service. The WCH Paediatric Emergency Department is a level 1 major trauma centre for children in South Australia. Each year, there are more than 30,000 admissions and about 5000 births at the hospital. In addition, more than 250,000 people come to the hospital as outpatients. The hospital has 295 beds, with 17 wards: 11 paediatric and 6 for women. The hospital's paediatric and adolescent wards cater for all paediatric specialties.

2.4 SYSTEMATIC REVIEW

A systematic review was undertaken and was reported following the MOOSE (Meta-analysis of Observational Studies in Epidemiology) recommendations. (55) The aim of the study was to systematically assess the current evidence of severity, complications and resource use experienced by children with SRMC who were hospitalised with influenza infection.

The review outcomes were the:

1. Probability of pneumonia
2. Intensive care unit (ICU) admission
3. Mechanical ventilation requirement
4. Neurological complications (encephalopathy or seizures)
5. Death
6. Hospital - Length of stay (LOS)
7. ICU - LOS

Full details of the protocol developed for the review, along with the search strategy are available in PROSPERO (CRD 42017074648) and included as an attachment (See Appendix A). Broadly, we searched MEDLINE and EMBASE for studies published from 1990 to March 2015, the reference lists of included studies and contacted investigators of studies containing data relevant for the review that was yet to be published. Studies were dual screened at full-text screening by two authors (SM and JT); disagreements were resolved by a third author (HM). We included English-language articles that presented quantitative information on hospitalisations of clinical influenza in children (aged ≤18 years) that included a breakdown by risk group(s) and additionally for any one of the listed outcomes. Two authors independently extracted all data and assessed study quality using The Quality in Prognosis Studies (QUIPS) tool. (56, 57) The quality

of evidence for each outcome was assessed according to the GRADE framework adapted to judge the quality of prognostic evidence.(58)

2.5 DETERMINING UPTAKE OF SEASONAL INFLUENZA VACCINE IN CHILDREN WITH SRMC

Recruitment for the study 'Determining uptake of seasonal influenza vaccine in children with special risk medical conditions' began in September 2015. The primary aim was to determine uptake of seasonal influenza vaccine in children with SRMC during each of two consecutive years (2014, 2015). Secondary aims included: i) examination of independent characteristics of influenza vaccination in children with SRMC including: demographic factors; medical history; parents' knowledge and attitudes about influenza and influenza vaccination; and access to influenza vaccine and whether they had received a recommendation to receive the influenza vaccine; ii) determine level of reporting of the influenza vaccine on the Australian Immunisation Register (AIR); iii) explore reasons why children do not receive the seasonal influenza vaccine; iv) determine vaccination status for routine immunisations (National Immunisation Program (NIP)) of children with SRMC.

Study Population

Children aged less than 18 years of age with a SRMC and current clients of the WCH were eligible for recruitment. Parents/ guardians were approached by study research assistants with the use of a plain language statement in the waiting area of the outpatient's department of the Women's and Children's Hospital, Adelaide. Clinics covered the subspecialties of pulmonary medicine, renal, endocrinology, neurology, cardiology, rheumatology, gastroenterology, general medicine and the home enteral nutrition service. While in certain specialist clinics, such as the diabetes clinic and medical day unit, all parents with children attending the clinic were approached, in other specialist general medical clinics the research assistants used screening questions to determine eligibility, such as age and presence of an ongoing diagnosed condition that

qualified for NIP influenza vaccine before being given information about the study and being invited to participate. In the cystic fibrosis clinic, parents (and children) were approached in individual clinic consultation rooms, in line with the hospital's infection control practices. At all times research assistants made themselves known to senior nursing staff before approaching parents. Additionally, current inpatients on three wards were approached. The three hospital wards approached cared for children aged from 12 months to <18 years. Exclusion criteria included: children over the age of 18 years or less than 6 month of age on the day of recruitment and/or children without a SRMC as defined by the Australian Immunisation Handbook (AIH) (4), children aged <6 months of age on the 31st December were excluded for that year's vaccination uptake analysis; having a parent unable to provide written informed consent or unable to understand written/spoken English without the need for a translator was also a reason for exclusion. Although the use of convenience sampling did not guarantee that all eligible children would have had an equal chance of being included in our sample, such as those who attended the hospital at another timepoint and who otherwise fit the study selection criteria, the decision to employ this method was justified on several levels. These were: i) lack of resources: a well-executed probabilistic sampling method would have been resource intensive and beyond the scope of this PhD; ii) the inability to identify members of this population, which coincidentally is part of the healthcare problem to begin with and iii) the need to establish the existence and extent of this healthcare problem.

A sample size of 451 respondents was determined by the population proportion of children with a SRMC who received the influenza vaccine with a precision estimate of +/- 4% and 95% confidence, based on an estimate of 25% uptake.

Following written consent from parents or guardians, the survey was undertaken, and additional data were collected. The questionnaire was completed at the time of recruitment, generally in the waiting area of the outpatient clinic or hospital ward. Consent was also obtained to view the child's AIR record, WCH medical record and contact the child's immunisation provider or current healthcare provider (HCP) to confirm influenza immunisation status. Additionally, we also sought permission to contact the child's general practitioner and treating specialist to administer a second survey (Project 4). This method ensured a group of medical practitioners currently treating children identified with a SRMC and allowed a more comprehensive understanding of the barriers to immunisation at a parent, provider and health service level.

Survey Instrument

In addition to demographic details, questionnaire items were based on existing evidence and covered adapted concepts from the Health Belief Model (59) and Protection Motivation Theory (59), in conjunction with existing evidence (27, 30, 35), representing perceived threat of influenza, perceived knowledge of the vaccine, self-efficacy and items assessing healthcare practices. To determine influenza vaccination status, we obtained details of the child's immunisation provider for 2014 and 2015 along with their current primary HCP. In some cases, details for current HCPs were provided as the name of a medical practice only, while others supplied the name of a specific medical practitioner (See Appendix C).

Medical 'at risk' Status

Medical at-risk status was collected during the parental interview and later confirmed by medical case note review. Special risk medical conditions were defined, using the AIH

as described above, as the presence of any underlying condition increasing the risks of complications from influenza infection (Table 1).

Table 1: Medical conditions associated with an increased risk of influenza disease complications and for which individuals are eligible for free vaccination under the National Immunisation Program (60)

Category	Vaccination strongly recommended for individuals with the following conditions
Cardiac disease	Cyanotic congenital cardiac disease, congestive cardiac failure, coronary artery disease
Chronic respiratory conditions	Severe asthma, cystic fibrosis, bronchiectasis, suppurative lung disease, chronic obstructive pulmonary disease, chronic emphysema
Chronic neurological conditions	Hereditary and degenerative CNS diseases, seizure disorders, spinal cord injuries, neuromuscular disorders
Immunocompromising conditions	Immunocompromised due to disease or treatment, asplenia or splenic dysfunction, HIV infection
Diabetes and other metabolic disorders	Type 1 or 2 diabetes, chronic metabolic disorders
Renal disease	Chronic renal failure
Haematological disorders	Haemoglobinopathies
Long-term aspirin therapy in children aged 6 months to 10 years	These children are at increased risk of Reye syndrome following influenza infection

All SRMC identified in the medical cases note were recorded, uncertainty regarding possible ineligibility was discussed with two senior paediatric specialists. The date from which they were deemed ‘special risk’ was also collected. In some cases, this included the day/month/year or month/year or just year. The reason for doing this was to confirm a child’s at-risk status for the 2014 and 2015 influenza seasons and to investigate the age at diagnosis as a possible contributing factor to vaccination.

Influenza vaccination status

Influenza immunisation status was collected during the parental interview and later confirmed by contacting the nominated immunisation provider. Additionally, the Women's and Children's Hospital immunisation records and the Australian Childhood Immunisation Register (ACIR) were checked. ACIR, established in 1996, recorded vaccinations provided to all children up to 7 years of age in Australia, linked to a Medicare account. Since 2017 this has expanded, and it is now called the Australian Immunisation Register (AIR) which records immunisations provided for people of any age. If vaccination status could not be determined using any of the above methods, where possible, we contacted the child's current healthcare provider (HCP). Influenza vaccination status was accessed for 2014 and 2015.

A record of receipt of the influenza vaccination through the AIR or an immunisation provider was accepted to be final. When contacting immunisations providers (GPs, pharmacies, councils, travel clinics, hospitals) we gave up to four (4) attempts before recording as unable to confirm. Where we were unable to confirm due to incorrect number or not a current HCP or a child not having a GP, we recorded these separately.

No distinction was made between "partially" and "fully vaccinated" for influenza according to age. However, for children who have ever had the flu vaccine parents were asked the age when their child first received it and if they recalled the child receiving two doses in the first year of receiving the vaccine. Confirmed influenza vaccination was defined as receipt of at least one dose of the influenza vaccine confirmed by the child's immunisation provider, the AIR, WCH or current HCP. In cases where this was not

attainable such as a child not having a GP, incorrect contact details or the HCP having no record of the individual child, then the child's parent reported vaccination was used.

For the purpose of determining parent reported validity of influenza vaccination and validity of the AIR to capture influenza vaccination, we included vaccination confirmed by the child's immunisation provider, WCH or current HCP only. Specific study eligibility by research question is described in Table 2.

Ethics, Consent and Confidentiality

The study was approved by the Women's and Children's Health Network (WCHN) Human Research Ethics Committee (HREC/15/WCHN/82). Formal notification to the University of Adelaide HREC was also provided. Standard ethical guidelines were followed whereby participation was voluntary, consent was sought, participants had the right to withdraw at any point and all information obtained for the study was treated confidentially. All data collected from parents or other sources as part of this study remains securely protected on secure file-walled servers managed by the University of Adelaide. Hard copies of all data are stored securely in a locked cupboard within the Vaccinology and Immunology Research Trials Unit, at the Women's and Children's Hospital.

Table 2: Project 2: Study eligibility by research question

	Influenza vaccination uptake	Parent reported validity of Influenza vaccination	Reporting of influenza vaccination uptake to AIR
Upper age limit	< 18 years	< 18 years	< 7 years on December 31, 2015/ < 7 years December 31st, 2014
Lower age limit	≥6 months at December 31, 2015	≥6 months at December 31, 2015	≥6 months at December 31, 2015
	If <6 months at December 31, 2014 then excluded from 2014 analysis	If <6 months at December 31, 2014 then excluded from 2014 analysis	If <6 months at December 31, 2014 then excluded from 2014 analysis
SRMC	Presence of SRMC according to AIH diagnosed prior to December 31st, 2015	not excluded	not excluded
	If not diagnosed prior to December 31st, 2014, then excluded for 2014.		
Influenza vaccination	no restrictions on confirmation[#]	those with data for both parent and provider confirmation	only those with data for provider confirmation

Footnote: AIH: Australian Immunisation Handbook; [#] Where this was not attainable parent reported was used.

2.6 COMMUNITY AWARENESS OF INFLUENZA VACCINATION RECOMMENDATIONS FOR CHILDREN

The study, 'Community awareness of influenza vaccination recommendations for children', utilised data collected in April- May 2016 as part of the Health Monitor Survey, a cross-sectional Computer Assisted Telephone Interview (CATI). The Health Monitor (HM) Survey was a service previously provided by Population Research Outcome Studies (PROS) at the University of Adelaide that enabled government and non-government organisations to collect population data focusing on the health and wellbeing of the South Australian Community. Generally, HM surveys sample around 3000 households per survey, yielding approximately 2000 completed interviews with South Australians aged 18 years and over. The study aim was to investigate awareness (among parents in the community) of current influenza vaccination recommendations for children and factors influencing influenza vaccine decision making. Data collected also enabled us to examine vaccine hesitancy and patterns of vaccine access, including information communication.

Study Population

The sample frame consisted of all households listed in the Electronic White Pages (EWP) for South Australia. Households to be included in the survey were randomly selected from the EWP telephone listings of metropolitan and rural households in SA. Prior to data collection commencing, an approach letter was sent to each household selected in the sample. Within households, the person who was last to have a birthday (aged 18 years or over) was selected to participate in the survey. Selected persons were non-replaceable, hence if the selected person was not available, interviews were not conducted with alternative household members. At least 10 call-backs were made to each household before the selected individual was classified as a non-contact. The

study population comprised a state-wide sample drawn from South Australia of adults aged ≥18 years who are parents or caregivers of a child aged <18 years (n=547).

Survey Instrument and Methods

Data analysed were obtained from SA Health following the Health Monitor survey conducted in 2016. As such, survey questions were not designed specifically for this analysis and were a limitation of the study. Respondents who identified as a parent (of a child aged <18 years) were asked their awareness of children's influenza vaccination recommendations and influencing factors towards future vaccine receipt for their child. Possible responses to future intentions towards influenza immunisation and immunisation service use were read to participants with the option for multiple response. Respondents could also specify another response, that was later recoded. To examine parental attitudes towards vaccines in general, parents were asked to state their beliefs towards vaccine necessity, side effects, access to services, behaviour towards their child receiving vaccines and their level of concern according to the Vaccine Communication Framework (VCF). (61) To examine immunisation service use, parents were asked their immunisation provider type, decision-making surrounding their choice as well as any difficulties with access. Parents were also asked their views on information surrounding where to obtain vaccinations and to rate their child's most recent vaccination service. Parents were instructed to answer all immunisation specific questions in relation to their youngest child. (See Appendix **Error! Reference source not found.**)

The interviews were conducted by an independent external research survey company using Computer Assisted Telephone Interviewing (CATI) methodology, which permitted data obtained from the interviewer's screen to be entered directly into a database. At

the beginning of the survey, the interviewer stated that they were calling on behalf of The University of Adelaide to conduct a survey on a range of health issues. An introductory sentence for each health topic covered in the survey was given. Specific questions could be asked of particular subgroups, such as parents. All data collected were non-identifiable. A pilot study of 50 randomly selected households was conducted to test question format and sequence. The questionnaire was designed so that each interview took an average of 15 minutes or less to be completed.

Following data collection, data were weighted by the inverse of the individual's probability of selection and the number of times their telephone number(s) is (are) listed in the white pages, then re-weighted to age group by sex and by section of state (metropolitan/country) benchmarks derived from the Australian Bureau of Statistics Estimated Resident Population. Data were weighted to correspond to the age, sex and geographic profile of South Australia and the probability of selection within a household so that the survey findings are applicable to that entire population. This design enabled a sample that is representative of parents of the South Australian population.

Ethics, Consent and Confidentiality

Ethical approval was granted for the Health Monitor survey methodology from The University of Adelaide, with an amendment letter sent to the SA Health HREC informing them of the questions to be submitted. Potential participants were informed of the purpose of the survey and timeframe, its voluntary nature and that they could decline or refuse questions at any stage of the survey or withdraw completely. Consent was implied by participation. The consent process was approved by The University of Adelaide Human Research Ethics Committee as part the survey methodology.

All Health Monitor survey data were de-identified and no personal or identifying information about participants were provided from SA Health with the dataset. All data collected from as part of this study remains securely protected on secure fire-walled servers managed by the University of Adelaide.

2.7 AWARENESS OF SEASONAL INFLUENZA VACCINATION RECOMMENDATIONS IN GENERAL PRACTITIONERS AND SPECIALISTS CARING FOR CHILDREN WITH SRMC: A MIXED METHODS STUDY.

This project follows on from the study with parents of children with a SRMC. Using the information provided in Project 2 we were able to identify a cohort of GPs whom we knew treated a child/ren with a SRMC. The study comprised a self-administered survey of the paediatric specialists and GP who were linked to the child (Project 2) and subsequent qualitative interviews with a subgroup of these participants. Figure 2 (Section 2.1 Chapter Outline) illustrates the link between participants in Projects 2 and 4 and subsequent papers from these projects.

The primary objective of the survey was to identify the vaccination practices of medical practitioners (MPs) (GPs and specialists) caring for children with SRMC. Secondary objectives were to:

i) examine provider sense of responsibility for immunisation of children with SRMC;

ii) describe health care professionals' decision making towards the seasonal influenza vaccination;

iii) determine if MPs are hesitant to discuss vaccination with these parents;

iv) determine if MPs recognise medical conditions associated with increased risk of more serious influenza disease; and

v) determine if GPs have processes to identify/ target these children for vaccination and whether this is a part of disease management for these children.

The primary objective of the qualitative interviews was to explore medical practitioners' decision making, practices and views of barriers and facilitators related to influenza vaccination and to categorise these using the COM-B model.

Secondary objectives were to:

i) describe provider practices in terms of recommending the vaccine to children with SRMC;

ii) describe perceived barriers/enablers to providing an influenza vaccine recommendation to children with SRMC;

iii) further examine provider responsibility for immunisation of children with SRMC and collaboration between specialists and GPs;

iv) explore the processes used to identify / target these children for vaccination and whether these form part of disease management; and

v) identify potential interventions to address these identified gaps.

Study Population

Medical practitioners of children less than 18 years of age with SRMC and identified from the participants of a parental study (Project 2). Paediatric specialists worked either privately or at the Women's and Children's Hospital (WCH) the major provider of tertiary paediatric healthcare services in South Australia. GPs were the child's current nominated GP, specified either by name or medical practice. In the separate study, "Determining uptake of seasonal influenza vaccine in children with special risk medical conditions", parents of children with various special risk medical conditions attending the outpatient clinics at the WCH will be approached to participate in a study. We asked participants for the contact details of their specialist (where some children may have more than one) and GP. For interviews (Project 4 - qualitative component) participants

may identify themselves as willing to participate or encourage other colleagues to participate (snowballing).

All participants were contacted via a mail survey sent to their workplace address, with the option to complete the survey online using Survey Monkey. In addition, where possible medical practitioners were sent an email with the option to complete the survey online (via a link) or they could download and print a hard copy and email/fax/post back. Practitioners willing to participate in the qualitative study were asked to provide their contact details on a participant information and consent form, returned with the survey. The survey and participant information and consent forms were separate documents and were separated from the surveys as they were returned, ensuring that all responses to the survey remained anonymous. We contacted all the general practitioners and specialists identified by parents; noting that some parents did not provide their GPs details and some children saw the same GP. Anticipating a response rate of approximately 50%, a sample size of 217 enabled us to determine the proportion of medical practitioners who provided a recommendation to receive the influenza vaccine to their patients (children with SRMC), (based on an original estimate of 10% providing this recommendation) with a sampling error of +/- 4%. We undertook interviews with GPs and Paediatric Specialists until data saturation was reached.

Use of Theoretical Model

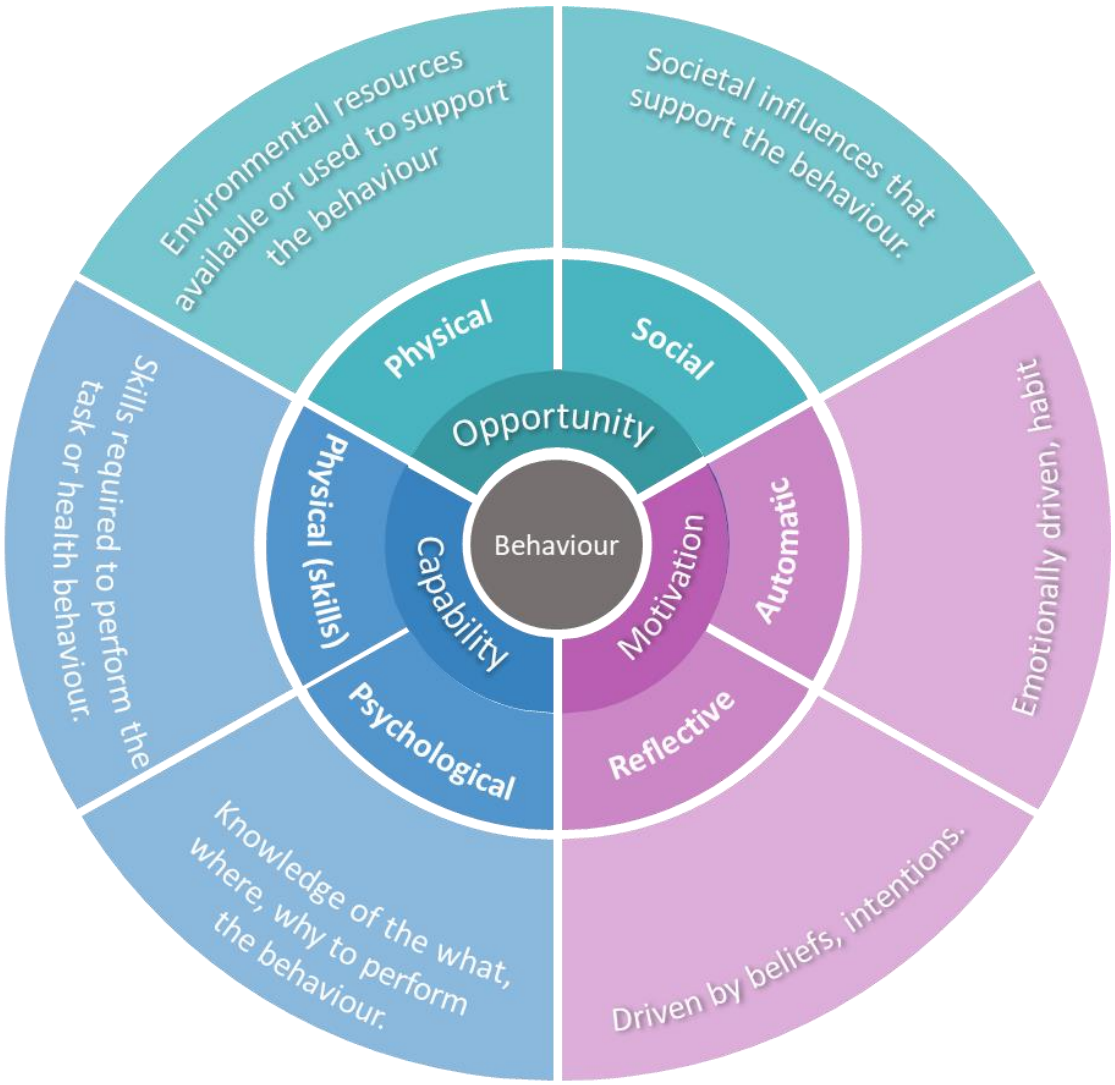
Understanding and implementing behaviour change is complex, particularly when multiple levels of stakeholders exist. In order to best address the drivers to influenza vaccination coverage for children with SRMC, evidence supports the use of interventions based on theory to identify the barriers and facilitators. (62) Use of an implementation science framework enables the systematic assessment and

development of such an intervention. (63) Additionally, implementation science strategies can improve the efficiency and reduce the resources required in the implementation of new behaviours. (64) Many theoretical models exist that attempt to explain behaviour and its underpinning drivers. (65) The Behaviour Change Wheel, which incorporates the COM-B Model, is a comprehensive theoretical framework that can be used as a guide to design evidence-based interventions, while providing structure to understand the fundamental factors that need to be addressed in the intervention. (66)

The Behaviour Change Wheel was developed following a systematic review of behaviour change intervention frameworks. It is unique in that it incorporates the breadth of all 19 frameworks identified in the review in terms of intervention functions and policies. (66) At the core of the Behaviour Change Wheel the COM-B explanatory model asserts that 'Capability', 'Opportunity' and 'Motivation' factors influence behaviour and that behaviour is part of an interacting system involving all these components; (66) with use of the COM-B model applied in the context of general practice and medical practitioner behaviours previously. (67-70) Each of the core COM-B components is further split into two types (Figure 4). Capability is separated into physical (having the skills, abilities or proficiencies acquired through practice to perform the behaviour) or psychological (having the knowledge, comprehension to engage in the necessary thought processes comprehension to perform the behaviour). Opportunity is separated into physical (opportunity facilitated by the environment to perform the behaviour - time, triggers, resources, locations, physical barriers) or social (including interpersonal influences, social cues and cultural norms). Motivation is divided into reflective (beliefs about what is good and bad and conscious intentions, decisions and plans) or automatic (processes driven by emotional responses, desires, impulses and habits resulting from

associative learning and physiological states). (71) Using the Behaviour Change Wheel, each of these behavioural drivers identified by the COM-B can be linked to nine potential intervention functions and seven supporting policy categories.(66)

Figure 4: Central components and sub-components of the COM-B Model



Quantitative Survey Instrument

In addition to demographic details, questionnaire items were developed in conjunction with existing evidence (72-74) and formulated around: knowledge of influenza disease and questions related to influenza vaccine attitudes, understanding of the official recommendations and practice. Additional questions asked participants to elaborate on barriers to recommending the influenza vaccine. (See Appendix D) Additionally, the Australian Health Practitioner Regulation Agency (AHPRA) website was used to determine baseline demographic details (practice location, gender and years practicing medicine) for the entire sample and compare those returning surveys with the eligible population.

Qualitative Interview Guide

Semi structured in-depth one-to-one interviews were completed over the telephone. The interview guide was informed by core constructs of COM-B (66) and also incorporated elements of Ajzen's Theory of Planned Behaviour (TPB) (75), such as the intensity of social pressure the medical professional perceives to provide a recommendation, and normalisation process theory (NPT) (76), such as cognitive participation and collective action. The interviews were guided by the following interview schedule:

1. Participant's role description/ information about the area of work/patient profile
2. Experience of dealing with parents of children with SRMC or complex medical issues and vaccination and discussing vaccination with parents
3. Beliefs regarding the need for different vaccines
4. Beliefs and experience with influenza and the influenza vaccine
5. Collaboration with other medical practitioner's regarding vaccinations
6. Workplace culture and practices towards influenza vaccination

All interviews were digitally recorded and transcribed verbatim. A thematic analysis was undertaken jointly by two authors to inductively code these data in NVivo 12. After initial coding of all data, the framework was reviewed by the candidate's primary supervisor and all other co-authors. The author group revisited the coding process part way through to discuss themes as they emerged. These inductively derived themes were then deductively mapped according to the COM-B ('capability', 'opportunity', 'motivation' and 'behaviour') theoretical framework for understanding barriers and potential interventions, according to sub-category thus enabling a solid foundation from which to conceptualise interventions. Steps taken to ensure the rigour of the qualitative research included multiple interviews (until saturation) with a diverse sample of GPs from metro and regional South Australia with varying lengths of time practising medicine. Dual coders were used with regular meetings with co-investigators, meetings and all decision making documented.

Ethics, Consent and Confidentiality

The study was approved by the Women's and Children's Health Network (WCHN) Human Research Ethics Committee (HREC/15/WCHN/82). Formal notification to the University of Adelaide HREC was also provided. Standard ethical guidelines were followed whereby participation was voluntary, consent was sought, participants had the right to withdraw at any point and all information obtained for the study was treated confidentially. For the survey, potential participants were informed of the purpose of the survey and timeframe, its voluntary nature and consent was implied by participation. Survey ID numbers were included for the purpose of sending reminders only and were not retained with survey responses. No identifying information was collected on participants and returned surveys were allocated a 'study ID' number prior to data entry.

For the qualitative interviews written informed consent was obtained prior to interview and reconfirmed at the beginning of each interview. Interviews were coded to protect the participants identity, GP#1 Metro, for example. For both studies, participants were made aware that all information collected would be stored confidentially and while information may be published, they would not be identified in any reports or publications arising from the research personally or in the case that there were small numbers working in certain specialities or geographical locations, by association. All data collected from medical professionals as part of this study remains securely protected on secure file-walled servers managed by the University of Adelaide. Hard copies of all data are stored securely in a locked cupboard within the Vaccinology and Immunology Research Trials Unit, at the Women's and Children’s Hospital.

CHAPTER 3 IMPACT - INFLUENZA IN CHILDREN WITH SRMC

3.1 HOSPITALISATIONS AND DEATHS FROM INFLUENZA INFECTION

Influenza is a highly contagious respiratory illness with symptoms including respiratory illness with systemic features to multisystem complications and death from primary viral or secondary bacterial pneumonia. (4) Long the scourge of populations, influenza was reported as far back as the era of Hippocrates. Deriving its name from "*influence of the stars"* in 15th century Italy, influenza has demonstrated its virulence over time with global pandemics that have killed millions.(77, 78) The most recent 2009 H1N1 pandemic was mild in comparison to the 1918, 'Spanish' influenza that infected about one-third of the world's population and killed an estimated 50 million people.(77)

Notwithstanding the potential for significant health consequences, the economic burden globally through lost productivity and direct and indirect health costs is substantial. In Australia, the cost to the health system attributable to influenza is significant. Influenza remains the leading cause of vaccine-preventable disease associated with hospitalisations and deaths annually in Australia. The most recent economic study estimated that between 2000 and 2006, influenza contributed to 18,400 hospitalisations and up to 3,457 deaths per annum with a cost to the healthcare system of $115AU million annually, (range of 72-170 million [$AUS]). (3) However, study results were estimated based on coded admissions and it is likely the actual figures are much higher.

The health system and hospitalisation costs reported from other countries, such as the USA, Canada, the UK and New Zealand are also substantial, noting that differences exist between public and private funding models between countries. In 2003, the cost of

influenza related hospitalisations in the USA was estimated at $76.5 million USD. (79) In a review of billing data between 2000-2004 for children <21 years in the USA, influenza related hospitalisations were found to cost more than $13,000USD per admission; with children identified at increased risk having higher mean costs than those considered low-risk. (80)

Most people recover from influenza infection with adequate rest and without sequelae and while the impact of influenza is most marked during a pandemic, seasonal influenza can have devastating consequences for affected individuals, including children.(78) The risk of more severe outcomes in the elderly is generally well understood and accepted, with previously much community attention focused on the elderly and a general classification of those at medical risk. Little attention has focused on awareness of the potential complications and availability of a vaccine for children with SRMC. People eligible for influenza vaccines funded on National Immunisation Program (NIP) in 2019 include Aboriginal and/or Torres Strait Islander persons aged ≥6 months, adults aged ≥65 years, pregnant women (during any stage of pregnancy) and all people aged ≥6 months who have certain medical conditions which increase the risk of influenza disease complications. (60) In general, the classification of those at 'increased risk' varies by country however these typically include asthma, respiratory, cardiovascular, renal, hepatic, neurologic, hematologic, or metabolic disorders or those who are immunocompromised. In Australia, the current medical conditions funded under the NIP include those listed in the Australian Immunisation Handbook. (4)

Overall, children (aged <18 years) who fall into the 'increased risk' group remain underrepresented in terms of influenza coverage and disease epidemiology data. This is likely attributable to the limited vaccination coverage data collected, with uptake data

reliant on survey methodology and a non-requirement to report some vaccines to the AIR. However, understanding the burden of any disease is important. This information helps to advance medical knowledge, plan educational strategies and allocate health system resources appropriately.

In general, the potential complications from influenza in children are well defined and include secondary bacterial pneumonia, sinusitis, bronchitis, acute otitis media, encephalitis, myositis, myocarditis, Guillain-Barre syndrome and Reyes syndrome, multi-organ failure and death. (12, 81-87) However, despite widespread recommendation for children with SRMC to receive the influenza vaccine, the increased risk for children with SRMC is less well categorised. Yet, understanding and quantifying this increased risk is valuable on many levels not least of all because it translates directly to the acceptance of recommendation polices by healthcare professionals and parents alike.

Studies have found children with SRMC are prone to a significant burden of illness high numbers of outpatient visits, hospitalisations and increased mortality. A retrospective cohort study (85) from the USA found that, children for whom influenza vaccination was recommended accounted for 56% of hospitalisations of children ≤18 years with laboratory confirmed influenza. Another study from the USA (88) found that rates of hospitalisation in children for influenza with conditions placing them at increased risk were higher at 3,562 admissions per 100,000 people compared to low risk children (509 per 100,000 people), which approached the same rate as adults who were at increased risk, aged 65-74 years. This finding is supported by a large retrospective study (89) that used data from 1973 to 1993 in children aged <15 years and discovered that compared to healthy children those with SRMC had 2-4 times excess hospitalisations. The same

data were also used to examine the burden of illness in children with asthma and other chronic conditions. On average, influenza accounted for an additional 19, 8 and 2 hospitalisations for acute cardiopulmonary disease per 1,000 children at increased risk aged <1 year, 1 to <3 years and 3 to <15 years respectively. (89) Another retrospective cohort study found that hospitalisation for acute respiratory disease among children with SRMCs was 4 to 21 times more likely than in healthy children of the same age. (13)

A systematic review (5) of 27 studies with data on 14,086 children, found the strongest risk factors for hospitalisation for influenza or influenza-like-illness were neurological disorders OR 4.62 (95%CI 2.82-7.55), sickle cell disease OR 3.46 (95%CI 1.63-7.37), immunosuppression OR 2.39 (95%CI 1.24-4.61) and diabetes OR 2.34 (95%CI 1.20-4.58); however it should be noted that 20/27 of these studies assessed pandemic rather than seasonal influenza. This was similar to Dharan et al who found that in children aged 6-59 months, hospitalisation for laboratory confirmed influenza was increased in those with SRMC including hematologic/oncologic OR 11.8 (95%CI 4.5-31.0), pulmonary OR 2.9 (95%CI 1.9-4.4) and neurologic OR 3.8 (95%CI 1.6-9.2) conditions. (90) Children with SRMCs are also overrepresented in deaths from influenza. One study (91) in the USA looking at influenza associated death in children with laboratory confirmed influenza over 8 years, found 57% of deaths were in children who had 1 or more SRMC.

While children with SRMCs experience a greater burden of disease through higher numbers of hospitalisations and deaths, once hospitalised they also experience greater severity of disease. (12, 83) Several studies report higher rates of complications from influenza in children with SRMC. A retrospective study from the US found that compared to healthy peers, special risk children were more likely to experience

complications at a higher rate (0-4 years: RR 1.4; 95%CI 1.1-1.6 and 5-14 years: RR 1.8; 95%CI 1.5-2.2). (12) A study examining laboratory confirmed community acquired influenza in children aged ≤ 21 years found children with SRMCs had a higher incidence of influenza related complications compared to healthy children of the same age (29% vs 21%; OR: 1.6; 95%CI 1.1-202) and were more likely to require intensive care (OR: 1.6; 95%CI 1.2-2.5) or develop respiratory failure (OR: 2.8; 95% CI: 1.3–6.1). (83)

Studies also report specific categories of SRMC to have a higher incidence of influenza related complications. Neurological and neuromuscular disorders (NNMD) have a risk of complications from influenza like illness and laboratory confirmed influenza that is approximately 3-6 times higher than healthy children (84, 92-94) and admissions that are more likely to be associated with a prolonged length of stay (LOS) (83). Those with cardiac diseases are also reported to have complications four times higher than healthy children (92, 94) with laboratory confirmed influenza and also experience a prolonged LOS (83). Children with SRMCs are also more likely to have a hospital acquired infection (HAI). In a retrospective cohort study from the USA that examined 6 years of admissions to the Paediatric Intensive Care Unit, a significantly higher proportion of children with SRMC had acquired a respiratory infection in the hospital environment. (95)

To answer the thesis' first research question, noting no previous reviews had focused on categorising the increased risk from influenza for children with SMRC, we conducted a systematic review of observational studies. The hypothesis was that in children hospitalised with influenza; there would be significant differences in terms of complications, severity and resources use in children with SRMC compared to healthy children. A literature search was conducted in MEDLINE and EMBASE for studies

published from 1990 to March 2018. Additional manuscripts from reference list searching and contact with colleagues of studies containing unpublished data relevant for the review were also included. Further details on the search can be accessed at PROSPERO (http://www.crd.york.ac.uk/PROSPERO/).

3.2 COMPLICATIONS AND SEVERITY OF INFLUENZA INFECTION

Outcomes from influenza hospitalisation including intensive care unit (ICU) admission, mechanical ventilation, development of pneumonia, death, neurological outcomes, as well as, hospital resource use (hospital length of stay (LOS) and Intensive Care Unit LOS) were compared between children with and without SRMC in a systematic review of the literature. After systematically identifying 22 relevant articles in the literature that reported data on the probability of complications or resource use in paediatric influenza hospitalisations for at least one SRMC, all published evidence central to our review were qualitatively and, when feasible, quantitatively synthesised. While this systematic review was not without its short comings, particularly highlighting methodological weakness within this research field, it provided sufficient evidence to support, and justify SRMC conditions as a risk group.

This chapter concludes theme 1 of this thesis which related to the impact of influenza infection in children identified at increased risk from influenza complications compared to healthy children. Describing this risk was a critical step in understanding the literature and interpreting the recommendations. This resurfaces in later chapters involving theme 2 – when examining parents' perception of disease severity and in theme 4 – exploring medical professionals communication resources.

The resulting publication entitled "Influenza in Children with Special Risk Medical Conditions: A Systematic Review and Meta-Analysis", was published in the journal "Pediatric Infectious Disease Journal".

3.2.1. Statement of Authorship

Statement of Authorship

Title of Paper	Influenza in Children with Special Risk Medical Conditions: A Systematic Review and Meta-Analysis
Publication Status	☑ Published ☐ Accepted for Publication ☐ Submitted for Publication ☐ Unpublished and Unsubmitted work written in manuscript style
Publication Details	Tuckerman J, Misan S, Crawford NW, Marshall HS. Influenza in Children with Special Risk Medical Conditions: A Systematic Review and Meta-Analysis. PIDJ. 2019 Sept

Principal Author

Name of Principal Author (Candidate)	Jane Tuckerman
Contribution to the Paper	JT contributed to study design, development of the search strategy and screening, extracted and analysed the data, prepared the first draft of the manuscript.
Overall percentage (%)	75%
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: 18 Dec 2019

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	Siobhan Misan
Contribution to the Paper	SM contributed to the systematic review protocol, screening, data extraction, interpretation and critical review of the manuscript.
Signature	Date: 09/12/19

Name of Co-Author	Nigel Crawford
Contribution to the Paper	NC contributed to data interpretation and critical review of the manuscript.
Signature	Date: 16/12/19

Name of Co-Author	Helen Marshall
Contribution to the Paper	HM contributed to study design and systematic review protocol, screening, data interpretation and critical review of the manuscript.
Signature	Date: 10 Dec 2019

3.2.2. Publication

Influenza in Children With Special Risk Medical Conditions

A Systematic Review and Meta-analysis

Jane Tuckerman, MPH,† Siobhan Misan, MBBS,‡ Nigel W. Crawford, PhD,§¶ and Helen S. Marshall, MD*†‖*

Background: Children with special risk medical conditions (SRMC) are over-represented in influenza hospitalizations. A systematic review was undertaken to determine whether children with SRMCs experience greater complications or severity following influenza infection.

Methods: Bibliographies of pertinent articles were searched in MEDLINE and EMBASE (1990 to March 2018) and contact made with the investigators of unpublished studies containing relevant data. Studies of children (aged ≤18 years) with a SRMC hospitalized with influenza were included. Outcomes were pneumonia, intensive care unit (ICU) admission, mechanical ventilation, neurologic outcomes (seizures, encephalopathy), death and length of stay in hospital or ICU.

Results: Twenty-two studies met inclusion criteria. Compared with healthy peers, children with SRMC had higher odds of ICU admission [pooled odds ratio (OR) 1.66 (95% confidence interval (CI): 1.25–2.21)], for mechanical ventilation [pooled OR 1.53 (95% CI: 0.93–2.52)] and death [pooled OR 1.34 (95% CI: 0.74–2.41)]. Additionally, children with SRMC were more likely to develop bacterial pneumonia (crude OR 1.7; 95% CI: 1.1–2.6) or experience prolonged hospital length of stay [adjusted rate ratio 1.75 (95% CI: 1.44–2.11)]. The level of GRADE evidence was low for all outcomes considered in this review.

Conclusions: While there was evidence that ICU management and bacterial pneumonia increases in children with SRMC, evidence showing an increase in the probability of death or need for mechanical ventilation was inconsistent. Further research using large datasets should evaluate the impact of complications and associated morbidity from influenza in SRMC children.

Accepted for publication May 7, 2019.

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The authors have no financial relationships relevant to this article to disclose. No funding was secured for this study. This review was initiated as part of studies toward a Doctor of Philosophy (PhD) undertaken by Ms Tuckerman; funded by an Australian Government Research Training Program Scholarship (formally Australian Postgraduate Award). Prof Marshall is supported by NHMRC Fellowship APP1084951. This review is not sponsored or financed by a third party.

H.M. is an investigator on clinical trials of investigational vaccines sponsored by Industry. Her institution receives funding from Industry (GSK, Pfizer, Novavax) for Investigator led research. She does not receive any personal payments from the Industry. H.M. is a member of the Australian Technical Advisory Group on Immunisation (ATAGI), Australian Government. This paper reports her own personal views and not those of the ATAGI. The other authors have no conflicts of interest to disclose.

Registration: PROSPERO CRD42017074648 web link: http:/www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017074648

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Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.pidj.com).

ISSN: 0891-3668/19/3809-0912
DOI: 10.1097/INF.0000000000002405

Key Words: influenza, children, complications, outcomes, medical condition

(*Pediatr Infect Dis J* 2019;38:912–919)

Influenza is a seasonal respiratory infection that causes a wide spectrum of disease. The risk for complications or severe disease varies depending on an individual's age, comorbidities, influenza strain and vaccination status.[1–5] For children in general, the predominate complications from influenza are well documented[6–12] and a recommendation for vaccination of children believed to be at increased risk is now recognized public health policy.[5,13–15]

Special risk medical conditions (SRMC) such as severe asthma, lung or heart disease, immune compromise or diabetes may predispose an individual to increased influenza severity. Infection in those with a SRMC can lead to exacerbations of underlying comorbidities, neurologic complications, primary viral or secondary bacterial pneumonia, and death.[5,16,17] For children with SRMC, influenza is thought to have a protracted disease course resulting from reduced immunity and the disease can compromise medical comorbidities translating to higher rates of hospitalization and more severe outcomes such as a requirement for higher-level care and/or death.[18] A recent review found neurologic and immune disorders, prematurity and age younger than 2 years to be strong risk factors for influenza-related hospitalization, although most were studies of pandemic influenza.[19] However, the impact that a SRMC has on the severity of influenza hospitalizations in children has yet to be clarified.

Quantifying complications from influenza in children with SRMC is necessary to facilitate both clinical and policy decision-making and assist in parents' education. We hypothesized that among children hospitalized with influenza infection both severity and prevalence of complications are increased in children with SRMCs compared with their healthy counterparts. The aim of this study was to systematically assess the current evidence of severity, complications and resource use experienced by children with SRMC who were hospitalized with influenza infection.

METHODS

Search Strategy

This systematic review is reported following the Meta-analysis of Observational Studies in Epidemiology recommendations.[20] Details of the protocol developed for this review, along with the search strategy are available in PROSPERO (CRD 42017074648). Broadly, we searched MEDLINE and EMBASE for studies published from 1990 to March 2018, the reference lists of included studies and contacted investigators of studies containing unpublished data relevant for the review. The review outcomes were selected based on current literature[16,17,19,21] and were the probability of pneumonia, intensive care unit (ICU) admission, mechanical ventilation requirement, neurologic complications (encephalopathy or seizures), death and length of stay (LOS) in the hospital and the ICU.

Study Selection

Studies were screened initially by one author (JT) based on title and abstract, followed by full-text screening by two authors (SM and JT); disagreements were resolved by a third author (HM) (see Figure, Supplemental Digital Content 1, http://links.lww.com/INF/D544). We included English-language articles that presented quantitative information on hospitalizations of clinical influenza in children (≤18 years of age) that included a breakdown by risk group(s) and additionally for any one of the listed outcomes. Where a study included individuals >18 years of age, we included only studies in which the majority were ≤18 years or if children's data were reported separately. Clinical influenza was defined as cases either confirmed through laboratory testing [laboratory-confirmed influenza (LCI)], ICD coding or hospital discharge coding.

We excluded studies with no breakdown by risk group for hospitalizations or where total numbers for an outcome were not presented. When studies with duplicate data sources were identified, we endeavored to include the first published study except where a subsequent study provided more comprehensive outcome data or a more recent recommendation was used to define those 'at risk.' If study cohorts overlapped in such a way that excluding one would have omitted valuable data, then both studies were retained.

Data Extraction and Quality Assessment

Two authors (JT and SM) independently extracted all data and assessed study quality using The Quality in Prognosis Studies tool[22,23]; with risk of bias (RoB) provided for all included studies in Table 1.

The following six domains were assessed: (1) study participation; (2) study attrition; (3) prognostic factor measurement; (4) outcome measurement; (5) study confounding and (6) statistical analysis and reporting. Judgments of low, moderate, high risk of bias were made for each domain.[23] Additionally, where insufficient information was reported, we included a judgment of 'unable to determine.' Differences were discussed with all reviewers, and a decision made by agreement. The quality of evidence for each outcome was assessed according to the GRADE framework adapted to judge the quality of prognostic evidence.[43]

Statistical Analysis

We presented individual study data on the proportion of children with a SMRC and summary data visually for each outcome. For dichotomous outcomes: probability of ICU admission, mechanical ventilation, death and neurologic outcomes, we calculated the odds ratio (OR) when sufficient data enabled construction of a 2 × 2 table. We calculated the average effect summary using a random effects model (Mantel Haenszel method) in ReviewManager 5.0 (Cochrane Collaboration)[44] including I^2. We classified an I^2 of 50% or above as a substantial level of heterogeneity.[45] We planned to explore heterogeneity by subgroup analysis of studies with LCI, RoB and influenza vaccination status. Outcomes with data unsuitable for a meta-analysis were presented using a qualitative summary only.

RESULTS

Selection of Studies

Electronic databases and searching the reference lists of included papers identified 1377 records, including one study in-press (since published). We assessed 129 full-text articles and included 22 articles that reported data on the probability of complications or resource use in pediatric influenza hospitalizations for at least one SRMC (see Figure, Supplemental Digital Content 1, http://links.lww.com/INF/D544). The review included data on 42,875 children, of whom 12,225 (28.5%) had a SRMC. Three studies[46–48] that met inclusion criteria were excluded as they presented either the same cohort or a subgroup of another included study. Additionally, two studies[27,39] comprised participants that overlapped with a third study, but due to the difference in age groups and study periods we retained the death and ICU admission outcomes,[27,39] in addition to those reported in the larger study[26] with more restrictive age range.

TABLE 1. Quality Appraisal of Included Studies

Study Reference Author	Participation	Attrition	PF Measurement	Outcome Measurement	Confounding	Statistical Analysis
Ampofo et al[9]	Mod	Unable	Low	Low	High	Low
Blyth et al[24]	Low	Unable	Unable	Low	Mod	Mod
Burton et al[25]	Low	Unable	Low	Low	High	Low
Chaves et al[26]	Mod	Mod	Mod	Low	High	Low
Coffin et al[7]	Mod	Unable	Low	Low	High	Mod
Dawood et al[27]	Mod	Unable	Low	Low	High	Low
Feldman et al[28]	Low	Unable	Mod	Mod	High	Unable
Hassan et al[29]	Low	Unable	Mod	Low	High	Unable
Ipp (2003)	Low	Mod	Low	Low	High	Low
Kaczmarek et al[30]	Low	Mod	Low	Low	High	Low
Launes et al[31]	Mod	Low	Mod	Mod	High	Unable
Lee et al[32]	Mod	Unable	Low	Low	High	Low
Leung et al[33]	High	Unable	Low	Low	High	Low
Moore et al[34]	Low	Unable	Unable	Low	High	Mod
PHAC[35]	Low	Unable	Low	Low	High	Low
Punpanich et al[36]	High	Unable	Unable	Low	High	Unable
Rojo et al[37]	Low	Unable	Unable	Low	High	Mod
Sam et al[38]	Low	Low	Low	Low	High	Low
Schrag et al[39]	Low	Mod	Low	Low	High	Low
Serwint et al[40]	High	Unable	Low	Unable	High	Low
Spaeder et al[41]	Mod	Unable	Low	Low	High	High
Suntarattiwong et al[42]	High	Unable	Unable	Low	High	Low

Public Health Agency Canada (PHAC). Study quality was assessed using The Quality in Prognosis Studies (QUIPS) tool,[21,22] with judgments of low, moderate, high risk of bias made for each domain plus an unable (unable to determine) category, used when there was insufficient information reported to permit RoB judgment.

Methodologic Quality

Overall, inadequate reporting restricted study quality assessment (Table 1). Study participation RoB was upgraded due to insufficient reporting of the source population or the methods used to identify participants such as ICD coding, the exclusion criteria and the proportion of eligible population who participated. Study attrition was largely unable to be determined, with only two studies providing the proportion of participants with complete data. While many studies had low RoB for prognostic factor measurement (presence of SRMC), few reported missing data or the validity of the method used. Few studies provided a clear definition for each outcome measurement such as calculation of bed days or ICU admissions; none reported the validity of the method used. Confounding RoB was upgraded due to inadequate reporting of potential confounders and adjustment methods. Many studies had insufficiently described the statistical methods used. Across all outcomes, we were restricted from further exploration of heterogeneity: few studies reported vaccination status; leaving subgrouping impossible, all pooled studies used laboratory confirmation of influenza, and subgrouping by risk of bias was not helpful because most evidence was from studies at moderate or unclear risk of bias.

Study Characteristics

Study characteristics are presented in Supplemental Digital Content 2, http://links.lww.com/INF/D545 (Table). Outcomes of influenza were associated with LCI (n = 18)[7,9,24–27,31,33–42,49] or an ICD or discharge code of influenza (n = 4).[28–30,32] Some studies limited recruitment to one influenza season (n = 3)[29,36,42]; while others restricted participation to only cases admitted during the official influenza season (n = 9).[24,25,27,31,32,34,35,39,40] Studies also excluded cases for the following reasons: being a subsequent influenza admission in the same influenza season (n = 1)[7]; onset of symptoms >5 days before admission (n = 1)[42]; diagnosis >14 days following positive influenza test (n = 1)[39]; co-viral infection (n = 2)[34,37]; LOS >100 days (n = 1)[49] or nosocomial influenza (n = 9).[7,25,34,35,37–39,41,49] In studies that defined nosocomial influenza infection, the timeframe for diagnosis ranged from 48 hours to 7 days post admission. Nosocomial influenza cases were either included (n = 3)[24,28,40]; excluded (n = 9)[7,25,34,35,37–39,41,49] or their inclusion not reported (n = 10).[9,26,27,29–33,36,42] When specified (n = 6), nosocomial cases ranged from 3.5% to 17.4% of the original cohorts, with SRMCs overrepresented in these data. Few studies reported vaccination status (9/22)[24,25,27,31,34–36,39,40] or use of antivirals (12/22).[24–27,31–36,38,39] Antiviral use ranged from 6.6% to 95.1%, with increased use for those with SRMC, although few studies (n = 4)[27,31,34,35] provided these specific data.

The underlying medical conditions included varied between studies with the majority using official recommendations to determine risk status of participants; however, these differed by country and study periods (1977 to 2013). Overall, 44 separate disorders or principle groups of conditions were reported. Often a risk group was listed as a number of separate disorders or clustered with others making comparison difficult. As children may have had more than one risk condition within a principle risk category, it was not possible to combine subgroups together. Most notably this occurred with neurologic disorders, neuromuscular disorders and immunocompromised conditions. Neurologic and neuromuscular disorders were reported as a principle group in 10 studies,[7,24–26,31,33,35,36,38,39] while an additional three studies[9,27,34] reported a neurologic and neuromuscular category in addition to other neurologic conditions such as myotonic muscular dystrophy, developmental disorders, febrile seizures, seizure disorder, spina bifida and cerebral palsy. Immunocompromised conditions and malignancies were often combined; when listed separately as immunosuppressive or immunodeficiency categories, there was insufficient detail as to what these specific conditions were.

Proportion of Pediatric Influenza Hospitalizations With a SRMC

The proportion of pediatric influenza hospitalizations that included a child with any SRMC ranged from 14.2% to 54% (see Table, Supplemental Digital Content 2, http://links.lww.com/INF/D545), while the proportion of pediatric influenza hospitalizations with a SRMC sub-risk category ranged from 0.1% for liver cirrhosis, diabetes and aspirin therapy and up to 24.3%–28.3% for asthma and pulmonary conditions respectively (see Table, Supplemental Digital Content 3, http://links.lww.com/INF/D546).

Probability of Pneumonia if Hospitalized

Only one study[7] presented data on the probability of pneumonia, more specifically bacterial pneumonia. Those with SRMCs were more likely to develop suspected bacterial pneumonia than healthy counterparts [crude OR 1.71; 95% confidence interval (CI): 1.13–2.59] (see Table, Supplemental Digital Content 2, http://links.lww.com/INF/D545).

Probability of ICU Admission

For children with SRMCs, the probability of ICU admission ranged from 8.3% to 22.6% (see Table, Supplemental Digital Content 4, http://links.lww.com/INF/D547).[7,24–26,31,34,35,37–39] Using crude data and excluding the study with zero events in healthy children, risk of ICU admission increased in children with SRMCs OR 1.66 (95% CI: 1.25–2.21; I^2 68%, n = 9) (Table 2 and Fig. 1A). In two studies[28,32] examining children with a specific SRMC (acute lymphoblastic leukemia ± other SRMCs; or liver transplant), the probability of ICU admission ranged from 10.5% to 25.9%. Two additional studies[30,41] reporting on ICU admissions only, indicated that 40.8%–44.1% of admissions comprised children with a SRMC.

Probability of Mechanical Ventilation

Estimates of the probability of mechanical ventilation ranged from 5.5% to 44% (median 8.3%) for those with SRMCs and 2%–34.8% (median 6.1%) for children without SRMCs (see Table, Supplemental Digital Content 5, http://links.lww.com/INF/D548).[7,9,25,26,31,34,35,38,40–42] The presence of a SRMC increased the requirement for ventilation [crude OR 1.53 (95% CI: 0.93–2.52); I^2 64% n = 10] (Table 2 and Fig. 1B).

Hospital LOS

Studies reviewed presented different measures of hospital LOS including the mean, median and study specific definitions such as LOS >6 or 14 days (see Table, Supplemental Digital Content 6, http://links.lww.com/INF/D549). Of those presenting the median difference in hospital LOS, comparing SRMC to healthy, all but one showed the LOS to be longer in the SRMC group.[9,25,26,31] While another study[24] found prolonged LOS for those with comorbidities after adjusting for indigeneity, ICU admission and antiviral use [adjusted rate ratio 1.75 (95% CI: 1.44–2.11)].

ICU LOS

Only one study[30] compared SRMCs to non-SRMC, finding longer mean ICU LOS in those with a SRMC over a 16-year period (see Table, Supplemental Digital Content 6, http://links.lww.com/INF/D549 and Table 2).

Probability of Neurologic Complications

Only two studies [7,34] presented data on the probability of neurologic outcomes following influenza infection. Both studies

TABLE 2. Summary of Findings and Quality Assessment of Outcomes

	Outcomes							
	Bacterial Pneumonia	ICU Admission	Mechanical Ventilation	Seizures	Influenza-Related Encephalopathy	Death	Hospital LOS	ICU LOS
Number of participants (studies)	745 (1)	8020 (9)	5461(10)	1250(2)	1250(2)	10,619(9)	34,617(12)	704(1)
Comparative difference								
Healthy (%)	44/382 (11.5)	520/5305 (9.8)	157/1868 (8.4)	53/675 (7.9)	9/675 (1.3)	24/4360 (0.55)	Unable*	Unable*
SRMCs (%)	66/363 (18.2)	506/2832 (13.2)	145/3593 (4.0)	46/575 (8.0)	4/575 (0.7)	24/6259 (0.38)	Unable*	Unable*
OR (95% CI)	1.71 (1.13–2.59)	1.66 (1.25–2.21)	1.53 (0.93–2.52)	Unable*	Unable*	1.34 (0.74–2.41)	Unable*	Unable*
Quality of the evidence								
Risk of bias†	Serious‡	Serious	Serious	Serious	Serious	Serious	Serious	Serious‡
Inconsistency	N/A‡	Serious§	Serious§	N/A¶	N/A¶	Very serious‖	Very serious**	N/A‡
Indirectness	No††	Serious§§	Serious§§	Serious¶¶	Serious¶¶	Serious§§	Serious§§	No‖‖
Imprecision	No***	No†††	Serious§§§	Serious§§§	Serious§§§	Very serious¶¶¶	N/A‖‖‖	N/A‡
Publication bias	Strongly suspected‡	Strongly suspected*****	Strongly suspected*****	Strongly suspected††††	Strongly suspected††††	Strongly suspected*****	Strongly suspected	Strongly suspected††††
Overall	Very low	Very low	Very low	Very low	Very low	Very low	Very low	Very low

*Unable Too few studies or data unable to be combined;

†Studies were deemed to have no serious limitations when most evidence was from studies at low risk of bias for most of the bias domains; serious limitations when most evidence is from studies at moderate or unclear risk of bias for most of the bias domains; or very serious limitations when most information is from studies at high risk of bias with respect to almost all of the domains.

‡Evidence was from one study only.

††Excluded repeat admissions and nosocomial influenza cases.

***Although a significant result was found only a crude estimate was provided.

§High statistical inconsistency may be due to children's ages across studies (study with the greatest weight included only children aged <1 year) and difference in study years.

§§Variation across studies in terms of medical conditions included and inclusion of nosocomial cases differed across studies.

†††The total number of events are low for both groups in a number of studies.

*****Clustering toward top of funnel plot.

§§§The total number of events are low for both groups in a number of studies with extremely wide CI and the CI for the pooled effect of SRMCs included the null.

¶Too few studies to combine, however the study point estimates show variation in effect size.

¶¶Excluded repeat admissions, nosocomial influenza cases and co-infections.

††††Too few studies to determine.

‖The study point estimates show variation in effect size and direction.

¶¶¶The total number of events are extremely low for both groups in a number of studies with extremely wide CI and the CI for the pooled effect of SRMCs included the null.

**The outcome measurement across studies meant we were unable to pool this outcome. However the estimates from individual studies did not vary in direction.

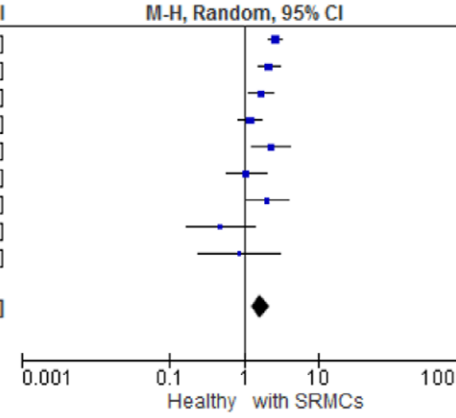
‖‖‖The outcome measurement across studies meant we were unable to pool this outcome and insufficient information in studies to determine.

‖‖Only one study included that does not report if any population groups are excluded.

A

Study or Subgroup	SRMCs Events	SRMCs Total	Healthy Events	Healthy Total	Weight	Odds Ratio M-H, Random, 95% CI
Chaves	162	796	210	2361	17.1%	2.62 [2.09, 3.27]
Blyth	113	572	71	696	15.4%	2.17 [1.57, 2.99]
Coffin	82	363	56	382	14.3%	1.70 [1.17, 2.47]
Schrag	43	339	104	969	14.3%	1.21 [0.83, 1.77]
Moore	32	212	21	293	10.6%	2.30 [1.29, 4.12]
Burton	22	188	20	183	9.6%	1.08 [0.57, 2.05]
PHAC	33	211	15	180	9.6%	2.04 [1.07, 3.89]
Launes	5	55	15	88	5.1%	0.49 [0.17, 1.42]
Sam	4	48	8	84	4.0%	0.86 [0.25, 3.03]
Total (95% CI)		**2784**		**5236**	**100.0%**	**1.66 [1.25, 2.21]**
Total events	496		520			

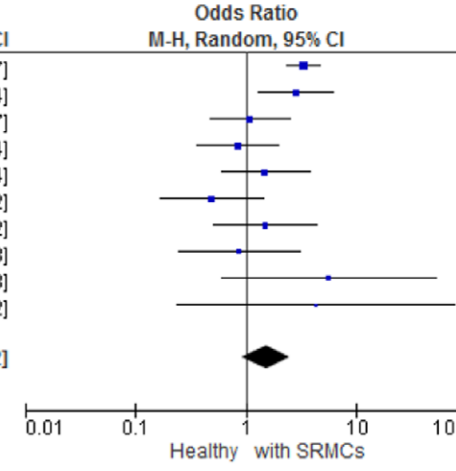
Heterogeneity: Tau² = 0.11; Chi² = 25.39, df = 8 (P = 0.001); I² = 68%
Test for overall effect: Z = 3.51 (P = 0.0004)



B

Study or Subgroup	Healthy Events	Healthy Total	with SRMCs Events	with SRMCs Total	Weight	Odds Ratio M-H, Random, 95% CI
Chaves	69	796	66	2361	16.9%	3.30 [2.33, 4.67]
Coffin	23	363	9	382	12.6%	2.80 [1.28, 6.14]
PHAC	14	211	11	180	12.3%	1.09 [0.48, 2.47]
Ampofo	9	120	18	205	12.1%	0.84 [0.37, 1.94]
Burton	12	188	8	183	11.3%	1.49 [0.60, 3.74]
Launes	5	55	15	88	9.9%	0.49 [0.17, 1.42]
Spaeder	16	36	8	23	9.9%	1.50 [0.51, 4.42]
Sam	4	48	8	84	8.5%	0.86 [0.25, 3.03]
Serwint	4	43	1	56	3.9%	5.64 [0.61, 52.43]
Suntarattiwong	1	8	1	31	2.6%	4.29 [0.24, 77.22]
Total (95% CI)		**1868**		**3593**	**100.0%**	**1.53 [0.93, 2.52]**
Total events	157		145			

Heterogeneity: Tau² = 0.35; Chi² = 25.14, df = 9 (P = 0.003); I² = 64%
Test for overall effect: Z = 1.69 (P = 0.09)



C

Study or Subgroup	Healthy Events	Healthy Total	High risk Events	High risk Total	Weight	Odds Ratio M-H, Random, 95% CI
Dawood	9	1894	8	2123	38.1%	1.26 [0.49, 3.28]
Chaves	2	796	6	2361	13.5%	0.99 [0.20, 4.91]
Blyth	2	696	3	572	10.8%	0.55 [0.09, 3.28]
Coffin	3	363	2	382	10.8%	1.58 [0.26, 9.53]
Moore	2	212	1	293	6.0%	2.78 [0.25, 30.87]
Sam	2	48	1	84	5.9%	3.61 [0.32, 40.88]
Serwint	2	43	1	56	5.9%	2.68 [0.24, 30.61]
Burton	1	188	1	183	4.5%	0.97 [0.06, 15.68]
Ampofo	1	120	1	205	4.5%	1.71 [0.11, 27.66]
Total (95% CI)		**4360**		**6259**	**100.0%**	**1.34 [0.74, 2.41]**
Total events	24		24			

Heterogeneity: Tau² = 0.00; Chi² = 2.53, df = 8 (P = 0.96); I² = 0%
Test for overall effect: Z = 0.96 (P = 0.34)

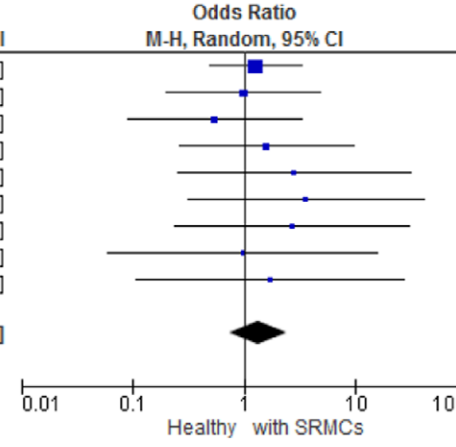


FIGURE 1. Meta-analyses of severity and complications from influenza infection in children with SRMC compared with healthy counterparts. "A: Probability for admission to ICU"; "B: Probability for mechanical ventilation"; "C: Probability of death."

showed influenza-related encephalopathy was higher for children without SRMCs (range 1%–1.7%) compared with SRMCs (range 0.5%–0.8%), yet the number of events captured was extremely low. In contrast, the same two studies reported conflicting evidence on the effect of a SRMC on the probability of seizures (SRMC range: 7.1%–9% versus without SRMCs: range 6%–10.2%) (Table 2).

Probability of Dying From Influenza

The probability of hospitalized mortality with influenza ranged from 0% to 4.88% (median 0.53%) in children with SRMC (see Table, Supplemental Digital Content 7, http://links.lww.com/INF/D550). In four studies, no deaths occurred.[31,33,35,36] The case fatality rate in studies that comprised only single risk categories such as malignancy or solid organ transplant ranged from 1.4% to 2.1 %.[28,32] In studies with more diverse special risk groups, using crude data and excluding studies with zero events, the probability of dying was increased for SRMC versus healthy [crude OR 1.34 (95% CI: 0.74–2.41; I^2 0% n = 9)][7,9,24–27,34,38,40] (Table 2 and Fig. 1C).

DISCUSSION

Influenza infection disproportionally affects children with SRMCs by increasing the risk of severe disease and complications. Our review found only limited data were available to differentiate between children with SRMC and healthy children in terms of influenza severity, complications and hospital resource use. This should be distinguished from finding evidence suggesting no difference in the probability of severity, complications or resource use in those with SRMCs compared with those without SRMCs.

While individual studies showed marginal differences across outcomes, overall there was evidence that the probability of ICU admission increased for children with SRMC. Despite an increase in the pooled point estimates, there was not strong evidence to suggest that having a SRMC had an effect on either the probability of mechanical ventilation or death. The more severe and prolonged disease course experienced by children with SRMC may be a consequence of enhanced susceptibility to infection due to reduced immune response, respiratory or cardiac compromise with less reserve when infected by influenza and a compromise to existing medical comorbidities. While ICU admission was most common in studies comprising large proportions of young children (<5 years) or where inclusion was restricted to the very young (<1 year), it is unclear why we identified such variation in the probability of ICU admission between studies. It is possible that one contributing factor was that smaller studies with less event data would have been insufficient to detect a meaningful difference between the two groups of children. Additionally, studies showed wide variation across years even when identical methodology was used, such as the requirement for ICU admission and mechanical ventilation in studies using data from Canada's Immunization Monitoring Program ACTive.[25,35] This suggests outcomes are potentially modified by variables related to the seasonal variation in the circulating strain of the virus, such as severity of the strain, efficacy and uptake of the vaccine, along with antivirals that may affect disease severity.

While the probability of death appeared higher among children with a SRMC the small number of overall deaths in individual studies limited further interpretation of this outcome, such as by country, which may have highlighted differences between the underlying health services. Studies reporting lower or zero deaths had increased use of antivirals. The difference in I^2 identified between outcomes is interesting. Although we found moderate to substantial heterogeneity for ICU admission and mechanical ventilation but conversely a zero I^2 for deaths is likely to reflect inconsistences across studies and CI that do not overlap for both ICU admission and mechanical ventilation. In contrast, the studies for the death outcome are less precise (wide CIs), and so disparities in the point estimates across studies are not necessarily reflected in the I^2 value, and it is possible that heterogeneity, similar to ICU admission and mechanical ventilation is also present. In terms of hospital resource use (hospital LOS, ICU LOS), we found limited data that distinguished between children with SRMC and healthy children. However, when differences in resource use were presented for both groups, it was not always in a uniform way that enabled comparison across studies. In the studies that did report a median hospital LOS, most of these studies comprised large proportions of children aged <5 years or excluded older aged children, limiting translation to the wider age group of children with SRMC.

Our review provides a comprehensive summary of the available evidence and included MEDLINE and EMBASE databases, as well as hand-searching included papers. Our resources restricted the inclusion to articles published in English only. The review is subject to the same limitations as the included studies, acknowledging the challenges of evidence synthesis and reporting of prognostic studies.[50–52] There were weaknesses related to study design, and reporting and publication bias was strongly suspected. In all but three studies, the data extracted were from secondary outcomes. Given children with SRMCs experience a higher burden of nosocomial influenza,[53] the results may not encapsulate all influenza episodes as nosocomial cases were often excluded. Additionally, there were differences between study groups and the assembly of each cohort in terms of influenza season, participant ages, country, method of influenza diagnosis and definition for SRMC; with comparisons across studies likely distorted by risk disorders not well defined. Accordingly, given the limited evidence identified, including low event numbers and quality of studies, the summary effect measures presented in this review should be interpreted with caution.

The absence of a transparent description comparing the characteristics between those with and without SRMC in studies was universal across studies, as was lack of adjustment for confounding factors such as children's age, influenza strain and vaccination status, consistent with similar reviews in this area.[19,21] Few studies contributed data on influenza vaccine uptake or antiviral use and when vaccination data were provided (often parent reported), there was uncertainty regarding receipt of the second dose of the vaccine for children (when indicated) and identifying these children was problematic. The fact that the majority of studies included a significant proportion aged <5 years is important. Given the very young are recognized as a risk group on their own and included in many official recommendations, this may have had consequences on the effect of SRMC. Additionally, vaccination may have attenuated the effect of influenza infection but not necessarily prevented hospitalization. If more children with SRMC received the vaccine (as they are recommended), then lower events for severe outcomes in this group would be expected. However, current literature suggests there is low uptake of the vaccine in children overall and for those with SRMCs.[1,54–67]

It is likely that the prognosis of influenza is determined by a number of factors, including the social climate toward both influenza and vaccination, parental expectations, health-seeking behavior, presence of SRMC or other risk factor, the level of care received and variation in influenza virulence by season. Additionally, seasons are often dominated by a particular influenza strain (A or B) or subtype such as H1 or H3, which is relevant as both B strains are not included in the Trivalent Influenza Vaccine which was the predominate vaccine available in these studies.

Despite a recommendation for children with SRMC to receive an influenza vaccination in many countries worldwide, estimates of vaccine uptake remain suboptimal.[50,51,55,61,65,66]

While the relative lack of eligible studies on seasonal influenza and clinical outcomes for these children was surprising, it was expected, given the absence of data on vaccination coverage at the population level. The implications of this review suggest an urgent need to further our understanding of the burden of influenza for children with SRMCs. This would enable clinicians and policy makers to contemplate alternative ways to improve protection and potentially reduce severity of influenza disease for these children. It would also empower clinicians to clearly communicate simple but important messages related to risk, tailor education toward a vaccination recommendation, and help improve levels of acceptance toward influenza vaccination and coverage in these children.

Ascertaining an accurate picture of complications and resource use from influenza in children with SRMCs will require well-designed studies reported with attention to the STROBE statement.[52] Notably, data collection should extend to potentially modifiable factors such age appropriate influenza vaccination status and use of antivirals. Data encompassing multiple influenza seasons powered to detect meaningful differences would help to progress further policy and clinical practice for this vulnerable group.

CONCLUSIONS

This systematic review provides a comprehensive summary of the available evidence to distinguish influenza severity, complications and hospital resource use in children with SRMC compared with healthy children. While there was evidence that ICU management and bacterial pneumonia increases in children with SRMC, evidence showing the probability of death or increased need for mechanical ventilation was inconsistent. The volume of evidence identified was limited, with major areas of weakness related to study design and reporting. Further research using large datasets should evaluate the impact of complications and associated morbidity from influenza in SRMC children. Policy-directed research to further support vaccination recommendations for clinicians and parents in this area is urgently warranted.

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Supplementary Digital Content 1

Proportion of influenza hospitalisations with SRMCs

Condition *Denotes total number of studies reporting this either as a principle group or singly as conditions that fall within this sub specialty, no study was counted twice.	**Number of Studies**	**Proportion of children with condition %**		
		Min	**Max**	**Median**
Respiratory*	18	0.8	28.3	10.3
Asthma	10	4.5	24.3	13.6
Pulmonary conditions including asthma	16	1.4	28.3	8.9
Cystic fibrosis	1	0.8	0.8	0.8
Cardiac*	18	0.1	10.6	3.6
Cardiac	17	1.5	10.6	4.0
Aspirin therapy	3	0.1	1.9	0.4
Immunological*	16	0.4	9.0	2.2
Immunosuppressive (not further described)	8	0.8	9.0	3.4
Immune deficiency (not further described)	6	1.1	4.9	2.1
Immunosuppressive[1]	4	0.4	7.9	3.1
HIV	2	0.9	1.4	1.2
Splenic dysfunction	1	2.2	2.2	2.2
Immunosuppressive medications	2	0.9	1.0	1.0
Solid organ transplant recipient (SOTR)*	2	0.3	100	0.6
Transplant (hepatic/renal/cardiac)	2	0.3	100	50.2
Bone marrow or organ transplant	1	0.6	0.6	0.6
Cancer*	6	0.3	100	3.2
Haematological: ALL	2	0.3	100	50.2
Stem Cell	1	1.8	1.8	1.8
Not specified	1	2.1	2.1	2.1
Non-Haematological: (type not reported)[2]	4	0.6	5.1	4.6
Haematological*	9	0.3	5.5	2.8
Haematological including sickle cell disease	8	0.3	5.5	3.2
Sickle cell disease	2	0.5	0.9	0.7
Anemia	2	0.5	1.6	1.1
Neurological disease*	14	0.9	16.1	4.2
Neurological / neuromuscular	13	2.1	16.1	5.3
Myotonia muscular dystrophy	1	0.9	0.9	0.9
Developmental disorder	2	4.2	4.8	4.5
Febrile seizures	1	1.0	1.0	1.0
Seizure disorder	3	2.4	4.6	4.5
Spina bifida	1	0.9	0.9	0.9
Cerebral palsy	3	1.5	2.5	2.0
Endocrine*	14	0.1	3.2	1.8
Adrenogenital syndrome	1	2.6	2.6	2.6
Metabolic including diabetes	13	0.1	3.2	1.7
Inborn error of metabolism	1	1.8	1.8	1.8
Obesity	1	0.6	0.6	0.6
Renal*	12	0.4	2.8	1.3
Renal condition	12	0.4	2.8	1.4
Genitourinary disorder	2	0.8	1.1	0.9
Gastrointestinal*	7	0.1	4.4	2.6
Gastro/hepatic condition	7	0.1	4.4	3.0
Nutritional	2	0.8	1.1	0.9
Rheumatology*	2	1.0	1.6	1.3
Prematurity*	6	0.3	14.2	4.6
Genetic*	1	2.6	6.0	4.3
Genetic (undefined)	1	6.0	6.0	6.0
Sotos syndrome	1	2.6	2.6	2.6
Unclassified*	3	0.3	0.3	3.3
Multisystem disorder syndrome	2	1.6	3.3	2.5
Severe skin disorder	1	0.5	0.5	0.5
Chronic infection	1	0.3	0.3	0.3
Concurrent acute infection	2	3.8	3.8	3.8
Other - not specified	1	4.4	4.4	4.4

Footnote: 1: these were immunoglobulin deficiency, congenital neutropenia, cancer/malignancies, congenital human immunodeficiency virus (HIV) & immunosuppressive treatment, leukaemia/lymphoma; 2: one study reported these as thalamic glioma and hepatocellular carcinoma.

Supplementary Digital Content 2

Probability of ICU admission and proportion of ICU admissions with SRMCs

Reference	Study years	Risk group	Age (years)	Number of children		Probability of ICU admission		
				Total N	SRMC n (%)	SRMC n (%)	Healthy n (%)	OR (95 % CI)
Probability of ICU admission if hospitalised - SRMCs vs 'healthy'								
Blyth (2018)	2017	AIH	≤16	1268	572(45)	113 (19.8)	71 (10.2)	2.17 (1.57-2.99)
Burton (2008)	2006-2007	NACI 2006-2007 + additional SRMC[1]	≤16	371	188 (50)	22 (11.7)	20 (10.9)	1.08 (0.57-2.05)
Chaves (2014)	2003-2012	SRMCs [2]	<1	3157	796 (25)	162 (20.4)	210 (8.9)	2.62 (2.09-3.27)
Coffin (2007)	2000-2004	ACIP 2005-2006	≤21	745	363 (49)	82 (22.6)	56 (14.7)	1.70 (1.17-2.47)
Launes (2013)	2010-2011	chronic conditions[3]	0.5-<18	143	55 (38)	5 (9.1)	15 (17.0)	0.49 (0.17-1.42)
Moore (2006)	2003-2004	chronic conditions[4]	≤18	505	212 (41)	32 (15.1)	21 (7.2)	2.30 (1.29-4.12)
PHAC (2006)	2004-2005	NACI 2004-2005 + additional SRMCs[6]	≤16	391	211(54)	33 (15.6)	15 (8.3)	2.04 (1.07-3.89)
Rojo (2006)	1996-2003	chronic conditions[5]	<3	117	48 (41)	10 (20.8)	0 (-)	-
Sam (2010)	2002-2007	ACIP 2008	<15	132	48 (36	4 (8.3)	8 (9.5)	0.86 (0.25-3.03)
Schrag (2006)	2003-2004	ACIP 2004 + neuromuscular or cognitive dysfunction	<18	1308	339 (26)	43 (12.7)	104 (10.7)	1.2 (0.83-1.77)
Probability of ICU admission if hospitalised - studies examining specific SRMC condition only								
Feldman (2017)	2004-2012	liver transplant	<18	143	143 (100)	37 (25.9)	-	-
Lee (2015)	1999-2011	ALL and other comorbidities[7]	<19	577	577 (100)	66 (10.5)	-	-
Proportion of ICU admissions with SRMCs								
Kaczmarek (2016)	1997-2013	AIH	<16	704	287 (41)	287 (40.8)	417 (59.2)	-
Spaeder (2011)	2002-2008	ACIP 2007	<18	59	36 (61)	36 (44.1)	23 (39)	-

Footnote: 1 Included neurological/ developmental disorder, genitourinary, gastrointestinal or hepatic disorder, nutritional disorder, bone joint or connective tissue disorder, multi system disorder or syndrome, relevant concurrent acute infection, prematurity, admitted within first year of life; 2: included lung and cardiovascular disease; metabolic disease; renal disease; neurologic and neuromuscular disorder; immunocompromised condition and prematurity (<37 weeks of gestation); 3: included in results as pulmonary, neurological, cardiac, renal, diabetes, immunodeficiency; 4: pulmonary disease, neurologic disease, immune deficiencies, hematologic, cardiac, gastrointestinal, malignancy, renal, endocrine/metabolic; 5: chronic lung disease, congenital heart disease, HIV, anticancer treatment, malnutrition, drepanocytosis, coeliac, mitochondrial diseases, chronic renal failure; 6: those listed at 1 and chronic infection or severe skin disorder; 7: chronic pulmonary, cardiac, neuromuscular or renal conditions.

Supplementary Digital Content 3

Probability of mechanical ventilation

Reference	Study years	Risk group	Age (years)	Number of children		Probability of mechanical ventilation		
				Total N	SRMC n (%)	SRMC n (%)	Healthy n (%)	OR (95% CI)
Probability of mechanical ventilation if hospitalised - special risk medical conditions vs 'healthy'								
Ampofo (2006)	2001-2004	ACIP 2005	≤18	325	120 (37)	9 (7.5)	18 (8.8)	0.84 (0.37-1.94)
Burton (2008)	2006-2007	NACI 2006-2007 + SRMCs[1]	≤16	371	188 (51)	12 (6.4)	8 (4.4)	1.49 (0.60-3.74)
Chaves (2014)	2003-2012	SRMCs [2]	<1	3157	796 (25)	69(8.7)	66 (2.8)	3.30 (2.33-4.67)
Coffin (2007)	2000-2004	ACIP 2005-2006	≤21	745	363 (49)	23(6.3)	9 (2.4)	2.80 (1.28-6.14)
Launes (2013)	2010-2011	chronic conditions[3]	0.5 - <18	143	55 (38)	5(9.1)	15 (17.0)	0.49 (0.17-1.42)
Moore (2006)	2003-2004	chronic conditions[4]	≤18	505	212(42)	(5.5)	(7.1)	-
PHAC (2006)	2004-2005	NACI 2004-2005 + SRMCs[7]	≤16	391	211 (54)	14 (6.6)	11 (6.1)	1.09 (0.48-2.47)
Sam (2010)	2002-2007	ACIP 2008	<15	132	48 (36)	4 (8.3)	8 (9.5)	0.86 (0.25-3.03)
Spaeder (2011)	2002-2008	ACIP 2007	<18	59	36 (61)	16(44.4)	8 (34.8)	1.50 (0.51-4.42)
Serwint (1991)	1988-1989	ACIP 1988	≤19	99	43 (43)	4(9.3)	1 (2.0)	5.64 (0.61-52.43)
Suntarattiwong (2007)	2004-2005	"underlying diseases"[5]	<5	39	8 (20)	1 (12.5)	1 (3.2)	4.29 (0.24-77.22)
Probability of mechanical ventilation if hospitalised - studies examining specific SRMC condition only								
Feldman (2017)	2004-2012	liver transplant	<18	143	143 (100)	29 (20.3)	-	-

Footnote: 1 Included neurological/ developmental disorder, genitourinary, gastrointestinal or hepatic disorder, nutritional disorder, bone joint or connective tissue disorder, multi system disorder or syndrome, relevant concurrent acute infection, prematurity, admitted within first year of life; 2: included lung and cardiovascular disease; metabolic disease; renal disease; neurologic and neuromuscular disorder; immunocompromised condition and prematurity (<37 weeks of gestation); 3: included as pulmonary, neurological, cardiac, renal, diabetes, immunodeficiency; 4: pulmonary disease, neurologic disease, immune deficiencies, hematologic, cardiac, gastrointestinal, malignancy, renal, endocrine/metabolic; 5: Not clearly defined but included: asthma, CP, ventricular septal defect, adrenogential syndrome, Sotos syndrome; 6: those listed at 1 and chronic infection or severe skin disorder.

Supplementary Digital Content 4

Hospital and ICU Length of Stay

Reference	Risk group	Sub group	LOS Risk Group	LOS Healthy
			Mean days; Median days (IQR)	Mean (days); Median days (IQR)
Studies reporting median hospital LOS				
Ampofo (2006)	ACIP 2005	6-23 months	Mean 4.69; Median 3 (2.0-6.5)	Mean 3.01; Median 2.0 (2.0-4.0)
		>2 years	Mean 5.83; Median 3.0 (2.0-6.0)	Mean 3.62; Median 2.0 (1.0-5.0)
Burton (2008)	NACI 2006-2007		Median 4.5	Median 2
	Additional SRMCs[1]		Median 3.5	_
Chaves (2014)	SRMCs [2]	< 3 months	Median 3(2-5)	Median 2(1-3)
		>3 to 6 months	Median 3(2-6)	Median 2(1-3)
		>6 to <12 months	Median 2(1-4)	Median 2(1-3)
Launes (2013)	chronic conditions[3]		Median 6.5 (IQR 4-10)	Median 6.0 (IQR 4-11)
Studies reporting mean hospital LOS				
Hassan (2009)	ACIP 2002/2003	Asthma	Mean 2.9	Mean 2.5
		Non-asthma SRMC	Mean 4.8	_
Ipp (2003)	NACI 2002		Mean 8.6	Mean 4.9
Moore (2006)	chronic conditions[4]		Mean 7.4	Mean 3.7
PHAC (2006)	NACI 2004-2005		Mean 5.5 (range 1-34)	Mean 3.1 (range 1-20)
	Additional SRMCs[5]		Mean 4.9 (range 1-20)	_
Sam (2010)	ACIP 2008		Mean 9.3	Mean 4.4
Studies reporting prolonged hospital LOS				
Blyth (2018)	AIH		aRR 1.75 (1.44-2.11) prolonged LOS[6]	
Coffin (2007)	ACIP 2005-2006		59/363(16%) LOS >6 days	31/382(8%) LOS >6 days
Serwint (1991)	ACIP 1988		19/43(44%) LOS >14 days	6/56(11%) LOS > 14 days
Single SRMC studies reporting hospital LOS				
Feldman (2017)	liver transplant		Mean 21; Median 4	NA
Lee (2015)	ALL + comorbidities[7]		Mean 8.9 (SD 13.5)	NA
Studies reporting ICU LOS				
Kaczmarek (2016)	AIH		Mean 7.1 (SD 9.7)	Mean 5.0 (SD 7.5)

Footnote: 1 Included neurological/ developmental disorder, genitourinary, gastrointestinal or hepatic disorder, nutritional disorder, bone joint or connective tissue disorder, multi system disorder or syndrome, relevant concurrent acute infection, prematurity, admitted within first year of life; 2: included lung and cardiovascular disease; metabolic disease; renal disease; neurologic and neuromuscular disorder; immunocompromised condition and prematurity (<37 weeks of gestation); 3: included in results as pulmonary, neurological, cardiac, renal, diabetes, immunodeficiency; 4: pulmonary disease, neurologic disease, immune deficiencies, hematologic, cardiac, gastrointestinal, malignancy, renal, endocrine/metabolic; 5: those listed at 1 and chronic infection or severe skin disorder; 6: aRR (adjusted rate ratio)- adjusted for indigeneity, ICU admission and antiviral use) for prolonged LOS using negative binomial regression; 7: chronic pulmonary, cardiac, neuromuscular or renal conditions; AIH: Australian Immunisation Handbook; SD: standard deviation.

Supplementary Digital Content 5

Probability of death

Reference	Study years	Risk group	Age (years)	Number of children		Probability of death		
				Total N	SRMC n (%)	SRMC n(%)	Healthy n(%)	OR (95% CI)
Probability of death if hospitalised - special medical risk conditions vs 'healthy'								
Ampofo (2006)	2001-2004	ACIP 2005	≤18	325	120 (37)	1 (0.8)	1 (0.5)	1.71 (0.11-27.66)
Blyth (2018)	2017	AIH	≤16	1268	572 (45)	3(0.5)	2(0.3)	0.55 (0.09-3.28)
Burton (2008)	2006-2007	NACI 2006-2007 + SRMC[1]	≤16	371	188 (51)	1 (0.5)	1 (0.5)	0.97 (0.06-15.68)
Chaves (2014)	2003-2012	HRMCs [2]	<1	3157	796 (25)	2 (0.2)	6 (0.2)	0.99 (0.20-4.91)
Coffin (2007)	2000-2004	ACIP 2005-2006	≤21	745	363 (49)	3 (0.8)	2 (0.5)	1.58 (0.26-9.53)
Dawood (2010)	2003-2008	ACIP 2007	<18	4015	1894 (47)	9 (0.5)	8 (0.4)	1.26 (0.49-3.28)
Launes (2013)	2010-2011	chronic conditions[3]	0.5 - <18	143	55 (38)	0 (0)	0 (0)	-
Leung (2014)	2009-2011	ACIP 2009	≤18	917	257 (28)	0 (0)	0 (0)	-
Moore (2006)	2003-2004	chronic conditions[5]	≤18	505	212 (41)	2 (0.9)	1 (0.3)	2.78 (0.25-30.87)
PHAC (2006)	2004-2005	NACI 2004-2005 + SRMC8	≤16	391	211 (54)	2(0.9)	0(0)	-
Punpanich (2014)	2010	ACIP 2010	≤18	289	41 (14)	2 (4.9)	0 (0)	-
Rojo (2006)	1996-2003	chronic conditions [6]	<3	117	48 (41)	0 (0)	9 (9)	-
Sam (2010)	2002-2007	ACIP 2008	<15	132	48 (36)	2 (4.2)	1 (1.2)	3.61 (0.32-40.88)
Serwint (1991)	1988-1989	ACIP 1988	≤19	99	43 (43)	2 (4.6)	1 (1.8)	2.68 (0.24-30.61)
Suntarattiwong (2007)	2004-2005	"underlying diseases"[7]	<5	39	8 (20)	0 (0)	0 (0)	-
Probability of death if hospitalised - studies examining specific SRMC condition only								
Feldman (2017)	2004-2012	liver transplant	<18	143	143 (100)	3 (2.1)	-	-
Lee (2015)	1999-2011	ALL + comorbidities[9]	<19	577	577 (100)	9 (1.43)	-	-
Probability of death – studies of ICU admissions only								
Kaczmarek (2016)	1997-2013	AIH	<16	704	287 (41)	13 (4.5)	14 (3.4)	1.36 (0.40-4.65)
Spaeder (2011)	2002-2008	ACIP 2007	<18	59	36 (61)	0 (0)	4 (17.4)	-

Footnote: 1 Included neurological/ developmental disorder, genitourinary, gastrointestinal or hepatic disorder, nutritional disorder, bone joint or connective tissue disorder, multi system disorder or syndrome, relevant concurrent acute infection, prematurity, admitted within first year of life; 2: included lung and cardiovascular disease; metabolic disease; renal disease; neurologic and neuromuscular disorder; immunocompromised condition and prematurity (<37 weeks of gestation); 3: included in results as pulmonary, neurological, cardiac, renal, diabetes, immunodeficiency; 5: pulmonary disease, neurologic disease, immune deficiencies, hematologic, cardiac, gastrointestinal, malignancy, renal, endocrine/metabolic; 6: chronic lung disease, congenital heart disease, HIV, anticancer treatment, malnutrition, drepanocytosis, coeliac, mitochondrial diseases, chronic renal failure; 7: Not clearly defined but included: asthma, CP, ventricular septal defect, adrenogential syndrome, Sotos syndrome; 8 : those listed at 1 and chronic infection or severe skin disorder; 9: chronic pulmonary, cardiac, neuromuscular or renal condition.

CHAPTER 4 COVERAGE AND VALIDATION - INFLUENZA VACCINATION IN CHILDREN WITH SRMC

4.1 LITERATURE REVIEW

4.1.1. The Influenza Vaccine

Influenza is a constantly evolving single-stranded RNA orthomyxovirus of which there are four antigenic types: A, B, C and D. (4, 96-98) Most often it is only influenza types A and B that lead to severe disease in humans, with influenza type C generally causing mild illness and type D primarily affecting cattle and not known to infect or cause illness in people. (4, 96-100) While Influenza A viruses are further divided into numerous subtypes based on virus surface proteins, influenza B viruses is only grouped into two lineages: B/Yamagata and B/Victoria.(4, 101)

Two influenza vaccines are available in Australia: quadrivalent and trivalent influenza vaccines.(4) These are based on the number of Influenza A virus subtypes and number of influenza B lineages included. Inactivated quadrivalent influenza vaccines have been in widespread use in Australia since 2016 (registered since 2014) and contain 4 influenza virus strains (2 influenza A subtypes and 2 influenza B lineages). (4) In contrast, inactivated trivalent influenza vaccines have been used since the 1970s and contain 3 influenza virus strains (2 influenza A subtypes and 1 influenza B lineage).(4) The only difference in strains contained in the vaccine each year between the quadrivalent and trivalent vaccine is the additional influenza B lineage. Infants and children benefit most from the broader protection from the inclusion of a second B virus strain in quadrivalent influenza vaccines due to a higher influenza B disease burden compared to older adults. (101, 102) More recently, additional formulations of trivalent

influenza vaccines, so called ‘enhanced trivalent influenza vaccines’ have become available for use in adults aged ≥65 years. (4)

Current Australian and international guidelines including the UK, USA, Canada and WHO (4, 60, 98, 103, 104) only recommend the vaccine from 6 months of age as there is no vaccine that protects against seasonal influenza for children <6 months of age. (105) Additionally, while young children can obtain similar levels of protection through vaccination to older children and adults, young children (<9 years) are considered immunologically naive to all strains of influenza and require 2 doses of the influenza vaccine when immunised for the first time, in order to maximise the immune response to all vaccine strains.(4)

Unlike any other vaccine on the NIP the seasonal influenza vaccine is required to be administered annually. This is because the surface antigens of influenza A and B viruses change constantly through small stepwise mutations; with influenza A viruses changing more rapidly than influenza B viruses. (106, 107) These accumulative changes in influenza antigens is called antigenic drift. (107, 108) While prior natural infection and vaccination can reduce likelihood of infection, antibodies produced against one influenza virus type or subtype offer little to no protection against another type or subtype and antigenic drift is the reason a new vaccine formulation is required each season. (4, 109) The Australian Influenza Vaccine Committee determines the formulation of influenza vaccines for use in Australia each year. This is based on recommendations from the WHO and information including data related to epidemiology, antigenic and genetic characteristics of recent influenza isolates circulating in Australia and the Southern Hemisphere, serological responses to the previous year’s vaccine and the availability of candidate vaccines viruses and

reagents.(110) Annual seasonal influenza statements containing advice on the use of influenza vaccines in Australia, including the vaccines registered by the Therapeutic Goods Administration and indicated ages for each vaccine are published by The Australian Technical Advisory Group on Immunisation (ATAGI).

4.1.2. Influenza Vaccine Safety and Effectiveness

While there is limited information available on the vaccine effectiveness (VE) for children aged less than two years, a recent West Australian study using a test negative study design found VE against laboratory confirmed influenza in all children to be 64.7%; those aged <2 years 85.8% and children ≥ 2 years to be 52%. (28) In slightly older children influenza VE varies significantly from years when there is good vaccine match to the circulating strain to years when there is a poor match. In healthy children, a systematic review in children aged from 6 months to 71 months found vaccine effectiveness against laboratory confirmed influenza to be between 60-85% for good years and 0-60% for years when there was poor match. (111) A study conducted in China showed VE against laboratory confirmed influenza to be 67% (95% CI 58-74%) for children aged 8 months to 6 years old. It also showed VE to be significantly higher in those children who were fully vaccinated children (73%) compared to partially vaccinated children (55%).(112) Additionally, influenza vaccination has been shown to be cost-effective in pre-school children and in children with SRMC (aged <15 years). (113, 114)

The influenza vaccine is safe (115), despite adverse events in children occurring in 2010 in Australia related to manufacturing issues of the bioCSL influenza 'Fluvax' vaccine.(116) This specific influenza vaccine was taken off the market, but did impact significantly on vaccine confidence.(117, 118) There is now annual, real-time monitoring

of influenza vaccines via AusVaxSafety, a prospective active surveillance system established in 2014, to monitor adverse events following immunisation with influenza vaccines in Australian children. (119, 120) Prior to this, a 2013 Australian prospective active surveillance of influenza vaccine safety study of children (aged 6 months to <10 years) (n=981) found a low proportion (5.5%–6.5%) had fever after vaccination and that any injection site or systemic reactions experienced were generally mild. (121) Of interest, 484 children (54.2%) had at least one medical condition and were recommended to receive the influenza vaccine in Australia. (121) More recent 2017 AusVaxSafety data show that the proportion of children aged 6 months to < 5 years experiencing fever or any adverse event following influenza vaccination was 2.3% and 8.4%, respectively. (122) These proportions were lower in children aged ≥5 to 14 years, with 1.3% experiencing fever and 6.7% experiencing any adverse event following influenza vaccination. (122)

4.1.3. Influenza Vaccine Recommendation for Children with SRMC

Globally, it is increasingly recognised that young children (< 5 years of age) have rates of serious illness and death similar to those aged ≥65 years and since 2012 the WHO has strongly recommended influenza vaccination for all individuals ≥6 months.(123, 124) Many countries currently include children amongst the groups targeted to receive the influenza vaccine. Several countries including New Zealand and most European Union countries such as Spain and Italy recommend and provide the vaccine to individuals > 6 months with SRMC. (29, 125-127) In the USA the Advisory Committee on Immunisation Practices (ACIP) has recommended at risk children (aged >6 months) to receive the influenza vaccine since 1965 which was extended to all children in 2003.(128) Several other countries including the UK, Finland, Estonia, Finland, Latvia, Poland, Slovakia and Slovenia and Canada also recommend the vaccine to young children.(127)

The seasonal influenza vaccination has been recommended in Australia through the National Immunisation Program (NIP) for all persons over 6 months of age considered at increased risk of influenza disease or complications since 1991.(19) Initially the vaccine was subsided under the Pharmaceutical Benefits Scheme (PBS) becoming fully funded (free) in 2010. (4, 19) It has also been recommended but not funded for all children (aged 6 months – 5 years) since 2013. Aboriginal or Torres Strait Islander children are recommended to receive the influenza vaccine and fully funded from ≥6 months – 5 years, with the 10-15 year old age group funded since 2015 and as of 2019, all Aboriginal or Torres Strait Islander peoples are fully funded to receive the influenza vaccine. (19, 60) However, there are little data about vaccine uptake specifically in children with SRMC and the seasonal influenza vaccine is not routinely recorded on the Australian Immunisation Register (AIR).

4.1.4. Uptake of Routine Vaccinations

Assessing uptake of routine vaccinations in children with SRMCs is problematic. In Australia there is no one database or registry that collects information on SRMC and accessing vaccination uptake in these children has relied on data collection. It has been suggested that parents of these children may be more hesitant to vaccinate or delay vaccinations due to fear of side effects or further complicating their child's existing condition.(82) Internationally there is a scarcity of information on uptake of routine vaccinations in children with SRMC and at the time of commencing candidature no studies from Australia. What evidence exists suggests uptake is lower and delayed in these children. A study from Italy (n=275) showed routine immunisations in children with SRMC at 12 months was poor at around 35% and at 24 months of age MMR was 62.4%. Uptake was lower as age increased however there was no comparison to

uptake for healthy children. (129) The study considered the greatest barrier against vaccine uptake to be concurrent disease or acute pathology preventing immunisations. A Swiss study found children with neurological deficits were delayed for the 3rd dose of DTP (Diphtheria 89% versus 97%; tetanus 91% versus 98%; pertussis 71% versus 89%) and 2nd + 3rd Hib doses (2nd dose 80% versus 88% and 3rd dose 69% versus 82%)(130) However the study was limited in size. No studies from Australia have examined delays and timeliness of routine vaccinations in children with SRMCs.

4.1.5. Uptake of the Influenza Vaccine

Despite high levels of evidence for the recommendation for children with SRMC to receive the influenza vaccine, uptake remains low. Influenza vaccine coverage amongst the different categories of SRMC is variable. Studies from the USA report overall coverage for children with SRMCs ranging from 8 to 52 %. (123, 131-133) In Europe coverage varies; Italy 5 to 60%; France (in children with cystic fibrosis) 86%; Israel 30%; Turkey 45.7%; Spain 19 to 27%. (29, 30, 32, 35, 123, 125, 129, 131, 132, 134-136) There is little published data on influenza vaccine uptake in Australian children with most studies undertaken prior to the 2009/2010 pandemic and in response to the influenza vaccine adverse events that occurred in 2010. It is estimated that less than 10% of children overall receive seasonal influenza vaccine each year. One study that examined hospitalised cases of influenza in children less than 5 years of age in New South Wales found vaccination against influenza to be 3.5%. (24) Another study, also from New South Wales in 2007 (n=122) of hospitalised cases of influenza found only 1 child to have documented influenza vaccination. (25) An informal survey (n=74) in 2004-2005 of SRMC paediatric patients at a tertiary paediatric hospital in Sydney, found coverage to be 42%. (26) This figure was supported by a more recent study also from Sydney, that found coverage in children with SRMC to be 41%.(27) In contrast, the

West Australian Influenza Vaccine Effectiveness (WAIVE) study, that was examining influenza VE in hospitalised children, found coverage in children with a SRMC to be 30.1%. (28) It should be noted that Western Australia introduced free seasonal influenza for all children aged ≥ 6 months to < 5 years in 2008, following several influenza related deaths in young children.(117, 137)

4.1.6. Barriers and Facilitators of Influenza Vaccination Receipt

Explanations often provided for the poor uptake of the influenza vaccine from parents of children with SRMC comprise: lack of awareness about recommendations, lack of information, not identifying children as being at risk, fear of the vaccine/side effects, inconvenience, lack of perceived severity of influenza, advised against receiving it, negative social influences, need for a priming dose in children < 9-10 years and perceived low efficacy of the vaccine. (27, 29-36) The majority of these studies were undertaken overseas; three in Italy, three in the USA, one in Israel and only one from Australia. While the study from Australia was undertaken in 2012, the small sample size (n=121) of children with SRMC may limit the generalisability of its findings. Several studies have attempted to determine the predictors of influenza vaccination uptake for these children, with a high number of studies reporting physician or a healthcare professional's recommendation being a significant predictor of uptake. (30, 33, 34, 132, 138) It has also been found that children are more likely to receive the vaccine if: parents have adequate awareness and knowledge, believe in the vaccine and that it is effective, believe it is safe, easy to access, children are younger in age (<6 years), previous vaccination, have more than one SRMC and that parents or relatives believe it is necessary along with positive social influences. (30, 33-35, 135, 138) The impact of social influences is supported by a large systematic review (139) on determinants of hesitancy towards childhood vaccines (for children <7 years) which found that,

encouragement in any form was a facilitator in all studies in which immunisation as a social norm was identified, suggesting that social and professional support of vaccination to be an important explanatory factor for uptake. Pearce et al., using data from the Longitudinal Study of Australian Children found that amongst mothers who did not disagree with immunisation, child health concerns such as above average medical needs was one of five barrier classes identified and had an elevated risk of incomplete immunisation.(140) Finally, Nakamura et al., who accessed influenza vaccination in adolescents with SRMCs over four years, found that adolescents aged 11-13 years were significantly more likely to be vaccinated than those aged 14-17 years and suggested that parents may have a greater influence on the health behaviours of younger adolescents. (131)

This chapter aims to answer two research questions:

- What is the uptake of the influenza vaccine in children with SRMCs and what characteristics are associated with receipt of the influenza vaccine? (Paper 2 in Section 4.2)
- How valid is parent reported receipt of influenza vaccination in children with SRMC and what is the level of reporting to the AIR? (Paper 3 in Section 4.3)

The next two sections report the results and data obtained from a face-to-face survey. The first survey collected as part of Project 1 interviewed parents (of children with SRMC) and collected information about their child's medical conditions and previous influenza vaccinations. It also sought permission to confirm vaccination status with their child's immunisation provider as well as access medical records and the AIR and answered the first and second research questions. Literature reviews relevant to each question are summarised in the associated publication.

4.2 INFLUENZA VACCINATION COVERAGE

Influenza vaccination and characteristics associated with uptake were evaluated in a cross-sectional survey with parents of children with a SRMC attending the Women's and Children's Hospital (WCH). Convenience sampling was used to recruit participants from September 2015 to February 2016, with 410 participants providing complete data to answer this research question. Influenza vaccination was verified with providers, the WCH and AIR. Characteristics associated with uptake were explored using univariable and multivariable analyses. While confirmed influenza vaccination was modest, provision of a recommendation from a paediatric specialist was strongly associated with vaccine uptake. The resulting publication entitled "Influenza vaccination: Uptake and associations in a cross-sectional study of children with special risk medical conditions", was published in the journal "Vaccine".

In any population understanding the key influencers to vaccination is key and although HCP recommendation is long established as a critical driver to vaccination receipt, understanding the patterns of care and the context in which parents want to be provided preventative care information, provides valuable insight into parental preferences for how this information should be delivered. The parental preference for receiving the influenza vaccine recommendation from a specialist compared to a GP was also confirmed in a later study published by Norman et al (2019) (141) also in the Australian context. This section concludes theme 2 (Coverage and Validation) of this thesis which related to determining seasonal influenza vaccination coverage of children identified at increased risk and exploring the characteristics associated with receipt. Describing the reasons for low coverage was instrumental in shaping the approach used in theme 4, particularly the interview guide and survey for medical professionals and additionally as useful when triangulating the results of community study (theme 3: parental awareness).

4.2.1. Statement of Authorship

Statement of Authorship

Title of Paper	Uptake and associations in a cross-sectional study of children with special risk medical conditions.
Publication Status	☑ Published ☐ Accepted for Publication ☐ Submitted for Publication ☐ Unpublished and Unsubmitted w ork w ritten in manuscript style
Publication Details	Tuckerman J, Misan S, Salih S, Joseph Xavier B, Crawford NW, Lynch J, Marshall HS. Influenza vaccination: Uptake and associations in a cross-sectional study of children with special risk medical conditions. Vaccine. 2018 Dec 18;36(52):8138-8147.

Principal Author

Name of Principal Author (Candidate)	Jane Tuckerman
Contribution to the Paper	JT contributed to the study design, collected and analysed the data, prepared the first draft of the manuscript.
Overall percentage (%)	80%
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 18 Dec 2019

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.

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Signature		Date	14/12/2019

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Contribution to the Paper	JL contributed to study design, statistical analysis interpretation and critically reviewed the manuscript.		
Signature		Date	11/12/19

Name of Co-Author	Helen Marshall		
Contribution to the Paper	HM contributed to study design, statistical analysis interpretation and critical review of the manuscript.		
Signature		Date	12 Dec 2019

4.2.2. Publication

Vaccine 36 (2018) 8138–8147

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Influenza vaccination: Uptake and associations in a cross-sectional study of children with special risk medical conditions

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ARTICLE INFO

Article history:
Received 8 May 2018
Received in revised form 17 September 2018
Accepted 18 September 2018
Available online 16 November 2018

Keywords:
Influenza
Children
Special risk medical condition
Vaccination
Facilitators
Recommendation

ABSTRACT

Objective: To determine uptake of influenza vaccination in children with special risk medical conditions (SRMC) and to explore associations with vaccination.
Design: Cross-sectional study.
Setting/participants: Parents of children with a SRMC attending either outpatient department clinics or being an inpatient at the Women's and Children's Hospital (WCH), Adelaide, Australia from September 2015 to February 2016 were recruited using convenience sampling.
Methods: Data were collected using a face-to-face survey. Influenza vaccination was verified with providers. Characteristics associated with uptake were explored using univariable and multivariable analyses.
Results: There were 410 participants with complete data. Confirmed influenza vaccination at least once in the last two years was 50%, annual uptake was 32.8%. 63.9% of parents were aware of the vaccination recommendation and 57.9% had been recommended by a specialist or general practitioner (GP). Characteristics strongly associated with uptake included: receiving a recommendation from a specialist or GP and having a parent receive the influenza vaccine annually.
Conclusions: Despite a long standing funded program, influenza vaccination uptake in children with SRMC is suboptimal. Parental vaccination behaviour, along with medical practitioner recommendation, particularly specialist recommendation, appear to be key influences in facilitating vaccination. Potential interventions could target the family rather than just the individual child. Understanding the barriers to recommendation from the perspective of general medical practitioners and specialists who treat these children is needed.

1. Introduction

Influenza is a serious disease, with seasonal peaks contributing to large numbers of hospitalisations, associated morbidity and mortality worldwide [1–3]. Numerous medical conditions increase an individual's risk of acquiring influenza infection or developing serious complications, including lung and cardiac diseases, neurological disorders, low immunity and other conditions that require regular medical follow-up or hospitalisation such as diabetes [4]. Influenza vaccination is the single most important measure to

Abbreviations: AIR, Australian Immunisation Register; CI, Confidence Interval; GP, general practitioner; HCP, Healthcare Provider; NIP, National Immunisation Program; OR, Odds Ratio; SRMC, special risk medical condition; WCH, Women's and Children's Hospital.

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https://doi.org/10.1016/j.vaccine.2018.09.039
0264-410X/

prevent or attenuate infection and prevent mortality. Several countries recommend the seasonal influenza vaccine annually for children with special risk medical conditions (SRMC) [5–7]. In Australia, SRMCs are defined in the Australian Immunisation Handbook [4] based on recommendations of the Australian Technical Advisory Group on Immunisation and approved by the National Health and Medical Research Council [8]. Individuals with these conditions have been funded under Australia's National Immunisation Program (NIP) to receive the vaccine annually since 2010 [8] with the National Seasonal Influenza Vaccination Program (NSIVP) generally commencing in the first month of autumn each year. However, the seasonal influenza vaccine is not routinely recorded on the Australian Immunisation Register (AIR) and consequently, there is little data about vaccine coverage, including in children with SMRC.

Most studies reporting influenza vaccine coverage in Australian children were prior to the 2009/2010 pandemic and serious adverse events that occurred in 2010 with use of the BioCSL Fluvax vaccine [9,10]. Two recent studies, both from New South Wales in children with SRMC, estimated coverage to be 41–42% [11,12]. In contrast, a study of hospitalised children in Western Australia, found coverage with a SRMC to be 30.1% [13]. Western Australia implemented a funded influenza vaccine program for children <6 years of age in 2010, with all other states commencing a similar program in 2018.

Besides reporting on coverage, understanding facilitators associated with uptake is useful in order to tailor vaccination recommendations, identify program weaknesses and guide policy changes. Studies from overseas [14–19] and Australia [12] suggest that provider recommendation is critical to uptake.

Current recommendations are for children aged 6 months to <9 years receiving influenza vaccine for the first time to receive 2 doses in the first year to maximise the immune response to the vaccine [4]. The upper age limit was <10 years of age until March 2015 [20]. However, there is limited data on adherence to this recommendation. A coverage report suggests that only half of the children aged <5 years with a first documented dose on the AIR also received their second dose in the same year [21].

The objectives of this study were to determine levels of influenza vaccination uptake in children with SRMC, and to explore characteristics associated with receipt of the influenza vaccine in children with SRMCs.

2. Methods

2.1. Study design

This was an observational cross-sectional study reported with consideration of the STROBE statement [22].

2.2. Study setting

The study population was recruited from September 2015 to February 2016 at The Women's and Children's Hospital (WCH), the major provider of tertiary paediatric healthcare services in South Australia.

2.3. Study recruitment

Parents or guardians, referred to hereafter as parents, of children with a SRMC attending clinics in the outpatient's department or current inpatients on three wards at the WCH were eligible for enrolment and were recruited using convenience sampling. Clinics covered the subspecialties of pulmonary medicine, renal, endocrinology, neurology, cardiology, rheumatology, gastroenterology, general medicine and the home enteral nutrition service. The three hospital wards approached cared for children aged from 12 months to <18 years.

A child was included in the study provided they were eligible to receive the vaccine at least once in the last two years. A child qualified for influenza vaccination in either of the previous two years (2014 or 2015) if they were aged ≥6 months and diagnosed with a SRMC before December 31st of that year. A child's data were included only once in the study. If multiple children of the same family were eligible, the eldest child was enrolled. Other exclusion criteria included: age ≥18 years or ≤6 months on recruitment day; absence of a SRMC according to the Australian Immunisation Handbook [4]; having a parent unable to provide written informed consent nor understand English without a translator.

2.4. Parental survey questionnaire

Following written consent from parents, a predominately closed-ended questionnaire was administered face-to-face in the clinic waiting area or hospital ward. Questionnaire items were based on adapted concepts from the Health Belief Model [23] and Protection Motivation Theory [23] in conjunction with existing evidence [12,15,24], representing perceived threat of influenza, perceived knowledge of the vaccine, self-efficacy and items assessing healthcare practices. Questions related to knowledge were asked directly. For example, "...did you know the flu vaccine is recommended for children aged >6 months with certain medical conditions? (yes, no). Attitudes towards the seriousness of influenza infection were asked on a scale of 0–10, while respondents indicated their level of agreement with attitudes toward healthcare worker (HCW) vaccination on a five-point Likert scale (strongly agree to strongly disagree) as well as views on their child's health status, "How is your child's health generally? (five options from excellent to poor). Parents whose child had never had the vaccine or who had it less than once in the last two years were asked to report their reasons using free-text ('What was the reason for not getting the influenza vaccine for your child or not getting it this year?'). To determine influenza vaccination status we obtained details of the child's immunisation provider for 2014 and 2015 along with their current primary healthcare provider (HCP). In some cases details for current HCPs were provided as the name of a medical practice only, while others supplied the name of a specific general medical practitioner (GP) (Family Physician).

2.5. Medical 'at risk' status

Medical case notes were reviewed to confirm parental report of a child's risk status. All SRMCs, including the diagnosis date, identified in the medical case notes were recorded using a data collection form. Uncertainty regarding eligibility was discussed with paediatric specialists.

2.6. Influenza vaccination status

Confirmed influenza vaccination was defined as receipt of at least one dose of the vaccine verified by the child's immunisation provider, the AIR, WCH influenza database or current HCP. When contacting immunisation providers (GPs and medical practices, pharmacies (drug stores), councils, travel health clinics, hospitals) four attempts were made before recording as unable to confirm. Vaccination status data for individual years were used to determine and create the variable, 'received the vaccine at least once in the last two years'.

For children with previous influenza vaccine receipt, parents were asked the child's age at first receipt and whether two doses were administered in that year.

2.7. Statistical analysis

A sample size of 451 respondents was determined by the population proportion of children with a SRMC who received the influenza vaccine with a precision estimate of ±4% and 95% confidence, based on an estimate of 25% uptake. Descriptive and inferential statistics were used to analyse data. Open ended questions were coded using content analysis. Although a number of potential response options were identified prior to the survey (these were not shown to participants), additional responses were coded and grouped into categories. Characteristics associated with a child receiving the influenza vaccine at least once in the last two years was explored in sequential multivariable logistic regression models. We included all individual variables that had been collected, grouped together in blocks. These variable blocks represent different constructs that may be important in understanding vaccination uptake. This enabled an understanding of each block's role in explaining influenza vaccination status. Five blocks of explanatory variables were entered: demographic variables, child health status, health service use, parental knowledge/attitudes and receiving a specialist or GP recommendation. Odds ratios (OR) were presented with their 95% confidence intervals (CI). In this paper we present the crude versus final model that includes all variable blocks. Supplementary Table 6 shows the addition of each block of variables.

Furthermore, we examined if there was any difference in the characteristics associated with receiving the influenza vaccine either: never, once only or in both of the last two years, using identical successive multinominal regression models. There was no evidence that suggested exploring characteristics in this way provided any additional insight (results not presented). Stata (Version 14.1) was used for all statistical analyses (StataCorp, Texas, USA). The study was approved by the Women's and Children's Health Network Human Research Ethics Committee.

3. Results

3.1. Study population

Approximately 10% of parents who were approached were ineligible or declined participation. Due to logistical reasons, we did not record numbers of those who were approached and declined or were ineligible at initial screening. Fig. 1 shows detailed information on study recruitment. A total of 443 parents completed the survey. Given less than 2% (n = 8) of children were inpatients at enrolment, all with previous hospital outpatient appointments and that 92.7% of our total sample were previously hospitalized, we combined those recruited from outpatient and inpatient settings for analysis. Influenza vaccination status was confirmed with providers for 93% of children with parental report substituted for the remainder. Validation of risk status was determined for all participants. Differences in eligibility due to the vaccine's licensed lower age limit and date of medical condition diagnosis left a final cohort of 410 children eligible in 2015 and 380 eligible in 2014; 410 were eligible to receive the vaccine at least once.

3.2. Study demographics

At the time of the survey, children's ages ranged from 11 months to 17.9 years (median 10.8 years) (Table 1). Marginally

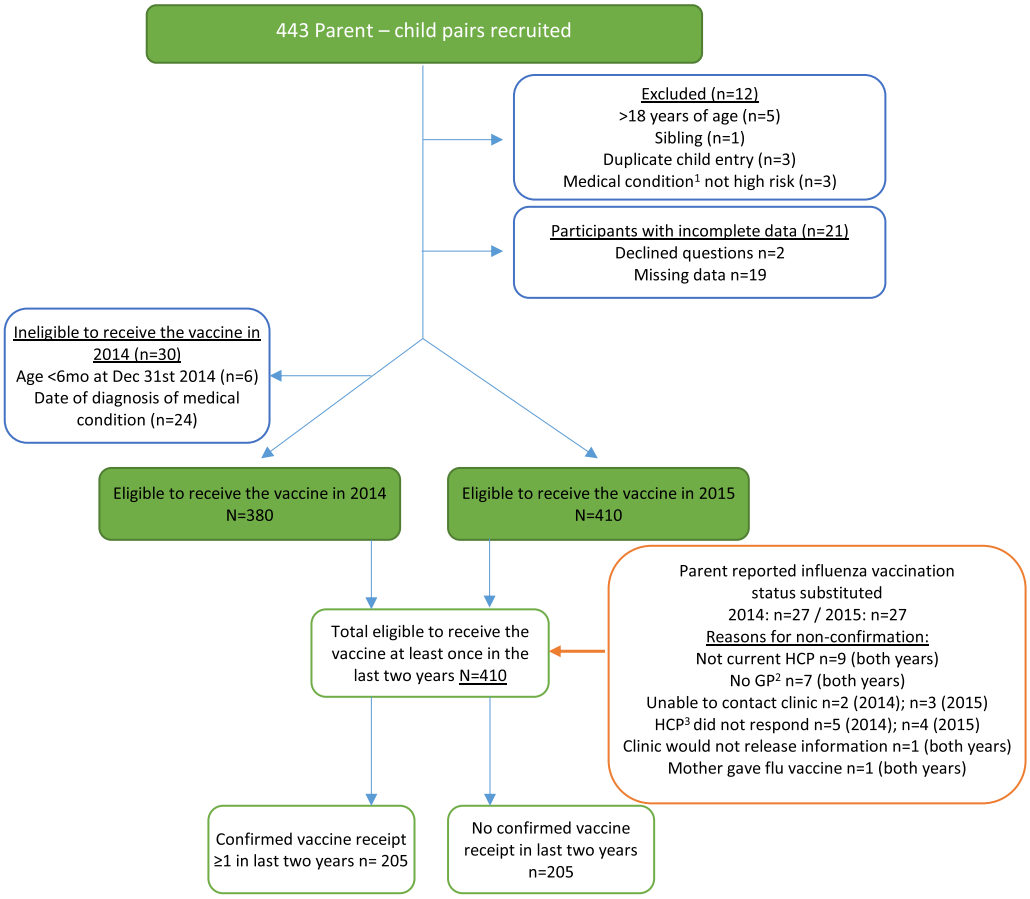

Fig. 1. Study recruitment. 1: Medical conditions: migraines, chronic osteomyelitis and seizure; 2: general practitioner (GP); 3: Healthcare provider (HCP).

Table 1
Demographic characteristics of eligible respondents and those with complete data.

Characteristic	Level	Eligible participants n = 431 n (%)	Participants with complete data n = 410 n (%)
Age of parent (years)	18–30	30 (7)	30 (7.3)
	31–40	152 (35.3)	146 (35.6)
	41–50	209 (48.5)	196 (47.8)
	>50	40 (9.3)	38 (9.3)
Place of residence	Metropolitan	320 (74.2)	306 (74.6)
	Rural[a]	111 (25.8)	104 (25.4)
Relationship to child	Mother	354 (82.1)	337 (82.2)
	Father	68 (15.8)	65 (15.9)
	Legal Guardian	9 (2.1)	8 (2)
Parents employment status	Full time employed	131 (30.4)	122 (29.8)
	Part time employed	115 (26.7)	106 (25.9)
	Casual	45 (10.4)	45 (11)
	Not working	140 (32.5)	137 (33.4)
Highest education level	High school or less	147 (34.1)	138 (33.7)
	Certificate or Diploma	164 (38.1)	158 (38.5)
	Bachelor	84 (19.5)	79 (19.3)
	Post Graduate	36 (8.3)	35 (8.5)
Member of household smoker		89 (20.6)	84 (20.5)
Born in Australia		360 (83.5)	347 (84.6)
English is not first language		27 (6.3)	25 (6.1)
Gender of child	Female	204 (47.3)	191 (46.6)
	Male	227 (52.7)	219 (53.4)
Child's health status (parent reported)	Excellent	80 (18.6)	78 (19)
	Very Good	153 (35.5)	145 (35.4)
	Good	125 (29)	119 (29)
	Fair	55 (12.8)	51 (12.4)
	Poor	18 (4.2)	17 (4.1)
Child is of Aboriginal or Torres Strait Islander decent		23[b] (5.3)	20 (4.9)
Child previously hospitalised		397 (92.1)	380 (92.7)
Child's age (years) at survey – median (IQR)		11.12 (6.7–14.7)	10.8 (6.7–14.4)
Child's age at diagnosis of SRMC – median (IQR)		2 (0–6.7)	1.9 (0–6.3)
Years since diagnosis of SRMC – median (IQR)		5.9 (2.5–10)	6.0 (2.6–10)

Footnote: a: postcodes were in defined rural areas of South Australia, New South Wales, Victoria and the Northern Territory; b: Of the eligible participants, 1 declined to answer; IQR: inter quartile range.

more children were male (53.4%), with 4.9% of children being Aboriginal or Torres Strait Islander ethnicity. In total, 54.4% of parents reported their child's health status to be very good to excellent, while 16.5% reported it to be fair to poor. One fifth (20.5%) of children were from smoking households. Table 2 shows the most common SRMC was Type 1 diabetes (37.1%), followed by cystic fibrosis (20.7%).

Of the children aged <10 years when first receiving the influenza vaccine (n = 210); 45% of parents recalled their child receiving two doses, another 22% reported one dose was received, while 33% could not recall the number of doses received.

3.3. Parental vaccination, knowledge and perceptions of influenza disease

A high proportion of parents reported having ever received influenza vaccine (73%), with 41% reporting annual receipt. The majority of parents (89.5%) agreed/strongly agreed that HCWs in a hospital should be obliged to be vaccinated against influenza; with parents who received the vaccine yearly more likely to be in favour of HCW vaccination ($p < 0.001$). Overall, parents reported a medical professional had spoken to 53% (n = 218) of parents about influenza and its potential severity for their child. In total, only 56% of parents perceived the severity to be higher for children with certain medical conditions than for the general community.

Overall, 64% (n = 263) of parents were aware of the recommendation that children with SRMCs receive the influenza vaccine and 61% (n = 252) received a positive recommendation from a HCP. Other sources of positive recommendation (3.4%; n = 14) included family, school and medical practice receptionist staff. HCP recommendations came from the child's specialist (61%), GP (26%), both specialist and GP (6%) or other HCPs (6%) such as Aboriginal HCP, diabetes educator, hospital nursing staff, medical practice nurses and immunisation providers. In contrast, 4% (n = 17) of parents reported a negative recommendation from a HCP, with GPs (n = 9) and specialists (n = 7) providing the majority. Additional sources of negative recommendation (5%; n = 21) included family/friends, 'others' e.g. work colleagues or shopkeepers and natural healthcare providers. In total, 71% (n = 27) of parents receiving a negative recommendation from any source (n = 38) also received a positive recommendation from a HCP. In those who also received a positive recommendation from a HCP in addition to a negative recommendation, vaccination at least once in the last two years was higher (78%; 21/27), compared to those only receiving a negative recommendation from any source (9%; 1/11) (Fisher's exact $p < 0.001$).

3.4. Uptake of the influenza vaccine and characteristics associated with uptake

Confirmed receipt of at least one dose of the influenza vaccine in the last two years was 50%; uptake was lower for individual years (2014: 39.7% and 2015: 43.9%) or annual receipt (33.2%) (Table 3). Provider- confirmed vaccinations were administered between January and September in 2014 (IQR: March 26th–May 1st) and February to September (IQR: 20th April–20th May) in 2015.

In the fully adjusted model (model 5), receipt of the vaccine at least once was strongly associated with recommendation from a specialist (OR 15.80, CI 6.69–37.29), parent receiving the vaccine

Table 2
Children's medical conditions (N = 410).

Sub-specialty Total number of children in subspecialty (%)*	Medical condition	n	%
Respiratory n = 149 (36.3)	Asthma	49	12
	Other – non asthma	32	7.8
	Cystic Fibrosis	85	20.7
Cardiac		7	1.7
Solid Organ Transplant Recipient		14	3.4
Neurological/neuromuscular n = 68 (16.6)	Muscular dystrophy	7	1.7
	Developmental delay	23	5.6
	Congenital -neurological	7	1.7
	Genetic – neurological	3	0.7
	Seizure disorder	31	7.6
	Cerebral palsy	14	3.4
	Neurological other[1]	33	8
Endocrine n = 155 (37.8)	Diabetes	152	37.1
	Obesity	2	0.5
	Endocrine	1	0.2
Renal n = 45 (11)	Renal transplant	11	2.7
	Dialysis	3	0.7
	Chronic renal condition	45	11
Gastro		35	8.5
Hepatic		8	2
Metabolic		23	5.6
Rheumatology		8	2
Prematurity		18	4.4
Immunosuppressed[2]		40	9.8
Other[3]		2	0.5
2 SRMCs		65	15.8
3 SRMCs		29	7.1
4 SRMCs		16	3.9
5+ SRMCs		8	1.9

Footnote: numbers will not total as participants could have more than one condition; 1 included: spina bifida, congenital or acquired brain injury, severe spasticity, hemiparesis, microcephaly, hydrocephalus, neurodegenerative or neuromuscular disease, structural brain abnormality, aspiration disorder; 2: participants were also allocated to the sub speciality for which they required immunosuppressive medication, these included: gastroenterology, neurological, renal, solid organ transplant recipient, rheumatology conditions; 3: other subspecialties were: haematology disorders and cancer – non-haematological. *Where the sub speciality contained more than one medical condition.

Table 3
Confirmed influenza vaccination in children with special risk medical conditions.

Confirmed influenza immunisation uptake	Number of participants (n)	Percentage (%)
At least once in last 2 years (N = 410)	205	50
2014 (N = 380)[a]	151	39.7
2015 (N = 410)	180	43.9

Footnote: a: N = 380 (30 excluded due to age < 6/12 and/or not yet diagnosed with SRMC).

annually (OR 11.12, CI 5.36–23.06) or recommendation from a GP (OR 6.76, CI 2.99–15.29) (Table 4). The model also showed that a child's medical diagnosis could affect parental vaccination decisions either negatively (OR 0.11, CI 0.02–0.60) or positively (OR 2.02, CI 0.93–4.42).

3.5. Barriers to influenza vaccination, despite recommendation (n = 78)

We examined reasons for non-receipt despite receiving a recommendation from a HCP. In total, 78 parents were previously recommended the vaccine for their child, but their child had never received it or received it only once. In those who had never previously received the vaccine (n = 36), reasons for non-receipt of influenza vaccine despite HCP recommendation were related to perceived influenza risk and vaccine side effects (Table 5). While in those who had only received it once before (n = 42), the greatest barrier was time. Common to both groups was medical concerns related to the child's condition. Considerably, more parents whose children had never received the vaccine cited safety concerns compared to those who had received the vaccine previously (Table 5).

3.6. Facilitators to influenza vaccination (n = 162)

In total, 162 parents (39.5%) reported their child had never received the vaccine. Of these, 54.3% were unaware of the recommendation, 59.3% were unaware it was free, 8.6% were unaware where to access it, while 62.4% were unaware of the availability of the hospital immunisation nurse. In total, 63% said they would not or were unlikely to use a (then) proposed hospital immunisation clinic. Barriers provided included: a preference for their GP administering vaccines, distance to the hospital, unsure or not wanting to receive the vaccine and coordinating with other hospital appointment times.

4. Discussion

Annual vaccination is the best way to protect children with SRMCs against seasonal influenza, with the vaccine recommended and funded under the NIP. Our study of children with SRMC found only half received the vaccine in the last two years, even less received it annually. Coverage for individual study years (40–44%) is similar to other Australian studies that report uptake from 30.1 to 42% [11–13]; other estimates from overseas report uptake of 5–60% [14,15,19,25–32].

In our study, the strongest characteristic associated with uptake was receiving a recommendation from a specialist. The change in OR from the crude analysis to the final model indicated little influence from other variables in the model. Receiving a recommendation from a general practitioner was also associated with uptake;

Table 4
Multivariable results for the effect of characteristics on receiving the influenza vaccine at least once in the last two years, crude versus fully adjusted (N = 410).

Characteristic		Level	No of children (%)	crude			Model 5 (fully adjusted)		
				OR	95% CI	p value	OR	95% CI	p value
Demographic	Age of parent (years)	18–30	30 (7.3)	ref	–	–	ref	–	–
		31–40	146 (35.6)	1.93	(0.86–4.34)	0.113	2.39	(0.66–8.66)	0.185
		41–50	196 (47.8)	1.80	(0.81–3.98)	0.147	1.61	(0.41–6.38)	0.495
		>50	38 (9.3)	1.40	(0.52–3.73)	0.503	0.36	(0.06–2.23)	0.274
	Place of residence	Metro	306 (74.6)	ref	–	–	ref	–	–
		Rural	104 (25.4)	1.23	(0.79–1.92)	0.364	1.26	(0.62–2.57)	0.529
	Relationship to child	Mother	337 (82.2)	ref	–	–	ref	–	–
		Father	65 (15.9)	0.92	(0.54–1.56)	0.750	1.13	(0.42–3.03)	0.813
		Legal Guardian	8 (2.0)	3.02	(0.60–15.17)	0.180	3.18	(0.28–36.59)	0.352
	Parents work status	Full time employed	122 (29.8)	ref	–	–	ref	–	–
		Part time employed	106 (25.9)	1.22	(0.73–2.06)	0.448	1.56	(0.64–3.82)	0.327
		Casual	45 (11.0)	1.35	(0.68–2.67)	0.394	2.81	(0.91–8.67)	0.072
		Not working	137 (33.4)	1.27	(0.78–2.07)	0.341	1.81	(0.74–4.43)	0.197
	Highest education level	High school or less	138 (33.7)	ref	–	–	ref	–	–
		Certificate of Diploma	158 (38.5)	0.78	(0.49–1.23)	0.277	0.88	(0.42–1.86)	0.743
		Bachelor	79 (19.3)	0.65	(0.37–1.13)	0.128	0.54	(0.21–1.39)	0.203
		Postgraduate	35 (8.5)	0.77	(0.37–1.62)	0.491	0.49	(0.14–1.72)	0.266
	Member of household is a smoker	Yes	84 (20.5)	0.70	(0.43–1.13)	0.143	0.94	(0.41–2.14)	0.879
	Born in Australia	Yes	347 (84.6)	1.04	(0.61–1.78)	0.891	1.00	(0.34–2.95)	0.996
	Parent's first language is not English	Yes	25 (6.1)	1.09	(0.48–2.45)	0.837	1.89	(0.41–8.65)	0.411
	Gender of child	Male	219 (53.4)	0.94	(0.64–1.39)	0.766	0.87	(0.46–1.66)	0.675
	Child is of ATSI decent	Yes	20 (4.9)	1	(0.41–2.46)	1.000	1.21	(0.30–4.90)	0.788
Child's health status	Child has received all NIP vaccines (parent reported)	Yes	390 (95.1)	1.92	(0.75–4.90)	0.175	2.13	(0.53–8.53)	0.283
	Child's health status (parent reported)	Excellent	78 (19.0)	ref	–	–	ref	–	–
		Very Good	145 (35.4)	1.39	(0.80–2.42)	0.242	1.64	(0.67–4.00)	0.281
		Good	119 (29.0)	1.21	(0.68–2.14)	0.518	0.98	(0.36–2.64)	0.962
		Fair	51 (12.4)	1.18	(0.58–2.40)	0.644	1.09	(0.31–3.82)	0.887
		Poor	17 (4.1)	1.38	(0.48–3.96)	0.546	0.52	(0.10–2.72)	0.436
	Child's age at diagnosis – median (IQR)	1.9(0–6.3)		0.88	(0.84–0.92)	<0.001	1.07	(0.97–1.19)	0.181
	Years since diagnosis – median (IQR)	6 (2.6–10)		1.17	(1.11–1.22)	<0.001	1.10	(1.00–1.21)	0.045
	Number of SRMCs – median (IQR)	1(1–2)		1.29	(1.04–1.60)	0.021	0.89	(0.63–1.27)	0.516
Health service use	Child previously hospitalised	Yes	380 (92.7)	1.34	(0.63–2.83)	0.449	1.33	(0.37–4.80)	0.666
	Number of child's GP visits per year	0–4 visits	315 (76.8)	ref	–	–	ref	–	–
		5–10 visits	63 (15.4)	0.58	(0.33–1.00)	0.050	0.60	(0.24–1.49)	0.272
		10 + visits	32 (7.8)	0.53	(0.25–1.11)	0.092	0.38	(0.12–1.22)	0.103
	Number of child's specialist visits per year	0–4 visits	202 (49.3)	ref	–	–	ref	–	–
		5–10 visits	138 (33.7)	2.74	(1.75–4.28)	<0.001	1.66	(0.78–3.53)	0.187
		10 + visits	70 (17.1)	7.07	(3.72–13.41)	<0.001	1.98	(0.59–6.67)	0.272
	Source of primary care	Hospital – WCH	36 (8.8)	ref	–	–	ref	–	–
		GP	374 (91.2)	0.18	(0.07–0.46)	<0.001	0.31	(0.09–1.15)	0.081
Parental knowledge/ attitudes	Parental vaccination decisions effected by child's condition	Neutral	303 (73.9)	ref	–	–	ref	–	–
		Negatively	12 (2.9)	0.44	(0.12–1.65)	0.222	0.11	(0.02–0.60)	0.011
		Positively	95 (23.2)	3.88	(2.32–6.50)	<0.001	2.02	(0.93–4.42)	0.077
	Parent receives influenza vaccine annually	Yes	168 (41.0)	5.33	(3.46–8.22)	<0.001	11.12	(5.36–23.06)	<0.001
	Parent talked to about influenza disease and their child	Yes	218 (53.2)	3.83	(2.54–5.77)	<0.001	0.82	(0.40–1.66)	0.572
	'Influenza can be serious' (Scale 0–10) – median (IQR)	8 (6–10)		1.09	(0.99–1.20)	0.084	1.04	(0.86–1.24)	0.712
	'Influenza can be serious for children with certain medical conditions' (Scale 0–10) – median (IQR)	10 (9–10)		1.56	(1.30–1.86)	<0.001	1.22	(0.90–1.66)	0.202
	Aware influenza vaccine recommended for	Yes	263 (64.1)	3.36	(2.19–5.15)	<0.001	1.26	(0.65–2.45)	0.488

(*continued on next page*)

Table 4 (*continued*)

Characteristic		Level	No of children (%)	crude			Model 5 (fully adjusted)		
				OR	95% CI	p value	OR	95% CI	p value
	children > 6 months of age with certain medical conditions								
	Aware of hospital immunisation nurse	Yes	188 (45.9)	2.31	(1.55–3.44)	<0.001	1.89	(0.98–3.66)	0.057
Receiving recommendation	Recommendation from specialist	Yes	174 (42.4)	12.19	(7.54–19.69)	<0.001	15.80	(6.69–37.29)	<0.001
	Recommendation from GP	Yes	83 (20.2)	1.58	(0.97–2.57)	0.066	6.76	(2.99–15.29)	<0.001

Footnote: ATSI: Aboriginal or Torres Strait Islander ethnicity; IQR: Interquartile range; GP: general practitioner.
Crude = unadjusted for all other variables.
Model 5 = variables adjusted for demographic, child's health status, health service use, parental knowledge/attitudes and receiving recommendation variables.

Table 5
Reasons for non-receipt of the influenza vaccine despite HCP recommendation by those who have never received or received only once, according to parent report (n = 78).

Reason	Examples	Overall (n = 78)	Never received (n = 36)	Received once only (n = 42)*
		n (%)	n (%)	n (%)
Medical (valid/perceived)	'worried about child's medical condition' 'child allergic to the influenza vaccine' 'thought vaccine contraindicated with child's medical condition'	19 (24.4)	8 (22.2)	11 (26.2)
Time	'too many appointments already' 'time poor' 'Forgot'	19 (24.4)	4 (11.1)	15 (35.7)
Risk (flu)	'don't think influenza is serious' 'don't think my child is at risk' 'my child rarely gets sick' 'wouldn't get any sicker than other children'	15 (19.2)	9 (25)	6 (14.3)
Vaccine – side effects	'side effects' or 'serious side effects' 'the vaccine can give you the flu' 'side effects are long term'	11 (14.1)	9 (25)	2 (4.8)
Vaccine–knowledge	'unaware of influenza vaccine recommendations' 'unaware of the minimum age for vaccination' 'unaware that vaccination is annual'	7 (8.9)	3 (9.1)	4 (9.5)
Child related	'child does not want the vaccine' 'child does not like needles'	4 (5.1)	2 (5.5)	2 (4.8)
No response provided		4 (5.1)	1 (2.8)	3 (7.1)
Medical advice	'conflicting views from healthcare providers' 'received advice directly against the vaccination'	3 (3.8)	1 (2.8)	2 (4.8)
Vaccine – confidence	'Don't think the vaccine works'	3 (3.8)	2 (5.5)	1 (2.4)
Object to vaccinations[a]		2 (2.6)	2 (5.5)	– (–)
Access	'Don't know where to get at the hospital' 'Immunisation nurse unavailable'	2 (2.6)	2 (5.5)	– (–)

Footnote a: participants were registered as conscientious objectors on AIR. *An additional four children in this group were ineligible to have received the vaccine more than once (too young or not yet diagnosed).

however the effect remained lower in the final model compared to a specialist recommendation. It is likely that the effect of GP recommendation was influenced largely by other variables in the model, the strongest of which appears to be a specialist's recommendation. A much higher proportion of those recommended by a specialist received the vaccine compared to those recommended by a GP; the reasons for this are unclear. It is possible that parents may perceive specialists to have more detailed knowledge and familiarity with their child's condition and in doing so more readily take on board preventative healthcare advice. Our finding of a medical professional's influence is consistent with studies from the USA and Italy [14–19]. In a recent Australian study [12] that looked at both healthy and medically at risk children, HCP recommendation was found to be the strongest stimulus for vaccination. Our findings highlight the need to better understand medical professionals' knowledge and prioritisation of influenza vaccination.

Our crude and adjusted models presented would indicate that confounding is present; as the difference in effect sizes between the crude and final adjusted model for some variables is considerable. Table 6, presented in the supplementary material shows the effect on variables after the inclusion of each additional group or block of variables. For example, the effect of annual parental receipt of the influenza vaccine on a child's influenza vaccination status, more than doubled from the crude to final model, indicating this variable, unlike a specialist recommendation, is influenced by other variables in the model. The effect of parental influenza vaccination behaviour we report is consistent with a United States study that found children of immunised parents were almost three times more likely to also be immunised for seasonal influenza and that any changes in parental influenza vaccination were mirrored in children [33]. All states in Australia have recently provided the influenza vaccine universally and free to children up to 5 years of

age, which could, aside from the benefit of protecting a greater number of children, potentially normalise receipt of vaccine and increase community acceptance leading to increased coverage in children with SRMC. Targeting the family unit with appropriate messaging about the herd immunity protective effect for their at risk child as well as the opportunity to normalise immunisation as an annual family activity may have a far greater effect for these children in improving coverage.

Our finding that a child's medical condition both positively and negatively influences parent's vaccination decision making, has not been identified previously in relation to influenza. However, the negative effect of a child's medical condition on vaccination decisions has been previously reported. An Australian study that examined potential barriers to infant immunisation in parents who did not disagree with immunisation found that compared to infants from families experiencing minimal barriers, those with child health issues or concerns had a higher risk of incomplete immunisation [34]. While data from the Millennium Cohort study in the UK showed 45% of partial immunisation was attributable to medical reasons [35]. It is possible that parents of children with ongoing medical issues may be more reluctant to vaccinate for fear of worsening the child's medical condition or lack of knowledge surrounding contraindications of the influenza vaccine in conjunction with their child's treatment. While the group of parents in our study whose vaccination decisions were negatively affected by their child's medical condition was small ($\sim$ 3% of the cohort), they are worth identifying as these parents may require more individualised approaches.

In Australia, uncertainty regarding the vaccine's safety as well as a decrease in its uptake followed the serious adverse events that occurred in 2010 with the BioCSL Fluvax vaccine. [36–38] Our study found a quarter of parents whose children have never received the vaccine, despite being recommended by a HCP, cited safety concerns as a barrier. Other studies support this, with several studies of parents [39–43] and specifically parents of children with SRMCs [15,24,44–45] reporting safety as a reason for non-receipt. Although one study's preliminary findings [46] suggested parents (with healthy children) perceived the vaccine to be safer in healthy children compared to those with a chronic health condition; limited evidence has examined if parents of children with SRMCs are more likely to perceive the vaccine to be less safe for children with SRMCs compared to children in general.

While just over half of parents understood influenza to be a potentially serious disease, the majority indicated that influenza was a potentially serious disease for children with SRMCs, suggesting that parents may not necessarily identify their child being 'at risk' and/or are unaware of what defines this risk. A recent Australian cross-sectional study found that, 43% of all parents (not just those with children with medical conditions) were uncertain of their child's eligibility for free influenza vaccine [47].

Our study also identified anomalies with some of the children's vaccination dates. In particular, confirmed receipt of the vaccine as early as January and February is interesting as the National Seasonal Influenza Immunisation Program usually starts mid-March, (in 2015 it was delayed until April) [48]. Moreover the previous year's stock has an expiry of December. Whilst this only included three participants, it may identify a broader issue. Given influenza activity occurs throughout the year, the appropriate extension of expiry dates should be considered to improve access to vaccination year-round, not just winter months. [2,49] This will include protection for those undertaking international travel.

The strengths of our study included utilising a personal face-to-face interview; confirmation of risk status using medical records, including date of diagnosis and confirming influenza vaccination status with the provider. Our study is not without limitations. Children were recruited from a single tertiary paediatric hospital and may have had more complicated comorbidities and therefore may not represent this at risk population more broadly in the community. While almost a quarter had less than three specialist visits per year, we may have missed those managed predominately in general medical practice. It is also possible that there was non-participation from non-vaccinators or those with no interest in influenza disease. Some at risk groups may have been under-represented, and some conditions over-represented in our sample, such as diabetes and cystic fibrosis. Our sample was limited to those who spoke English and as such, the sample of parents with English as a second language was small. This is important given ethnicity has previously been cited as an important factor in vaccination status [50–52]. In particular, limited evidence has identified that not speaking a countries' dominant language is an important barrier for influenza vaccination [53]. Additionally, when unable to confirm influenza vaccination status we substituted parental report. However, while parents are more likely to over report influenza vaccination [17,54,55], it is unlikely that we over estimated uptake as less than 10% of those substituted reported receiving the vaccine. Although it is possible that our uptake figure is a slight overestimate. Social desirability bias could have affected parent's responses [56] with parents responding in a manner that would be viewed favourably by others, leading to more positive responses towards influenza vaccination. Recall bias [57] could also have meant vaccinators were potentially more likely to recall their reasoning, such as provider recommendation or awareness of guidelines.

5. Conclusion

Influenza vaccination uptake in children with SRMC is low and many children are unprotected against severe disease. Parental vaccination acceptance and behaviour strongly effects a child's vaccination status and for that reason targeting the family unit may prove more successful to increase uptake in this target group. This study confirms previous studies showing the influence of medical professional's recommendation. Understanding barriers to recommendation and prioritisation from the perspective of these children's general practitioners could identify areas for improvement.

Author contribution

JT contributed to the study design, collected and analysed the data and prepared the first draft of the manuscript. SS, SM and BJX contributed to data collection, statistical analysis interpretation and critically reviewed the manuscript. HM contributed to the study design, statistical analysis interpretation and critical review of the manuscript. NC and JL contributed to statistical analysis interpretation and critical review of the manuscript. The manuscript has been read and approved by all named authors.

Conflicts of interest

JT, NC, JL, SS, SM and BJX report no conflict. HM is an investigator on clinical trials of investigational vaccines sponsored by Industry. Her institution receives funding from Industry (GSK, Pfizer, Novavax) for Investigator led research. She does not receive any personal payments from Industry.

Acknowledgments

The authors would like to thank Larissa Au, Mary Premnath, Emma Lane, Kathryn Riley, Chris Heath and Iann Homer for their assistance with data collection.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2018.09.039.

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Supplementary Table 6: Multivariable results for the effect of selected characteristics on receiving the influenza vaccine at least once in the last two years, crude versus each sequential model with blocks of additional variables (N=410)

Characteristic	Level	No of children	crude			Model 1			Model 2			Model 3			Model 4			Model 5		
			OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
Age of parent (years)	18-30	30	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-
	31-40	146	1.93	(0.86-4.34)	0.113	2.16	(0.93-5.00)	0.073	2.29	(0.94-5.61)	0.069	1.75	(0.66-4.64)	0.260	2.18	(0.69-6.85)	0.183	2.39	(0.66-8.66)	0.185
	41-50	196	1.80	(0.81-3.98)	0.147	1.99	(0.87-4.56)	0.102	1.77	(0.68-4.64)	0.244	1.64	(0.59-4.57)	0.347	1.46	(0.43-5.01)	0.543	1.61	(0.41-6.38)	0.495
	>50	38	1.40	(0.52-3.73)	0.503	1.35	(0.48-3.79)	0.568	1.28	(0.36-4.60)	0.706	0.97	(0.25-3.80)	0.965	0.63	(0.13-3.02)	0.561	0.36	(0.06-2.23)	0.274
Place of residence	Metro	306	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-
	Rural	104	1.23	(0.79-1.92)	0.364	1.18	(0.74-1.89)	0.485	1.42	(0.85-2.37)	0.179	1.60	(0.93-2.76)	0.089	1.50	(0.79-2.83)	0.214	1.26	(0.62-2.57)	0.529
Relationship to child	Mother	337	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-
	Father	65	0.92	(0.54-1.56)	0.750	1.10	(0.59-2.06)	0.768	1.17	(0.59-2.32)	0.647	1.21	(0.59-2.50)	0.605	1.30	(0.54-3.13)	0.556	1.13	(0.42-3.03)	0.813
	Legal Guardian	8	3.02	(0.60-15.17)	0.180	3.76	(0.70-20.15)	0.122	3.41	(0.55-21.07)	0.187	2.13	(0.34-13.45)	0.420	1.61	(0.22-11.95)	0.641	3.18	(0.28-36.59)	0.352
Parents work status	Full time employed	122	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-
	Part time employed	106	1.22	(0.73-2.06)	0.448	1.33	(0.74-2.38)	0.343	1.47	(0.77-2.79)	0.243	1.46	(0.75-2.86)	0.268	1.54	(0.68-3.49)	0.298	1.56	(0.64-3.82)	0.327
	Casual	45	1.35	(0.68-2.67)	0.394	1.28	(0.61-2.66)	0.514	1.18	(0.54-2.61)	0.676	1.05	(0.45-2.45)	0.915	1.49	(0.54-4.10)	0.437	2.81	(0.91-8.67)	0.072
	Not working	137	1.27	(0.78-2.07)	0.341	1.34	(0.76-2.36)	0.312	1.31	(0.70-2.45)	0.398	1.29	(0.66-2.52)	0.464	1.44	(0.65-3.21)	0.371	1.81	(0.74-4.43)	0.197
Highest education level	High school or less	138	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-
	CertDip	158	0.78	(0.49-1.23)	0.277	0.75	(0.46-1.21)	0.231	0.95	(0.56-1.60)	0.844	0.86	(0.49-1.50)	0.599	0.80	(0.41-1.55)	0.507	0.88	(0.42-1.86)	0.743
	Bachelor	79	0.65	(0.37-1.13)	0.128	0.61	(0.34-1.12)	0.111	0.69	(0.35-1.35)	0.277	0.66	(0.32-1.33)	0.244	0.40	(0.17-0.96)	0.041	0.54	(0.21-1.39)	0.203
	Postgraduate	35	0.77	(0.37-1.62)	0.491	0.71	(0.32-1.57)	0.396	0.89	(0.38-2.08)	0.794	0.82	(0.33-2.04)	0.675	0.43	(0.13-1.36)	0.15	0.49	(0.14-1.72)	0.266
Member of household is a smoker		84	0.70	(0.43-1.13)	0.143	0.66	(0.40-1.10)	0.109	0.69	(0.40-1.19)	0.183	0.68	(0.37-1.23)	0.198	0.92	(0.45-1.89)	0.819	0.94	(0.41-2.14)	0.879
Born in Australia		347	1.04	(0.61-1.78)	0.891	0.92	(0.47-1.81)	0.805	0.92	(0.44-1.92)	0.831	0.93	(0.43-2.02)	0.854	1.02	(0.38-2.72)	0.972	1.00	(0.34-2.95)	0.996
Parent's first language is not English		25	1.09	(0.48-2.45)	0.837	0.97	(0.36-2.64)	0.953	1.18	(0.39-3.58)	0.766	1.35	(0.42-4.30)	0.615	1.81	(0.44-7.37)	0.408	1.89	(0.41-8.65)	0.411
Gender of child	Male	219	0.94	(0.64-1.39)	0.766	0.98	(0.66-1.46)	0.919	1.03	(0.67-1.59)	0.895	1.14	(0.72-1.82)	0.572	1.12	(0.64-1.97)	0.684	0.87	(0.46-1.66)	0.675
Child is of ATSI decent		20	1	(0.41-2.46)	1.000	0.94	(0.37-2.38)	0.888	1.36	(0.49-3.77)	0.559	1.26	(0.44-3.62)	0.667	1.10	(0.31-3.96)	0.878	1.21	(0.30-4.90)	0.788
Child has received all NIP vaccines		390	1.92	(0.75-4.90)	0.175				2.16	(0.74-6.29)	0.157	2.26	(0.77-6.67)	0.140	2.93	(0.86-9.96)	0.086	2.13	(0.53-8.53)	0.283
Child's health status (parent reported)	Excellent	78	ref	-	-				ref	-	-	ref	-	-	ref	-	-	ref	-	-
	Very Good	145	1.39	(0.80-2.42)	0.242				1.48	(0.79-2.79)	0.223	1.41	(0.73-2.72)	0.299	1.94	(0.87-4.31)	0.103	1.64	(0.67-4.00)	0.281
	Good	119	1.21	(0.68-2.14)	0.518				1.29	(0.66-2.51)	0.454	0.91	(0.44-1.87)	0.802	1.14	(0.48-2.72)	0.766	0.98	(0.36-2.64)	0.962
	Fair	51	1.18	(0.58-2.40)	0.644				1.28	(0.57-2.87)	0.557	0.66	(0.25-1.72)	0.390	1.05	(0.34-3.21)	0.935	1.09	(0.31-3.82)	0.887
	Poor	17	1.38	(0.48-3.96)	0.546				1.22	(0.36-4.15)	0.754	0.42	(0.11-1.59)	0.200	0.53	(0.12-2.44)	0.419	0.52	(0.10-2.72)	0.436
Child's age at diagnosis - median (IQR)	1.9(0-6.3)		0.88	(0.84-0.92)	<0.001				0.94	(0.88-1.01)	0.102	0.99	(0.92-1.07)	0.889	1.03	(0.94-1.13)	0.478	1.07	(0.97-1.19)	0.181
Years since diagnosis - median (IQR)	6 (2.6-10)		1.17	(1.11-1.22)	<0.001				1.14	(1.07-1.22)	<0.001	1.14	(1.06-1.22)	<0.001	1.12	(1.03-1.22)	0.011	1.10	(1.00-1.21)	0.045
Number of SRMCs - median (IQR)	1(1-2)		1.29	(1.04-1.60)	0.021				1.07	(0.83-1.37)	0.607	0.88	(0.67-1.16)	0.349	0.87	(0.64-1.18)	0.369	0.89	(0.63-1.27)	0.516
Child previously hospitalised		380	1.34	(0.63-2.83)	0.449							0.78	(0.33-1.85)	0.573	1.05	(0.35-3.16)	0.931	1.33	(0.37-4.80)	0.666

Characteristic	Level	No of children	crude			Model 1			Model 2			Model 3			Model 4			Model 5		
			OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
No child's GP visits per year	0-4	315	ref	-	-							ref	-	-	ref	-	-	ref	-	-
	5-10	63	0.58	(0.33-1.00)	0.050							0.84	(0.42-1.67)	0.619	0.66	(0.29-1.48)	0.315	0.60	(0.24-1.49)	0.272
	10+	32	0.53	(0.25-1.11)	0.092							0.61	(0.24-1.55)	0.297	0.40	(0.14-1.19)	0.099	0.38	(0.12-1.22)	0.103
No child's Specialist visits per year	0-4	202	ref	-	-							ref	-	-	ref	-	-	ref	-	-
	5-10	138	2.74	(1.75-4.28)	<0.001							2.59	(1.51-4.44)	0.001	2.63	(1.37-5.05)	0.004	1.66	(0.78-3.53)	0.187
	10+	70	7.07	(3.72-13.41)	<0.001							10.00	(3.91-25.57)	<0.001	4.84	(1.69-13.87)	0.003	1.98	(0.59-6.67)	0.272
Source of primary care	Hospital - WCH	36	ref	-	-							ref	-	-	ref	-	-	ref	-	-
	GP	374	0.18	(0.07-0.46)	<0.001							0.47	(0.16-1.34)	0.156	0.29	(0.09-0.99)	0.049	0.31	(0.09-1.15)	0.081
Parental vaccination decisions effected by child's condition	Neutral	303	ref	-	-										ref	-	-	ref	-	-
	Negatively	12	0.44	(0.12-1.65)	0.222										0.24	(0.04-1.29)	0.097	0.11	(0.02-0.60)	0.011
	Positively	95	3.88	(2.32-6.50)	<0.001										2.41	(1.20-4.83)	0.013	2.02	(0.93-4.42)	0.077
Parent receives influenza vaccine annually		168	5.33	(3.46-8.22)	<0.001										8.85	(4.71-16.63)	<0.001	11.12	(5.36-23.06)	<0.001
Parent talked to about influenza disease and their child		218	3.83	(2.54-5.77)	<0.001										1.84	(1.03-3.30)	0.039	0.82	(0.40-1.66)	0.572
'Influenza can be serious' (Scale 0-10) - median (IQR)	8 (6-10)		1.09	(0.99-1.20)	0.084										1.00	(0.84-1.19)	0.981	1.04	(0.86-1.24)	0.712
'Influenza can be serious for children with certain medical conditions' (Scale 0-10) - median (IQR)	10 (9-10)		1.56	(1.30-1.86)	<0.001										1.22	(0.92-1.62)	0.171	1.22	(0.90-1.66)	0.202
Aware influenza vaccine recommended for children >6 months age with certain medical conditions		263	3.36	(2.19-5.15)	<0.001										2.18	(1.21-3.93)	0.009	1.26	(0.65-2.45)	0.488
Aware of hospital immunisation nurse		188	2.31	(1.55-3.44)	<0.001										1.42	(0.79-2.53)	0.241	1.89	(0.98-3.66)	0.057
Recommendation from specialist		174	12.19	(7.54-19.69)	<0.001													15.80	(6.69-37.29)	<0.001
Recommendation from GP		83	1.58	(0.97-2.57)	0.066													6.76	(2.99-15.29)	<0.001

Footnote: IQR: Interquartile range.

Model 1: demographic variables (age of parent (years), place of residence, relationship to child, parents work status, highest education level, member of household is a smoker, born in Australia, parent's first language is English, gender of child, child is of ATSI decent)

Model 2: model 1 + child's health status (child has received all NIP vaccines, child's health status (parent reported), child's age at diagnosis of SRMC, years since diagnosis of SRMC, number of SRMCs)

Model 3: model 2 + health service use (child previously hospitalised, number child's GP visits per year, number child's Specialist visits per year, source of primary care)

Model 4: model 3 + parental knowledge/attitudes (vaccination decision effected by child's condition, parent receives influenza vaccine annually, parent talked to about influenza disease and their child, parent thinks getting influenza can be serious disease, parent thinks getting influenza can be serious, disease for children with certain medical conditions, aware influenza vaccine recommendation for children with medical conditions, aware of hospital immunisation nurse)

Model 5: model 4 + receiving recommendation

4.3 CAPTURING INFLUENZA VACCINATION STATUS

In this study, validity of parent reported influenza vaccination and provider reporting to the AIR in children with SRMC were evaluated using data collected as part of project 1. The results are published in “Human Vaccines & Immunotherapeutics”. Concordance of 794 available parent-provider influenza vaccination records were evaluated using the Kappa index and the sensitivity, specificity, positive predictive value and negative predictive value were calculated. With the same methods applied to provider-AIR influenza vaccination data.

The publication, “Are children with special risk medical conditions receiving influenza vaccination? Validity of parental and provider report, and to a National Immunisation Register” demonstrated that parents tend to over report influenza vaccination and that there is also poor reporting of child’s influenza vaccination encounters to AIR, with almost 70% of encounters not reported to the AIR. Our finding implies that a significant number of parents wrongly believe their children are protected against influenza when they are not. The need for timely and accurate coverage data is imperative to facilitate vaccination and evaluate program coverage. This section address’ theme 2 (Coverage and Validation) of this thesis which related to verify parent reported influenza vaccination compared to provider report and the Australian Immunisation Register. Examining the level of reporting to AIR was important. Together with understanding parental recall, determining AIR reporting, this chapter provided insight into immunisation provider practices and helped to direct questions asked in the interview guide and survey of medical professionals. Further illustrating the need to explore direct capture of vaccinations and systems based solutions.

4.3.1. Statement of Authorship

Statement of Authorship

Title of Paper	Are children with special risk medical conditions receiving influenza vaccination? Validity of parental and provider report, and to a National Immunisation Register.
Publication Status	☑ Published ☐ Accepted for Publication ☐ Submitted for Publication ☐ Unpublished and Unsubmitted work written in manuscript style
Publication Details	Tuckerman J, Crawford NW, Lynch J, Marshall HS. Are children with special risk medical conditions receiving influenza vaccination? Validity of parental and provider report, and to a National Immunisation Register. Hum Vaccin Immunother. 2019;15 (4):951-958.

Principal Author

Name of Principal Author (Candidate)	Jane Tuckerman
Contribution to the Paper	JT contributed to the study design, collected and analysed the data, prepared the first draft of the manuscript.
Overall percentage (%)	80%
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: 18 DEC 2019

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	Nigel W Crawford
Contribution to the Paper	NC contributed to statistical analysis interpretation and critical review of the manuscript.
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Contribution to the Paper	JL contributed to statistical analysis interpretation and critical review of the manuscript.
Signature	Date: 11/12/19

Name of Co-Author	Helen Marshall
Contribution to the Paper	HM contributed to study design, statistical analysis interpretation and critical review of the manuscript.
Signature	Date: 12 Dec 2019

4.3.2. Publication

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2019, VOL. 15, NO. 4, 951–958
https://doi.org/10.1080/21645515.2018.1554966

Taylor & Francis
Taylor & Francis Group

RESEARCH PAPER

Are children with special risk medical conditions receiving influenza vaccination? Validity of parental and provider report, and to a National Immunisation Register

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ABSTRACT

Background: To investigate the validity of parent reported influenza vaccination and provider reporting to the Australian Immunisation Register (AIR) in children with special risk medical conditions (SRMC).
Methods: Cross-sectional survey with parents of children with a SRMC aged ≥ 6 months and <18 years attending the Women's and Children's Hospital, Adelaide, Australia from September 2015 to February 2016. Children aged <7 years provided data to assess provider-AIR reporting. Influenza vaccination status was ascertained from the child's parent, immunisation provider and the AIR. Concordance was made using the Kappa index and the sensitivity, specificity, positive predictive value and negative predictive value were calculated.
Results: 389 and 395 parent-provider influenza vaccination records were available for 2014 and 2015 respectively. 78% of parent reported vaccinations were substantiated by a provider with the kappa indicating good (κ = 0.677) to very good agreement (κ = 0.814) for 2014 and 2015 respectively. Discordance was higher in 2014, largely attributable to parents over reporting vaccination. More fathers over reported compared to mothers (Fisher's exact = 0.052). There were 241 provider-AIR influenza vaccination records. Sensitivity of the AIR to reflect a child's influenza immunisation status was low (32.6%).
Conclusions: Parental report over estimates confirmed influenza vaccination status and is affected by time and relationship to the child. Only a third of influenza vaccinations were reported to the AIR. Timely accurate data is critical to facilitate vaccination and evaluate program coverage.

ARTICLE HISTORY
Received 16 September 2018
Revised 11 November 2018
Accepted 26 November 2018

KEYWORDS
Special risk medical condition; validity; parental report; influenza vaccination; immunisation register

Background

Many countries recommend the seasonal influenza vaccine to children with special risk medical conditions (SRMC).[1–3] SRMCs include severe asthma, lung or heart disease, low immunity or diabetes and increase an individual's risk of influenza complications or severity. In Australia, SRMCs who are at increased risk for inferior influenza outcomes are defined as per the Australian Immunisation Handbook[4] which is approved by the National Health and Medical Research Council and for which the Australian Technical Advisory Group on Immunisation specifically recommends vaccination.[5] Individuals with SRMCs, including children, have been funded under Australia's National Immunisation Program (NIP) to receive the vaccine since 2010[5]

Under the NIP, vaccines are routinely scheduled at specific ages and additionally for people at special risk or requiring catch-up according to the program and eligibility. While other vaccines may be recommended, all vaccines listed under the NIP are free. Of those routinely given to children, traditional NIP immunisation providers include, general medical practitioners (GPs) (family physicians) and practice nurses who administer the vaccines in general medical practices (78.8%), government community immunisation clinics (8.9%) and community children's health clinics or Aboriginal Health Services (7.5%).[6] Australia's National Seasonal Influenza Vaccination Program (NSIVP) generally commences in the first month of autumn each year. Under the NSIVP, the vaccine is free to eligible people, but GPs may charge a consultation fee for the visit with non-eligible people able to obtain the vaccine privately. The influenza vaccine is widely available at general medical practices, community immunisation clinics, hospitals, community children's health clinics and Aboriginal health centres. Additionally, travel clinics may also provide the vaccine and in South Australia, since early 2015, pharmacists, working in pharmacies (drug stores) can administer influenza vaccine to people over the age of 16 at a cost. Unlike for children's routinely scheduled vaccines there is no information available on the distribution of provider types who administer the influenza vaccine from Australia. However, it is thought few parents would seek alternatives beyond

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traditional NIP immunisation providers due to the cost implications and age restrictions.

In South Australia (as in many states of Australia), legislation requires immunisation encounters to be both recorded by the provider and a handheld record given to the patient. However, there is no requirement for immunisation providers to report immunisations to the person's primary healthcare provider (HCP), and while this is encouraged from those outside of the traditional health care delivery system, such as pharmacists, this also requires patient consent.

Ascertaining coverage of this recommendation assists in program planning and monitoring of influenza vaccination uptake over time, in line with strategic priority areas of Australia's National Immunisation Strategy, 2013–2018.[7] At the population level, a number of methods are available to determine coverage including data from healthcare providers, health insurance records, population surveys, as well as administrative and registry data.[8] Population surveys can include a representative sample of the population specific target groups but rely on self-report as a proxy for the true vaccination record. Parent reported influenza vaccination status of children is thought to overestimate vaccination[9-12] with suggestion that this is greater in children with SRMC.[11,13,14]

The use of a population registry with accurate data removes the need for data validation with multiple immunisation providers. Registry data has a use in epidemiological research and health service planning and also a role in examining vaccine effectiveness.[15–17]

Established in 1996, the Australian Childhood Immunisation Register (ACIR) was the first purpose-built immunisation register in the world.[18] With the exception of influenza, until 2016, the ACIR routinely recorded universal and targeted vaccines given under the NIP for all children aged < 7 years of age.[4,19] In September 2016, the registry became the Australian Immunisation Register (AIR) with the capability of capturing all NIP and most privately purchased vaccines, given to people of all ages.[20] The AIR is linked to the Medicare enrolment register,[4] and given approximately 99 per cent of children are registered with Medicare by 12 months of age and the AIR is 'opt-out' it is intended to constitute a nearly complete population register.[19,20]

However, as influenza is not required to be recorded on the AIR, and it does not currently attract notification payments for providers, as is the case for other childhood vaccines, concerns about the completeness and validity of AIR data have restricted its use in evaluating uptake of the vaccine.[21] Particularly so for children with medical conditions, Indigenous children and those aged under five years for whom it is currently provided in all states in Australia.[4]

Given the current limitations of the AIR to identify children with SRMC, determining parent reported validity would assist in evaluation of the NIP program's coverage in this priority group. Determining immunisation provider- AIR reporting would also provide much needed information. The aim of this study was to investigate the validity of parent-provider report and determine the accuracy of the AIR for recording provider reported influenza vaccination.

Results

A total of 443 surveys were completed; approximately 10% of those approached did not participate (Figure 1). Validation of risk status was determined for all participants with three participants included without a current SRMC.

Parent-provider record

A total of 389 parent-provider influenza vaccination records with complete data were available in 2014 and 395 in 2015 (Figure 1). Reasons for provider non-confirmation included: not the child's current HCP, incorrect clinic details, immunisation provider did not respond to request or would not release information, not having a GP, and mother (nurse) administered influenza vaccine.

Provider-AIR reporting

Complete data were available for 241 provider-AIR influenza vaccination records from 138 children (2014: 130 records; 2015:111 records) (Figure 1). By using the first day of the NSIVP to calculate a child's age at that time-point, no data were included from children aged >7 years at the time of vaccination in either year; nor were data excluded from children aged <7 years at the time of vaccination. Reasons for provider non-confirmation were not current HCP, incorrect clinic details, immunisation provider did not respond to request or not having a GP. All eligible children had an AIR record.

Characteristics of study participants

Of the 398 children with parent-provider vaccination data, age at the time of the survey ranged from 10 months to 17.9 years (median 11.2 years) (Table 1).

Parents interviewed were predominately the child's mother (83%). Six children were inpatients at the time of enrolment, but all had previously had outpatient appointments at the hospital.

Of the 138 children contributing provider-AIR reporting data, ages at the time of vaccination ranged from 10 months to 6.9 years (median 4.1 years) in 2014 and from 7 months to 6.3 years (median 3.6 years) in 2015.

Parent reported influenza vaccination uptake

Parent reported uptake of the influenza vaccine was 54.5% (212/389) for 2014 and 53% (209/395) for 2015 (Table 2). Across both years, the majority of influenza vaccinations were confirmed with the Women's and Children's Hospital (WCH) database (n = 162; 48%) or a medical practice (n = 164; 49%) (Table 3).

Parent-provider record

A total of 78% (328/421) of parent reported vaccinations were confirmed by a provider. There was higher agreement for

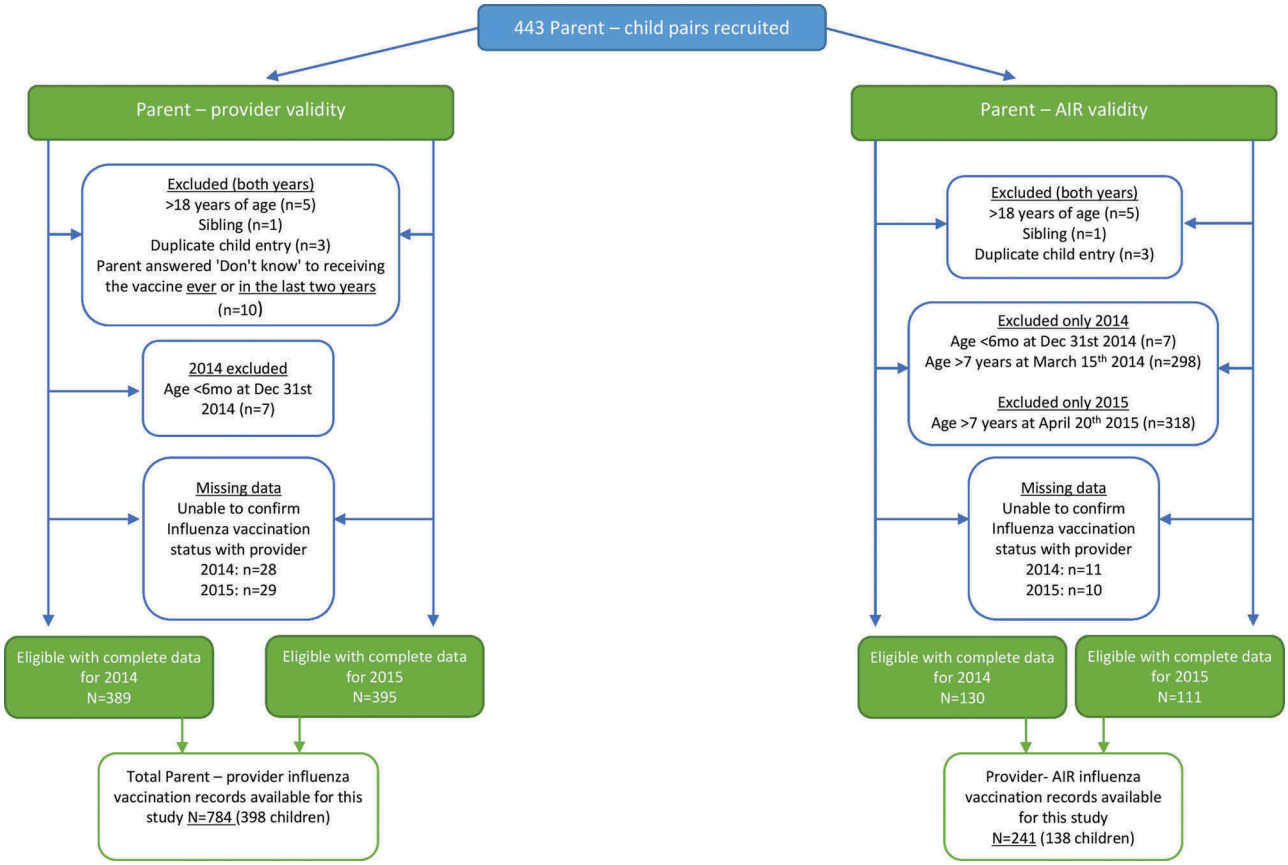

Figure 1. Study sample.

Table 1. Characteristics of study participants.

		Parental report		Provider – AIR reporting	
Characteristic	Level	Eligible N = 424	Complete data n = 398	Eligible N = 148	Complete data n = 138
Age of parent	18–30	30 (7.1)	25 (6.3)	25 (16.9)	20 (14.5)
	31–40	149 (35.1)	137 (34.4)	86 (58.1)	82 (59.4)
	41–50	206 (48.6)	200 (50.3)	37 (25)	36 (26.1)
	>50	39 (9.2)	36 (9)	-	-
Place of residence	Metro	316 (74.5)	298 (74.9)	104 (70.3)	97 (70.3)
	Rural[a]	108 (25.5)	100 (25.1)	44 (29.7)	41 (29.7)
Relationship to child	Mother	350 (82.5)	329 (82.7)	124 (83.8)	116 (84.1)
	Father	66 (15.6)	61 (15.3)	22 (14.9)	20 (14.5)
	Legal Guardian	8 (1.9)	8 (2)	2 (1.4)	2 (1.4)
Parent's highest education level	High school or less	147 (34.7)	138 (34.7)	43 (29.1)	40 (29)
	Certificate or Diploma	160 (37.7)	151 (37.9)	55 (37.2)	53 (38.4)
	Bachelor	82 (19.3)	77 (19.3)	33 (22.3)	30 (21.7)
	Postgraduate	35 (8.3)	32 (8)	17 (11.5)	15 (10.9)
Parents work status	Full time employed	129 (30.4)	119 (29.9)	37 (25)	34 (24.6)
	Part time employed	113 (26.7)	109 (27.4)	40 (27)	39 (28.3)
	Casual	45 (10.6)	42 (10.6)	17 (11.5)	16 (11.6)
	Not working	137 (32.3)	128 (32.2)	54 (36.5)	49 (35.5)
Born in Australia		355 (83.7)	335 (84.2)	126 (85.1)	119 (86.2)
English is first language		397 (93.6)	374 (94)	138 (93.2)	130 (94.2)
Gender of child	Male	225 (53.1)	209 (52.5)	82 (55.4)	75 (54.3)
Child is of Indigenous decent [b]		23 (5.4)	19 (4.8)	8 (5.4)	7 (5.1)
Child had specified GP[c]	No GP	35 (8.4)	30 (7.6)	14 (9.5)	10 (7.3)
	Specified GP	258 (61.6)	250 (63.1)	87 (59.2)	84 (61.3)
	Non – Specific GP[d]	126 (30.1)	116 (29.3)	46 (31.3)	43 (31.4)
Age at survey median (IQR)		11.2 (6.7–14.9)	11.2 (6.7–14.9)	5.7 (3.6–6.8)	5.7 (3.6–6.8)

Footnote: a: postcodes were in defined rural areas of South Australia, New South Wales, Victoria and the Northern Territory; b: Of the eligible participants 1 participant declined to answer; c: data were missing for 1 participant; d: child was a patient of a medical practice but did not see a specific doctor at the practice; GP: general practitioner; IQR: inter quartile range.

Table 2. Comparison of parent reported influenza vaccination and AIR record with provider record, by year.

		Vaccination status			Agreement		Sensitivity	Specificity	Positive predictive value %	Negative predictive value %
		Parent report (%)	Provider report (%)	AIR	%	Kappa	% (95% CI)	% (95% CI)	(95% CI)	(95% CI)
Parent – Provider report										
Overall		421/784 (53.7)	336/784 (42.9)	-	87.1	0.745	97.6 (95.4–99.0)	79.2 (75.2–82.9)	77.9 (73.6–81.8)	97.8 (95.7–99.0)
Year	2014[a]	212/389(54.5)	156/389(40.1)	-	83.5	0.677	97.4 (93.6–99.3)	74.2 (68.1–79.7)	71.7 (65.1–77.7)	97.7 (94.3–99.4)
	2015[b]	209/395(52.9)	180/395(45.6)	-	90.6	0.814	97.8 (94.4–99.4)	84.7 (79.1–89.2)	84.2 (78.5–88.9)	97.8 (94.6–99.4)
Provider reporting to AIR										
Overall		-	89/241 (36.9)	30/241 (12.4)	74.7	0.370	32.6 (23.0–43.3)	99.3 (96.4–100)	96.7 (82.8–99.9)	71.6 (65.0–77.5)
Year	2014[c]	-	47/130 (36.2)	18/130 (13.8)	77.7	0.442	38.3 (24.5–53.6)	100 (95.7–100)	100. (81.5–100)	74.1 (65.0–81.9)
	2015[d]	-	42/111 (37.8)	12/111 (10.8)	71.2	0.287	26.2(13.9–42.0)	98.6(92.2–100)	91.7(61.5–99.8)	68.7(58.6–77.6)

Footnote: a: N = 389 children had complete data; b: N = 395 children had complete data; c: N = 130 encounters had complete data; d: N = 111 encounters had complete data.

2015 (90.6%) than 2014 (83.5%); with the kappa indicating good (κ = 0.677) to very good agreement (κ = 0.814) for 2014 and 2015 respectively (Table 2). The sensitivity and specificity of parental report to reflect a child's influenza immunisation status was 97.4% and 74.2% respectively for 2014 and 97.8% and 84.7% respectively for 2015. Across both seasons, between 15.3–25.8% of children with no provider confirmed vaccination, were reported as being vaccinated by their parent.

Discordance was different across years (16.2% versus 9.4%; Fisher's exact = 0.004). The majority of discordance resulted from parents over reporting their child was vaccinated, which was almost double in 2014 compared to 2015 (15.4% versus 8.4%; Fisher's exact = 0.018). The inverse was true of parental relationship (the parent completing the survey). Overall, fathers were more likely to over report vaccination compared to mothers (Fisher's exact = 0.052); which was more likely in 2015 (Fisher's exact p = 0.020) than in 2014 (Fisher's exact p = 0.483). There were no other differences associated with agreement observed including place of residence, parents' age, education level, work status, place of birth, first language being English and child's gender, indigeneity or having a specific GP (data not reported).

Reporting of the influenza vaccine to the AIR

Confirmed influenza vaccination was 36.2% (47/130) for 2014 and 37.8% (42/111) for 2015; with 38.3% (18/47) and 26.2% (11/111) of these reported to the AIR respectively. There was only one first dose recorded on the AIR that had not been confirmed by an immunisation provider; which incidentally had been given on the same day/month as the previous year. The majority of influenza vaccinations were administered by WCH immunisation providers (2014: 61.7%; 2015: 54.7%), compared to medical practices (2014: 29.8%; 2015: 42.8%), with others provided by a travel health clinic and community immunisation clinics.

Second dose

In 2014, there were four second dose provider confirmed vaccinations, with 2/4 reported to the AIR; while an additional two second dose records were identified on the AIR only. For 2015, five second dose vaccinations were provider reported, with 3/5 reported to the AIR; while one second dose record was identified on the AIR only.

Provider-AIR agreement

There was fair agreement overall (κ = 0.3701) with higher agreement for 2014 (κ = 0.442) than 2015 (κ = 0.287) (Table 2). In total, a quarter of cases (25.4%) were discordant, with almost all discordance a result of vaccinations not reported to the AIR. The sensitivity and specificity of AIR to reflect a child's influenza immunisation status was 32.6% and 99.3% respectively. There was slightly higher sensitivity in 2014 (38.3%) than 2015 (26.2%). Across both years, 67.4% of children with a provider confirmed influenza vaccination were not reported to the AIR. Between the two highest providers, medical practices and the WCH, a much higher

Table 3. Children's nominated and confirmed providers of influenza vaccination in 2014 and 2015.

	2014		2015	
Provider type	Parent reported (N = 212) n (%)	Confirmed (N = 156) n (%)	Parent reported (N = 209 n (%)	Confirmed (N = 180) n (%)
General medical practice	116 (54.7)	67 (43)	109 (52.2)	81 (45)
Current HCP*	-	6 (3.8)	-	10 (5.6)
Women's and Children's Hospital	88 (41.5)	80 (51.3)	90 (43)	82 (45.6)
Other Hospital	1 (0.5)	-	1 (0.5)	1 (0.6)
Community immunisation clinic	6 (2.8)	2 (1.3)	4 (1.9)	4 (2.2)
Pharmacy/drug store	-	-	4 (1.9)	2 (1.1)
Travel health clinic	1 (0.5)	1 (0.6)	1 (0.5)	-

Footnote: *: were general medical practitioners (family physicians) nominated as a child's current healthcare provider (HCP).

proportion of influenza vaccinations given at medical practices (48.6%; 17/35) compared to the WCH (23.1%; 12/52) were reported to the AIR (χ^2= 6.12; p = 0.013).

While there was no difference between years (2014–2015) in the proportion of vaccinations reported to the AIR by medical practices (range reported, 41.2–55.6%), significantly less vaccinations administered at the WCH were reported to the AIR in 2015 (4.3%; 1/23) compared to 2014 (38%; 11/29) (Fisher's exact p = 0.007).

Discussion

At the population level, accurate influenza vaccination data are required to determine coverage, as well as guide and evaluate future programs. For children in special risk groups, such as those with underlying medical conditions, an accurate vaccination status has a role in the provision of healthcare at the individual level. Our data suggests that in children with SRMC, parents tend to over report influenza vaccination with 15–26% of vaccinations unconfirmed. AIR coverage is also not an accurate reflection of a child's influenza vaccination status, with almost 70% of encounters in our study not reported to the AIR. Our finding of parental over reporting of influenza vaccination status is consistent with previous studies of children and adolescents, both of children in general (specificity range: 86– 92%)[9,12] and in those with SRMCs, where specificity ranged from 68 to 82.3%.[11,13,14] We found two characteristics to be associated with over reporting: time and parental relationship. In regards to parental relationship, we speculate that it is not fathers solely who over report but any 'parent' who is not the child's primary carer, particularly when children may have complex medical conditions and multiple appointments. The misclassification (parental over reporting) could also be due to the fact that in addition to multiple medical treatments, parents can confuse the many different vaccines offered to children in general and are likely to be influenced by social desirability bias if they can't recall. The finding that between 15 to 26% of parents over report influenza vaccination is important as it identifies that a proportion of parents incorrectly believe their child is protected against influenza when they are not. The effect of time on recall has previously been demonstrated in a study of self-reported influenza vaccination in healthcare workers that found accuracy decreased with increasing time since vaccination.[22]

While the accuracy of the AIR to capture additional NIP vaccines has previously been highlighted and under reporting suspected,[18,21,23] to our knowledge this is the first study to investigate the AIR in terms of accurate reporting on influenza for children. Of the two major providers, there was low reporting (WCH: 18%; medical practices: 35%) of influenza vaccination encounters suggesting that barriers to reporting are likely to be common across all provider types. As children may see multiple medical practitioners including specialists, and as influenza vaccines become more available outside of traditional settings, such as in pharmacies and travel health clinics, the requirement for reporting to a centralised register (the AIR) becomes paramount.

Unlike the national Danish and Norwegian vaccination registers and some state based registers in the USA in which reporting of all vaccines is mandatory,[24–26] the AIR relies on the passive reporting for some NIP vaccines, particularly those used for targeted programs. While provider incentives have previously been shown to improve reporting and data accuracy, this method requires ongoing financial support.[17,23] The methods used to report to the AIR have changed over time with increasing numbers electronically reporting[21,23] and taking advantage of Medical Practice Management Software (PMS) that directly uploads to the AIR.

Aside from countries that link national or state-wide registers to health data,[27,28] evaluating the uptake of influenza vaccination in at risk groups is a problem worldwide, with considerable gaps in monitoring coverage. In a recent report into seasonal influenza vaccination recommendations and coverage in Europe, only 9 of 32 European Member States were able to provide data on uptake in people with chronic medical conditions; with a previous report indicating even less reliability for children.[3,29]

Whilst in 2016, the AIR transitioned to a registry that captures all age groups, identifying priority groups targeted for influenza vaccination with the current socio-demographic data collected remains a considerable obstacle that limits the evaluation of all current NIP programs. Establishing a way that target groups can be identified on the AIR would enable timely estimates of coverage and enhance program planning for these special vaccination groups.

In our study, the influenza vaccine was predominately delivered through medical practices or hospitals and less frequently by pharmacies/drug stores and community or travel health clinics. In comparison with delivery of the routinely scheduled NIP vaccines in which the majority (78%) (nationally) are received in medical practices, less of our study

participants received them in this way (49%)[6] However, this is likely to reflect the SRMC status of these children and availability of the vaccine in their specialist treatment centre (WCH).

One of the strengths of this study was the comprehensive method used to determine vaccination status. A child's influenza vaccine status was initially confirmed with the child's nominated provider. If this was negative other health care providers, (current HCP, WCH) were contacted to determine whether influenza vaccine had been administered and the date. We accept the possibility that some parents may not have accurately supplied immunisation provider details to us and these children could be incorrectly classified. However, we expect that only small numbers would be vaccinated outside of the traditional influenza vaccination delivery system and so being able to contact each child's current HCP was a strength of the study.

Our study also identified an issue with recommendations in relation to immunisation providers and age restrictions for administering vaccines. In particular, all children (n = 4) reported to have received the vaccine at a pharmacy/drug store in 2015 were aged <14 years. Two children's vaccinations were confirmed at separate pharmacies, with their age at administration below recommended practice (≥16 years for administration in a pharmacy in South Australia). Additionally, these children or their parents would have needed to pay for the vaccine, rather than receive it free as per recommendations.

There are several limitations to our study. In regards to parental report, individual years were analysed separately because of the difference in discordance. However, we acknowledge the fact that parents may report similarly from one year to the next, although if this were the case we would have expected similar discordance between years. We also did not account for the fact that some children attended the same medical practice each year or that multiple children attended the same medical practice when examining provider-AIR reporting; yet this is reflective of real world immunisation practice and we accept that our sample may limit generalizability to all immunisation providers. Our study data limited exploration of possible reasons for low reporting at the provider level. As these data came from a parent-based survey, possible confounders at the provider level were not collected, such as method of reporting to the AIR (PMS, Medicare Australia website or paper encounter forms) and size of the practice. Additionally, as almost all children in our study had a SRMC and were eligible for funded influenza vaccine, this may have prompted a higher level of provider reporting to the AIR compared to children not eligible. However, we cannot see any reason this would occur, given those who administer the vaccine are often different to those who oversee practice reporting. Whilst only undertaken in one Australian jurisdiction (South Australia), we believe the results would be applicable to other regions of Australia as the AIR is a national database.

Conclusion

Fundamental to having a vaccination program targeting children at increased risk of severe influenza is the ability to evaluate it. Parental report overestimates provider confirmed influenza vaccination status and this should be taken into account if using parental report as a proxy in population surveys. Influenza vaccination is significantly underreported to the AIR. Besides encouraging and potentially funding providers to report influenza vaccinations to the AIR, future research should focus on investigating provider level barriers in order to address them.

Methods

Study design

We report study findings for an observational cross-sectional study with consideration of the STROBE statement.[30]

Study setting

The study population was recruited from September 2015 to February 2016 at a paediatric hospital in Adelaide. The Women's and Children's Hospital (WCH) is the major provider of tertiary healthcare services for children with acute and chronic conditions in South Australia.

Study recruitment

Parents or guardians, referred to hereafter as parents, were approached at the outpatient's department or in hospital wards at the WCH. Exclusion criteria for this study included: age < 6 months or ≥ 18 years on the day of recruitment or children without a SRMC as defined by the AIH;[4] parent unable to provide written informed consent or understand English without a translator. If multiple children of the same family were eligible, the eldest child was enrolled. For both analyses, parental validity and AIR reporting, a child's data were ineligible in a given year if they were aged <6 months' old (prior to December 31st in that year). Additionally, the provider–AIR analyses were restricted to a subset of children from the parental validity analyses. This was due to the limited capability of the ACIR at the time of the study to record only the vaccinations of children aged less than 7 years at the time of vaccination. In order to capture those children aged less than 7 years at the time of vaccination (due to the capability of the ACIR at the time of the study), we used the first day of the National Seasonal Influenza Vaccination Program (NSIVP) in each year. A child's data were ineligible in a given year if they were >7 years old on the first day of the NSIVP. In 2014, this was March 15th, while in 2015 this was April 20th, due to a delay in vaccine availability as a result of multiple strain changes in the vaccine.[31]

Parental survey questionnaire

Following parental consent, data were collected using a predominately closed-ended questionnaire in a face-to-face interview. Parents were asked questions related to influenza vaccination, including vaccination in 2014 and 2015. More specifically, we asked, "Has your child ever received a seasonal influenza vaccine?" If yes, "Have they received a seasonal

influenza vaccine in the last two years?" If yes, this was followed by, "Has your child received the vaccine this year?" and "Did your child receive the vaccine last year? (2014)" with additional questions asked to extract reasons for receipt/non-receipt of the vaccine in either or both years. To confirm vaccination status we collected the child's immunisation provider for each year along with details of their current primary HCP. For some participants this was the name of the medical practice only, while others provided the details of a specific general medical practitioner (GP) within the practice. The questionnaire was completed in the waiting area of the outpatient clinic or hospital ward. Medical case notes were reviewed to confirm risk status.

Influenza vaccination status

Provider report of influenza vaccination was defined as receipt of at least one dose of the vaccine verified by the child's nominated immunisation provider, current HCP or WCH immunisation database. Nominated immunisation providers included general medical practitioners/medical practices, pharmacies (drug stores), community immunisation clinics, travel health clinics and hospitals. While the purpose of this study was not to consider a "gold standard", we considered that if their nominated provider had vaccinated a child, then in keeping with relevant legislation they (the nominated immunisation provider) should be able to verify a child's immunisation record. When contacting the child's nominated immunisation provider four attempts were made to establish contact with the provider before recording as unable to confirm and if we could not verify receipt of the vaccine elsewhere (current HCP, WCH) then these cases were excluded. The AIR was used to confirm influenza vaccination status for 2014 and 2015. Additionally, since children aged 6 months to <9 years receiving influenza vaccine for the first time are recommended to receive 2 doses[4] we examined provider and AIR record of a 2nd dose. In line with AIR coverage calculations, we allowed a minimum 3-month delay for late notification of influenza vaccinations to the AIR.[32]

Statistical analysis

The sample for both analyses was derived from the recruited sample. Influenza vaccination status from parent-provider record and provider-AIR record were compared in each year. The Kappa was used to measure the percent agreement between reporting.[33] We interpreted Kappa using the classification proposed by Altman,[34] where a kappa coefficient of 0.81–1.0 is considered to be very good; 0.61–0.80 good; 0.41–0.60 moderate; 0.21–0.40 fair and <0.20 poor. We examined the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). Concordance of parent-provider record was investigated and discordant unvaccinated cases further examined, by year and demographic characteristics. Additionally, the effect of year and provider type on provider-AIR reporting was investigated. Stata (Version 14.1) was used for all statistical analyses (StataCorp, Texas, USA). The study was approved by the Women's and Children's Health Network Human Research Ethics Committee.

Abbreviations

AIR	Australian Immunisation Register
HCP	healthcare provider
GP	general practitioner
NIP	National Immunisation Program
NPV	negative predictive value
NSIVP	National Seasonal Influenza Vaccination Program
PPV	positive predictive value
SRMC	special risk medical condition
WCH	Women's and Children's Hospital

Disclosure of potential conflicts of interest

JT, NC and JL report no conflict. HM is an investigator on clinical trials of investigational vaccines sponsored by Industry. Her institution receives funding from Industry (GSK, Pfizer, Novavax) for Investigator led research. She does not receive any personal payments from Industry.

Acknowledgments

The authors would like to thank Siobhan Misan, Salma Salih, Bridget Joseph Xavier, Larissa Au, Mary Premnath, Emma Lane, Kathryn Riley, Chris Heath and Iann Homer for their assistance with data collection. HM is supported by a NHMRC CDF APP1084951.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contribution

JT contributed to study design, collected and analysed the data and prepared the first draft of the manuscript. HM contributed to study design, statistical analysis interpretation and critical review of the manuscript. JL and NC contributed to statistical analysis interpretation and critical review of the manuscript. The manuscript has been read and approved by all named authors.

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CHAPTER 5 COMMUNITY AWARENESS - CHILDREN'S INFLUENZA RECOMMENDATIONS FROM A COMMUNITY PERSPECTIVE

5.1 LITERATURE REVIEW

In Australia, the age-specific influenza disease burden is U-shaped, with the highest rates of notifications and hospitalisations occurring at either end of the age spectrum. (1) As such, young age (< 5 years) is increasingly recognised as a risk factor in its own right. Australian children <5 years' experience a considerable influenza disease burden, including a higher annual incidence and hospitalisations compared to adults. (142-146) Children shed higher levels of the virus over a longer period, contributing to the virus' circulation within the community (25, 147, 148), with subsequent direct and indirect healthcare costs and lost productivity. (3, 18, 80) Influenza vaccine coverage in Australian children has been poor, although not well documented. While uptake in children has previously been reported between 14-23% (27, 149-151), more recent data from 2018 reports coverage of children aged 6 months to <5 years ranges between 19-43.4% across jurisdictions (25.6% overall) (21) In children with SRMCs, estimated coverage is 30-44% (27, 152).

Although knowledge alone is often insufficient to overcome a behaviour gap, understanding community knowledge and awareness often provides important insight as to a communities' current values and is therefore important to evaluate in the context of vaccination coverage and program planning. Evidence suggests a doctor's recommendation to receive the vaccine is central to uptake in children (27, 29, 30, 33, 34, 132, 153), and while research has examined facilitators and barriers to uptake of the influenza vaccine in children in both Australia and elsewhere (27, 30, 33, 34, 131, 132, 153-156), much of this work was undertaken in children hospitalised or with SRMC. It is

likely that parental awareness of children's influenza recommendations also contributes to uptake and there is limited research on parental awareness from a community perspective.

Few studies have directly examined awareness of recommendations from a community perspective. However, most community focused studies report high levels of misconceptions surrounding influenza vaccination moderated by social norms/expectations – yet are inconsistent. In a US survey, 71% of parents reported their child was vaccinated for influenza yet 47% of parents thought their child was unlikely to get influenza. (157) In multivariable analysis, social norms were associated with uptake (OR 1.32; 95%CI 1.03-1.69) while anticipating negative barriers (not being able to source the vaccine or an appointment) were negatively associated (OR 0.68 (95% CI 0.49-0.95). In contrast, a recent Singaporean study (158) found low uptake despite high parental influenza knowledge and perceived benefit. The mismatch between vaccine receipt despite a perceived lack of concern towards influenza severity was also reiterated in a qualitative meta-analysis of 29 US studies (159) and suggests other factors interplay with decision making and behaviour. The 29 unpublished primarily qualitative CDC sponsored studies (undertaken 2000-2013) focused on influenza vaccination knowledge, attitudes and beliefs (KABs) involving focus groups, in-depth interviews, message testing and surveys, with seven of these studies involving parents, primarily mothers. The review found that in studies that involved the general public (community) and parents, recurring themes included limited understanding of influenza and immunisation recommendations, indications of greater sub-group recognition of the value of flu vaccination, continued resistance to vaccination among many, and overestimation of the effectiveness of non-vaccine measures. Many adults did not appear to know there was a universal recommendation, nor believe that they

were in an at-risk group. Many parents believed it more important that their children were vaccinated than themselves (despite low-moderate levels of personal concern about influenza) while some parents, (even those following the recommended schedule) perceived the influenza vaccine to be optional. (159) The legitimacy of the vaccine through its inclusion on an official schedule was also echoed in a recent Australian qualitative study (160) conducted with GPs, parents, pharmacists and Maternal and Child Health nurses. The study also found a lack of disease and vaccination knowledge, uncertainty over the vaccine's safety, practical barriers such, as opportunity and cost along with a lack of normalisation to receive it.

In a 2017 Australian study (149), only 50% of parents knew the vaccine was recommended for children < 5 years; while another found children more likely to be vaccinated if parents believed the vaccine was recommended for their child's age group or with the same medical condition as their child (27). Some studies suggest lack of parental awareness of the recommendation to be a common reason for non-vaccination in children with SRMC (32) and hospitalised children (132).

Participants of target groups are often unaware of vaccine recommendations and along with children at increased risk of influenza, pregnant women remain a prime example of this. (161-164) However, awareness of recommendations (or lack of) also extends to recommended but unfunded children's vaccines. (165) Previous research on awareness of influenza recommendations has focused on pregnant women and healthcare workers (HCWs) (161, 162, 166) and there is limited research from an Australian perspective surrounding awareness of influenza recommendations towards children. Therefore, the community perspective is vital to indirect vaccine messaging. Understanding how parental awareness (knowledge) of recommendations is retained and understood can

inform and strengthen future messaging and is essential in planning and developing strategies to increase uptake.

This chapter aims to answer the fourth research question in this thesis:

- Amongst parents in the community, what is the level of awareness towards influenza vaccination in children; what characteristics are associated with awareness; and what influences future receipt of the influenza vaccine? (Paper 4; Section 5.2.2)

The next section reports the results and data obtained in a CATI survey. The survey as part of Project 3 quantitatively evaluated data collected as part of the Health Monitor survey undertaken in April-May 2016 and answered the fourth research question.

5.2 COMMUNITY AWARENESS

Parental awareness of influenza vaccination recommendations for children aged < 5 years were evaluated in a state-wide telephone survey. The cross-sectional survey was completed by 2006 South Australian adults (aged ≥18 years). After weighting the data there were 532 parents. Characteristics associated with awareness were explored using univariable and multivariable analyses with the survey data weighted to reflect the population of SA and the probability of selection within a household. At the time of the study, parents showed low awareness that all children (<5 years) were recommended influenza vaccine annually with only modest awareness of the recommendation that children with SRMCs should receive the influenza vaccine each year.

This section address' theme 3 (Community Awareness) of this thesis which related to parental awareness of children's influenza recommendations from a community perspective. Gaining this perspective was important in forming a broader picture now only of community knowledge to the recommendations but influencers within the social environment to future vaccine receipt. Our publication reporting this work, "Disparities in parental awareness of children's seasonal influenza vaccination recommendations and influencers of vaccination" showed decreased awareness of the recommendations from those in regional areas or who used a combination of immunisation providers. In terms of influential cues to future receipt, more parents indicated a preference for a GP recommendation than provision of the vaccine at no cost. In terms of general vaccination, vaccine hesitant parents were more likely to report the belief that their children's vaccinations (in general) were unnecessary, as other children in the community were vaccinated. Describing and understanding the social and environmental supports that may be required for wider paediatric influenza vaccination programs is valuable. The information obtained in this study helped to set the scene

more broadly in the community and lay the foundations, for how a future intervention may be received in the community.

5.2.1. Statement of Authorship

Statement of Authorship

Title of Paper	Disparities in parental awareness of children's seasonal influenza vaccination recommendations and influencers of vaccination.
Publication Status	☑ Published ☐ Accepted for Publication ☐ Submitted for Publication ☐ Unpublished and Unsubmitted w ork w ritten in manuscript style
Publication Details	Tuckerman J, Crawford NW, Marshall HS. Disparities in parental awareness of children's seasonal influenza vaccination recommendations and influencers of vaccination. PLOS One

Principal Author

Name of Principal Author (Candidate)	Jane Tuckerman		
Contribution to the Paper	JT contributed to the study design, sought these data from SA Health, analysed the data and prepared the first draft of the manuscript.		
Overall percentage (%)	80%		
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	30/7/2020

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	Nigel W Crawford		
Contribution to the Paper	NC contributed to study design, statistical analysis interpretation and critical review of the manuscript.		
Signature		Date	30/7/20

Name of Co-Author	Helen Marshall		
Contribution to the Paper	HM contributed to study design, statistical analysis interpretation and critical review of the manuscript.		
Signature		Date	27 July 2020

5.2.2. Publication

PLOS ONE

RESEARCH ARTICLE

Disparities in parental awareness of children's seasonal influenza vaccination recommendations and influencers of vaccination

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Citation: Tuckerman J, Crawford NW, Marshall HS (2020) Disparities in parental awareness of children's seasonal influenza vaccination recommendations and influencers of vaccination. PLoS ONE 15(4): e0230425. https://doi.org/10.1371/journal.pone.0230425

Editor: Italo Francesco Angelillo, University of Campania, ITALY

Received: August 1, 2019

Accepted: February 28, 2020

Published: April 9, 2020

Data Availability Statement: Data is not owned by the authors and data ownership rests with a third-party (SA Health). Interested researchers could replicate our study findings by directly obtaining the data from SA Health (contact via health.PrevandPopHealth@sa.gov.au) and following the analysis as set out in our methods section. The authors did not have any special access privileges to these data.

Funding: "Helen Marshall acknowledges NHMRC Fellowship APP1155066 funding. The funders had

Abstract

Objective

To determine parental awareness of influenza vaccination recommendations for children and explore associations with awareness.

Design

Cross-sectional survey.

Setting/participants

South Australian parents with a telephone listing in the Electronic White Pages were randomly selected.

Methods

Participants were interviewed using Computer Assisted Telephone Interviewing (CATI) during May–July 2016. Univariable and multivariable analyses explored characteristics associated with awareness; with the survey data weighted to reflect the population of SA and the probability of selection within a household.

Results

Of 539 parents, 33% were aware of the recommendation that all children (<5 years) should receive the influenza vaccine annually with 51.9% aware that children with special risk medical conditions (SRMC) should also receive the vaccine annually. Characteristics strongly associated with parental awareness of the recommendation for children aged < 5 years were knowledge of recommendation for children with a SRMC (adjusted Odds Ratio [aOR]

no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript."

Competing interests: JT and NC report no conflict. HM is an investigator on clinical trials of investigational vaccines sponsored by Industry. Her institution receives funding from Industry (GSK, Pfizer, Novavax) for Investigator led research. She does not receive any personal payments from Industry. This does not alter our adherence to PLOS ONE policies on sharing data and materials.

10.46, CI 4.44–24.63) or living in a metropolitan area (aOR 2.91, CI 1.19–7.09). There was lack of awareness in those not working (aOR 0.13, CI 0.04–0.47), with trade level education (compared with high school) (aOR 0.25 CI, 0.09–0.71) and in those born in the UK or Ireland (aOR 0.19, CI 0.04–0.85). Awareness of the recommendation for children with SRMC to receive the vaccine was strongly associated with knowledge of the influenza recommendation for children <5 years (aOR 10.22, CI 4.39–23.77) or not being born in Australia [UK/ Ireland (aOR 7.63, CI 1.86–31.31); other (aOR 3.93, CI 0.94–16.42)]. The most influential cues to future receipt were a general practitioner (GP) recommendation (63.8%) and providing influenza vaccine free for all children (37.6%). More parents who delayed or excluded vaccines believed that their children's vaccinations (in general) were unnecessary, as other children were vaccinated (42.8%) compared to those with no or minor concerns (11.1%) ($p<0.0001$).

Conclusions

Parental awareness of children's influenza vaccine recommendations is low. Targeted communication strategies and resources are required to establish broader community awareness of recommendations. Healthcare provider endorsement of the vaccine remains key and health care professionals, particularly GPs and paediatric specialists should be encouraged to discuss influenza vaccine with parents at every opportunity. Many parents have vaccine concerns and addressing concerns across the spectrum of hesitancy is crucial.

Introduction

Influenza is the leading cause of vaccine preventable hospitalisations for Australian children aged under 5 years. [1, 2] Children experience considerable disease burden with a higher annual incidence than adults. Ten to forty percent of children are infected each year, which increases considerably in children attending day-care. [3–5] Children also shed higher levels of the virus for a longer period, contributing to the virus' circulation within the community.[6–8] Attributable healthcare costs of influenza in children are substantial, as are indirect economic losses including lost productivity through parents needing time off work to care for infected children and subsequent secondary transmission in households. [9–11]

In recent times, changes to recommendations, funding, the 2009/2010 pandemic and a cluster of serious adverse events with use of the BioCSL Fluvax vaccine have contributed to the changing landscape of children's influenza vaccination in Australia (Fig 1). Influenza vaccine coverage in Australian children has been poor, with previous uptake reported between 14–23% in children aged <18 years [12–15]. More recent 2018 data reports coverage for children aged <5 years ranges between 19–43.4% across jurisdictions (25.6% overall). [16] Estimated coverage is 30–44% for children with special risk medical conditions (SRMC)[12, 17, 18].

SRMC: Special Risk Medical Condition; mo: months; yrs: years. ACT: Australian Capital Territory; NSW: New South Wales; QLD: Queensland; SA: South Australia; TAS: Tasmania; VIC: Victoria; NT: Northern Territory; WA: Western Australia. Reference: National Centre for Immunisation Research and Surveillance (NCIRS). Significant events in influenza vaccination in Australia: NCIRS Fact sheet. Significant events in influenza vaccination in Australia: NCIRS Fact sheet April 2019. [19]

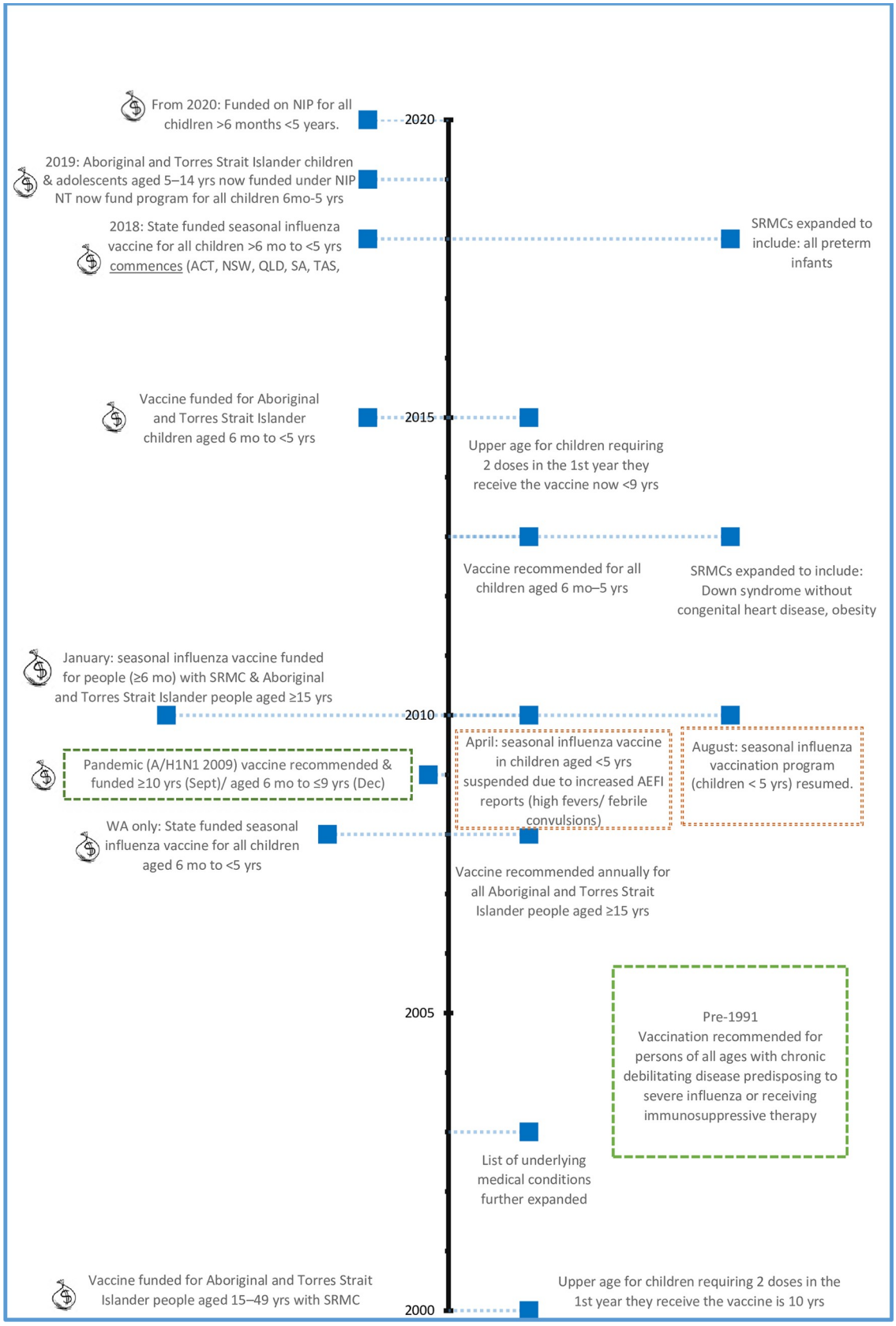

Fig 1. Brief timeline of children's seasonal influenza vaccination recommendations, funding and events in Australia.

https://doi.org/10.1371/journal.pone.0230425.g001

The influenza vaccine is free to those eligible under Australia's National Seasonal Influenza Vaccination and at a cost to non-eligible people, with the vaccine accessible through medical practices, community immunisation clinics, hospitals, community children's health clinics and Aboriginal Health Centres. Community pharmacies may also administer the vaccine at a cost, dependent on the jurisdiction and a person's age.

While a doctor's recommendation is considered central to influenza vaccine uptake in children [12, 17, 20–24], much of the previous research examining factors related to vaccine uptake in children in both Australia and elsewhere [12, 17, 20–23, 25–28] was undertaken in children hospitalised or with SRMC. However, it is likely that general parental awareness of children's influenza recommendations also contributes to uptake and there is limited research on parental awareness from a community perspective.

Only 50% of parents in a recent Australian study knew the vaccine was recommended for children < 5 years, while another found higher uptake if parents believed the vaccine was recommended for their child's age group or with the same medical condition as their child. [12, 13] Lack of parental awareness of the recommendation is cited as a common reason for non-vaccination in children with SRMC [29] and hospitalised children [20].

Understanding parental awareness towards recommendations is essential in planning and developing strategies to increase uptake. The primary aim of this study was to examine parental awareness of influenza vaccine recommendations and explore associated characteristics. The study also sought to describe influences towards future receipt of the influenza vaccine, examine patterns of information provision and decision making towards vaccination in general, from a random sample of parents residing in South Australia (SA).

Methods

Study design

This study used data collected as part of a cross-sectional telephone survey. Study findings are reported with consideration of the STROBE statement.[30]

Study setting

The survey was performed as part of the 'Health Monitor' program administered by the Population Research and Outcomes Studies Unit, University of Adelaide, with the study population recruited from the approximate 765,786 households located in metropolitan and rural South Australia during May–July 2016.

Study recruitment

For this study, South Australian adults aged >18 years who were the parent or caregiver, referred to hereafter as parents, of a child aged <18 years were eligible to participate. Participants were members of households randomly selected from the SA Electronic White Pages (EWP) telephone listings in SA. For each household, the adult aged 18 years or older with the most recent birthday was selected for an interview. Each individual parent interviewed represents a separate household. Selected persons were non-replaceable, and interviews were not conducted with alternative household members if the selected person was not available. Up to 10 call-backs were made to each household before the selected individual was classified as a non-contact.

Ethical approval was granted from The University of Adelaide, and the SA Health HREC. Potential participants were informed of the purpose of the survey and timeframe, its voluntary nature and that they could decline or refuse questions at any stage of the survey or withdraw completely at any time. Consent was implied by participation.

Parental survey questionnaire

An independent external research company conducted Computer Assisted Telephone Interviews (CATI) whereby the interviewer followed a script provided by a computer and entered participant responses directly into a database. At the beginning of the dialogue, interviewers stated that they were calling on behalf of The University of Adelaide to conduct a survey on a range of health issues. There was an introductory sentence for each health topic covered in the survey and specific questions could be directed towards subgroups, such as parents. All data collected were non-identifiable. A pilot study of 50 randomly selected households tested question format and sequence. The questionnaire was designed so that each interview took on average 15 minutes or less to be completed.

Respondents who identified as a parent (of a child aged <18 years) were asked their awareness of children's influenza vaccination recommendations and influencing factors towards future vaccine receipt for their child. Possible responses to future intentions towards influenza immunisation and immunisation service use were read to participants with the option for multiple response. Respondents could also specify another response, that was later recoded. To examine parental attitudes towards vaccines in general, parents were asked to state their beliefs towards vaccine necessity, side effects, access to services, behaviour towards their child receiving vaccines and their level of concern according to the Vaccine Communication Framework (VCF). [31] To examine immunisation service use, parents were asked their immunisation provider type, decision-making surrounding their choice as well as any difficulties with access. Parents were also asked their views on information surrounding where to obtain vaccinations and to rate their child's most recent vaccination service. Parents were instructed to answer all immunisation specific questions in relation to their youngest child.

Statistical analysis

The survey data were weighted by the inverse of the individual's probability of selection and the number of times their telephone number(s) is(are) listed in the EWP, then re-weighted to age group by sex by section of state (metropolitan/country) benchmarks derived from the June 2014 ABS Estimated Resident Population. Weighting corrected the distributions in the sample data to approximate those of the SA population. The weights generated for the wider study population were then maintained for the parental subset. Both as an expansion of the data and as a matter of adjustment for non-response and non-coverage, resulting in data that is representative of the population rather than limited to the households that responded.

Additional response questions were coded using content analysis and grouped into categories. Characteristics associated with awareness of the current influenza recommendations for children were explored in successive multivariable logistic regression models. All the variables were included and grouped together in blocks, facilitating an understanding of each group of variables role in explaining awareness.

These variable blocks representing different constructs, may be important in understanding vaccination awareness. The explanatory variable blocks were demographic variables, parental beliefs/attitudes and health service use/awareness of other influenza recommendations. Unadjusted odds ratios (OR) and adjusted OR (aOR) were presented with their 95% confidence intervals (CI). In this paper, the crude versus final model is presented, with S1 and S2 Tables showing full models. We examined level of parental concern according to the VCF. To further explore this, we summed the total number of questions each participant had responded to, in a negative or opposing way to 4 other questions related to vaccination beliefs and safety. Those who responded in the neutral category were not included (neither agree/disagree) as an expression of hesitancy. We used Stata (Version 14.1) for all statistical analyses (StataCorp, Texas, USA).

Results

Study population

From 5,200 households randomly selected to participate, 2,118 households could not be contacted or were non-residential telephone numbers. From the remaining 3,082 telephone numbers, 2,006 interviews were conducted, a participation rate of 64.8%. After the raw data were weighted, 547 (27.3%) participants were parents, with 539 providing complete data.

Description of study sample

In the weighted sample, the mean age of parents was 41.5 years (95% CI 40.0–42.9) (Table 1). There were slightly more female parents (53.3%), with the majority Australian born (n = 436; 80.9%) and speaking English as the predominant household language (91.9%, n = 496). Most households were situated in metropolitan Adelaide (77.5%, n = 418) while 22.5% (n = 121) were rural/regional residences, closely reflecting the proportion of households in metropolitan versus rural South Australia.

Table 1. Household demographics of survey participants.

Participant characteristic		Eligible parents[#]	Parents[#] with complete data †	
		Raw N = 285	Raw N = 279	Weighted (N = 539)
	Level	n (%)	n%	n%
Age (years)	25–34	27 (9.5)	26 (9.3)	121 (22.5)
	35–44	102 (35.8)	101 (36.2)	236 (43.8)
	45–54	117 (41.1)	115 (41.2)	152 (28.2)
	55 and over	39 (13.7)	37 (13.3)	30 (5.6)
Gender	Male	105 (36.8)	105 (37.6)	252 (46.7)
	Female	180 (63.2)	174 (62.4)	288 (53.3)
Residence	Regional	94 (33.0)	93 (33.3)	121 (22.5)
	Metropolitan	191 (67.0)	186 (66.7)	418 (77.5)
Country of Birth	Australia	238 (83.5)	234 (83.9)	436 (80.9)
	U.K. / Ireland	18 (6.3)	18 (6.5)	33 (6.1)
	Other	29 (10.2)	27 (9.7)	70 (13.1)
Main language in household	English	276 (96.8)	270 (96.8)	496 (91.9)
	Non-English	9 (3.2)	9 (3.2)	44 (8.1)
Educational attainment	High School or less	75 (26.3)	72 (25.8)	148 (27.4)
	Trade Certificate	101 (35.4)	99 (35.5)	173 (32.0)
	Bachelor or higher	109 (38.3)	108 (38.7)	219 (40.6)
Employment	Full time	137 (48.1)	135 (48.4)	292 (54.2)
	Part time/casual	99 (34.7)	99 (35.5)	166 (30.8)
	Not working	49 (17.2)	45 (16.1)	82 (15.1)
Household income	Up to $30,000	19 (6.7)	18 (6.5)	36 (6.7)
	$30,001 - $50,000	36 (12.6)	34 (12.2)	48 (8.9)
	$50,001 - $80,000	41 (14.4)	40 (14.3)	90 (16.6)
	$80,001 - $100,000	44 (15.4)	44 (15.8)	75 (13.9)
	More than $100,000	116 (40.7)	115 (41.2)	231 (42.8)
	Don't know/not stated	29 (10.2)	28 (10.0)	60 (11.1)

weighting can result in minor rounding variations.

#Participants who indicated they were the parent or caregiver of a child under the age of 18 years.

† We removed participants listwise with missing data for any of the variables included in the analysis (raw data n = 6).

https://doi.org/10.1371/journal.pone.0230425.t001

Awareness of seasonal influenza vaccination recommendations for children and characteristics associated with awareness

In total, 32.8% (n = 177) of parents were aware that all children aged >6months to 5 years are recommended to receive the influenza vaccine whereas 51.4% of parents (n = 277) were aware of the recommendation that children with SRMCs should receive the influenza vaccine. Only 26% (n = 141) of parents were aware of both recommendations. The proportion of parents who were aware of the recommendation for children with a SRMC to receive the vaccine was higher in parents who were aware of the recommendation towards all children < 5 years (140/177, 79.1%) compared with parents who were not aware of the recommendation for children < 5 years (136/362, 37.6%) (p<0.0001).

In the fully adjusted models (Table 2), awareness of the recommendation for children <5 years to receive the vaccine was strongly associated with knowledge of the influenza recommendation for children with a SRMC (aOR 10.46, CI 4.44–24.63) or living in a metropolitan area (aOR 2.91, CI 1.19–7.09) (Table 2). The model also indicated a lack of awareness in those not working (aOR 0.13, CI 0.04–0.47), with trade level education (compared with high school) (aOR 0.25 CI, 0.09–0.71) and in those born in the UK or Ireland (aOR 0.19, CI 0.04–0.85). Whilst awareness of the recommendation for children with SRMC to receive the vaccine was

Table 2. Multivariable results for the effect of characteristics on awareness of the influenza vaccine recommendations for children aged < 5 years and children with SRMC (N = 539).

				Awareness of the influenza vaccine recommendations for children aged < 5 years						Awareness of the influenza vaccine recommendations for children with SRMC					
Characteristic		Level	Number of parents	crude			Adjusted Model all covariates			crude			Adjusted Model all covariates		
				OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
Demographic	Age (yrs)	-	539	0.99	(0.94–1.03)	0.562	0.99	(0.94–1.05)	0.787	1.01	(0.97–1.05)	0.513	1.02	(0.97–1.06)	0.460
	Gender	Female	288	0.98	(0.48–2.01)	0.957	1.00	(0.38–2.62)	0.998	1.78	(0.95–3.34)	0.071	2.47	(0.97–6.31)	0.058
	Residence location	Metropolitan (versus Regional)	418	2.03	(1.01–4.10)	0.047	2.91	(1.19–7.09)	0.019	1.12	(0.60–2.10)	0.712	0.77	(0.34–1.76)	0.535
	Country of birth	Australia	436	ref	-	-	ref	-	-	ref	-	-	ref	-	-
		UK/Ireland	33	0.27	(0.07–1.10)	0.067	0.19	(0.04–0.85)	0.030	3.72	(1.03–13.48)	0.046	7.63	(1.86–31.31)	0.005
		Other	70	1.36	(0.47–3.91)	0.566	0.48	(0.12–1.99)	0.313	1.48	(0.51–4.28)	0.469	3.93	(0.94–16.42)	0.060
	Household speaking language	Non-English (versus English)	44	1.64	(0.39–7.00)	0.502	2.83	(0.48–16.61)	0.250	0.85	(0.20–3.57)	0.827	0.28	(0.04–1.89)	0.190
	Highest educational level	High school or less	148	ref	-	-	ref	-	-	ref	-	-	ref	-	-
		Trade Certificate	173	0.29	(0.12–0.73)	0.008	0.25	(0.09–0.71)	0.010	0.88	(0.38–2.03)	0.770	1.64	(0.69–3.89)	0.266
		Bachelor or higher	219	0.64	(0.26–1.55)	0.321	0.55	(0.21–1.45)	0.230	0.77	(0.33–1.77)	0.535	0.89	(0.36–2.19)	0.808
	Employment type	Full time	292	ref	-	-	ref	-	-	ref	-	-	ref	-	-
		Part time/ casual	166	1.02	(0.45–2.31)	0.958	0.63	(0.26–1.56)	0.319	1.65	(0.82–3.34)	0.162	1.37	(0.59–3.19)	0.460
		Not working	82	0.16	(0.06–0.42)	<0.001	0.13	(0.04–0.47)	0.002	0.89	(0.36–2.18)	0.797	0.85	(0.31–2.33)	0.748

(*Continued*)

Table 2. (Continued)

Characteristic		Level	Number of parents	Awareness of the influenza vaccine recommendations for children aged < 5 years						Awareness of the influenza vaccine recommendations for children with SRMC					
				crude			Adjusted Model all covariates			crude			Adjusted Model all covariates		
				OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
Parental attitudes to immunisation	Vaccines are necessary to protect my children	Disagree*	9	ref	-	-	ref	-	-	ref	-	-	ref	-	-
		Neutral	29	0.56	(0.07–4.51)	0.588	1.00	(0.11–9.14)	0.997	1.40	(0.14–13.98)	0.775	1.13	(0.12–10.88)	0.917
		Agree**	502	0.45	(0.13–1.57)	0.211	0.51	(0.14–1.85)	0.305	0.92	(0.27–3.16)	0.895	0.63	(0.15–2.66)	0.531
	Belief that "immunisation is important to my everyday life"	No/ low importance#	15	ref	-	-	ref	-	-	ref	-	-	ref	-	-
		Neutral	13	0.35	(0.03–3.75)	0.388	1.62	(0.08–31.57)	0.749	0.71	(0.07–7.52)	0.773	0.15	(0.01–2.30)	0.173
		Important##	511	0.58	(0.09–3.82)	0.568	1.10	(0.13–9.45)	0.930	1.28	(0.19–8.40)	0.798	0.88	(0.09–8.77)	0.912
Health service use	Immunisation service provider	GP	355	ref	-	-	ref	-	-	ref	-	-	ref	-	-
		Community clinic	44	0.29	(0.09–0.94)	0.040	0.27	(0.05–1.48)	0.132	0.65	(0.24–1.79)	0.408	0.85	(0.18–4.10)	0.843
		Child health clinic	23	0.96	(0.19–4.92)	0.960	0.47	(0.09–2.61)	0.389	2.37	(0.66–8.56)	0.187	2.55	(0.77–8.48)	0.128
		Combination†	85	0.70	(0.26–1.86)	0.471	0.44	(0.18–1.06)	0.067	1.20	(0.52–2.78)	0.669	1.48	(0.62–3.51)	0.373
		Other††	23	0.53	(0.10–2.78)	0.450	0.19	(0.05–0.80)	0.024	4.32	(1.24–15.06)	0.022	13.40	(2.93–61.23)	0.001
		Don't vaccinate	9	1.29	(0.21–8.08)	0.782	0.92	(0.12–7.05)	0.933	0.76	(0.12–4.67)	0.763	0.23	(0.02–2.23)	0.203
	Youngest child has SRMC	Yes	26	0.48	(0.13–1.77)	0.271	0.95	(0.20–4.59)	0.949	0.92	(0.26–3.27)	0.899	0.74	(0.15–3.65)	0.713
Awareness other recommendations	Aware of influenza recommendation for children with SRMC	Yes	277	6.421	(2.73–15.11)	<0.001	10.46	(4.44–24.63)	<0.001						
	Aware of influenza recommendation for children <5 years	Yes	177							6.42	(2.73–15.11)	<0.001	10.22	(4.39–23.77)	<0.001

GP: general practitioner; SRMC: Special Risk Medical Conditions; Disagree

* included disagree/ strongly disagree; Agree

** included agree/ strongly agree; No/ low importance

included responses 'Not at all/somewhat important'

included Important/ Very important

† included a combination of providers (from MP or clinics)

††other were school (n = 9), hospital (n = 4), chemist (n = 4), Aboriginal Health Service (n = 4) and 'Could not recall' (n = 2).

https://doi.org/10.1371/journal.pone.0230425.t002

strongly associated with knowledge of the influenza recommendation for children <5 years (aOR 10.22, CI 4.39–23.77) or not being born in Australia [UK/ Ireland (aOR 7.63, CI 1.86–31.31); other (aOR 3.93, CI 0.94–16.42)]. The model also indicated awareness in female participants (aOR 2.47, CI 0.97–6.31).

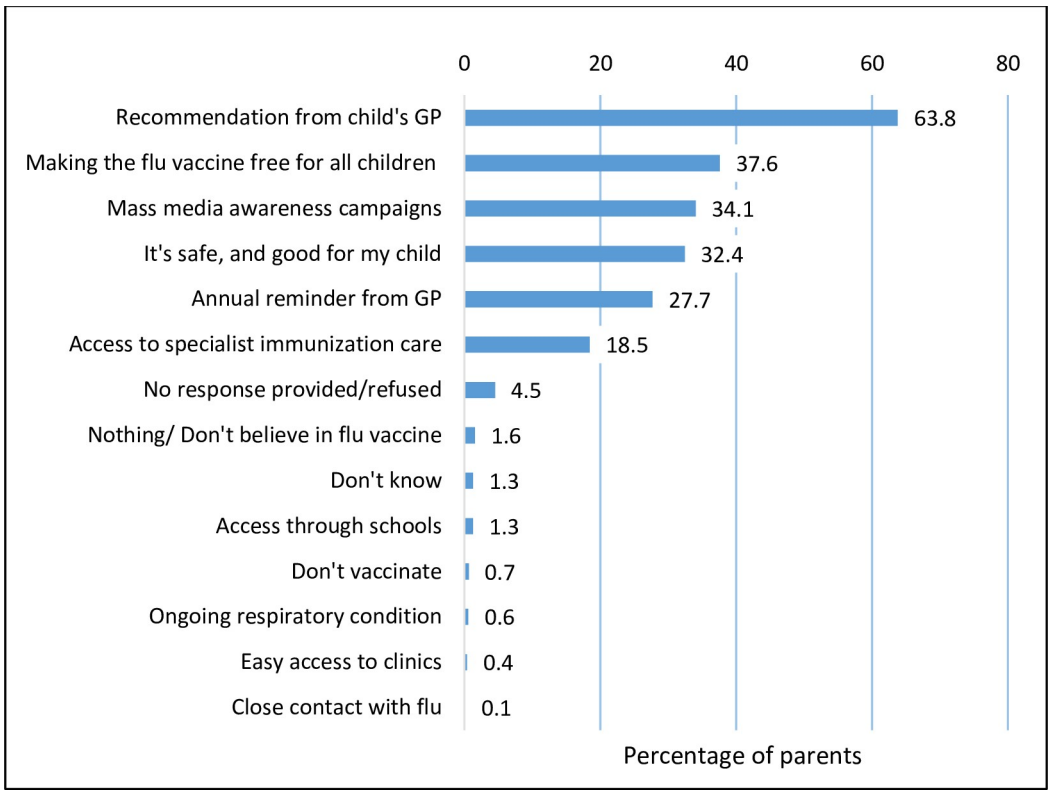

Fig 2. Potential influences towards future influenza vaccine receipt (N = 539).

https://doi.org/10.1371/journal.pone.0230425.g002

Future influenza vaccination cues to action

Parents indicated a GP recommendation as the most influential cue to future influenza vaccination receipt (63.8%, n = 344) (Fig 2). This was followed by access to the vaccine at no cost for all children (37.6%, n = 203), greater awareness through mass media (34.1%, n = 184) with a third (32.4%, n = 175) citing the belief in the benefit of the vaccine as a key influence. Excluding parents who did not vaccinate altogether(n = 9), 41.6% (221/530) vaccinating parents were in favour of their child receiving the influenza vaccine from a pharmacy in the future, 48.3% were opposed and 10% undecided. Higher support for pharmacy provision came from parents in regional areas (48.8% versus 39.7% metropolitan), those working full (45%) or part time (45.7%) compared with those not working (21.7%) and in parents with lower educational attainment (high school (47.7%), trade 42.2% or bachelor (37.2%)).

"What would be most influential for you in deciding to have your child receive a flu vaccine?" Multiple response—numbers will not total. GP: general practitioner.

Vaccination in general

Decision-making. Overall, 23.8% expressed either minor (19.8%) or high (4.0%) concern towards vaccination in general yet still vaccinated; 1.9% delayed or excluded vaccines and 1.7% did not vaccinate at all. While 72.6% of parents reported having no concerns towards vaccination 15.2% (59/391) of this group's responses to other vaccination belief questions indicated views opposing vaccination (S1 Fig). Of those reporting no concerns, 3.6% believed that vaccination is unnecessary to protect children, 10.2% thought vaccination was unnecessary as others are vaccinated, while 4.5% of this group held safety concerns. There were significant

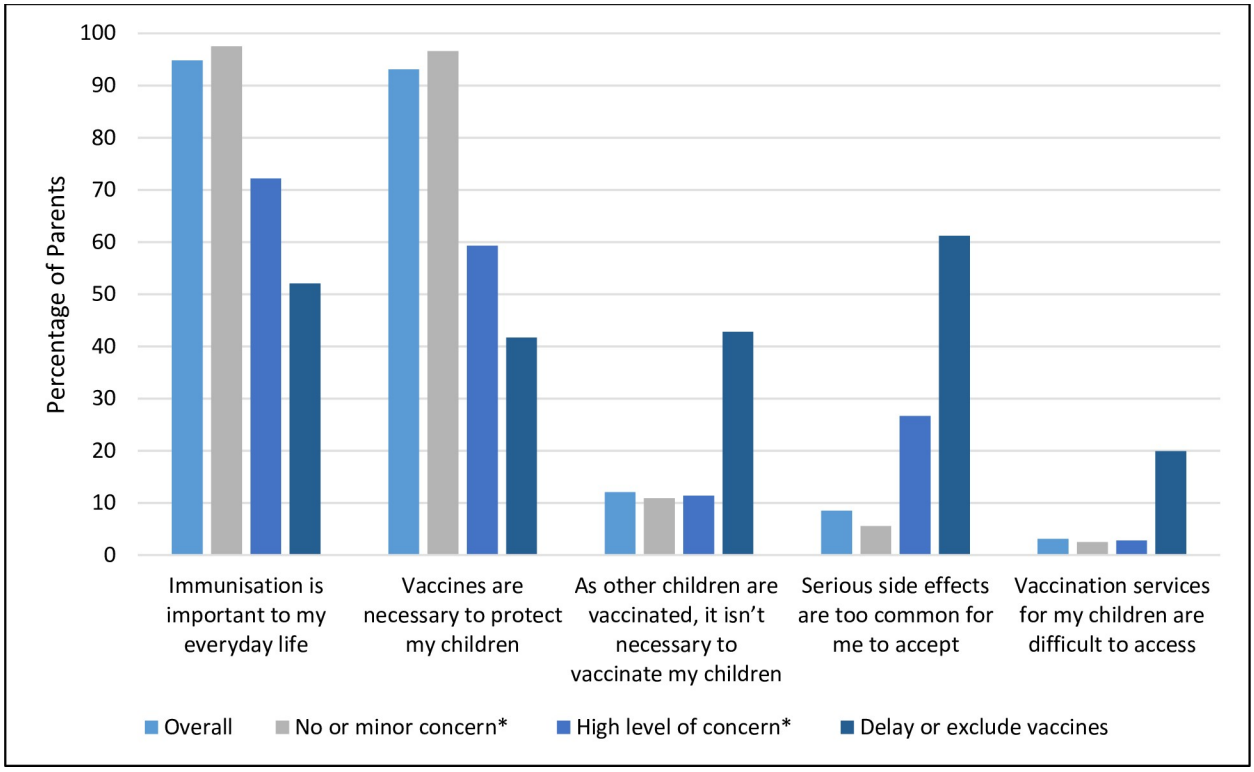

Fig 3. Parental agreement towards vaccination beliefs by level of concern towards vaccination (N = 539). * parent has vaccination concerns, but child receives all vaccines.

https://doi.org/10.1371/journal.pone.0230425.g003

differences for specific vaccination beliefs based on a parent's level of concern and behaviour towards vaccination (Fig 3). A higher proportion of parents who had no or minor concerns towards vaccination agreed/ strongly agreed that vaccines were necessary to protect their children (96.6%) compared to parents who reported a high level of concern (59.3%) or who delayed or excluded vaccines (41.7%) ($p < 0.0001$) (S3 Table). Of concern, a higher proportion of parents who delayed or excluded vaccines reported agreeing /strongly agreeing that their children's vaccinations were unnecessary as other children were vaccinated (42.8%) compared to those with no or minor concerns (10.9%) ($p<0.0001$). Over half of parents who delayed or excluded vaccines agreed/ strongly agreed that serious side effects were too common to accept (61.2%) compared to those with no or minor concerns (5.6%) ($p<0.0001$). A higher proportion of parents who delayed or excluded vaccines agreed/ strongly agreed that vaccination services were difficult to access (19.9%) compared to parents who reported a high level of concern (2.8%) or who had no or minor concerns (2.5%) ($p = 0.005$).

Immunisation service use (n = 530). All parents except those (n = 9) who indicated that their child did not receive any vaccinations provided information on their child's most recent immunisation service. Children's immunisations were received from their general practitioner (GP) (67%, n = 355.3), community immunisation clinic (8.4%, n = 44), child health clinic (4.3%, n = 23) or combination of clinics (16.2%) (Fig 4). Choice of immunisation provider was driven by proximity of the service to their home or easy access to (47.4%, n = 251) (S4 Table). Additionally, parents cited the immunisation service having their medical records (30.3%), being trustworthy (25.7%) or that a medical doctor provided the service (16.2%) as a reason for their choice of provider.

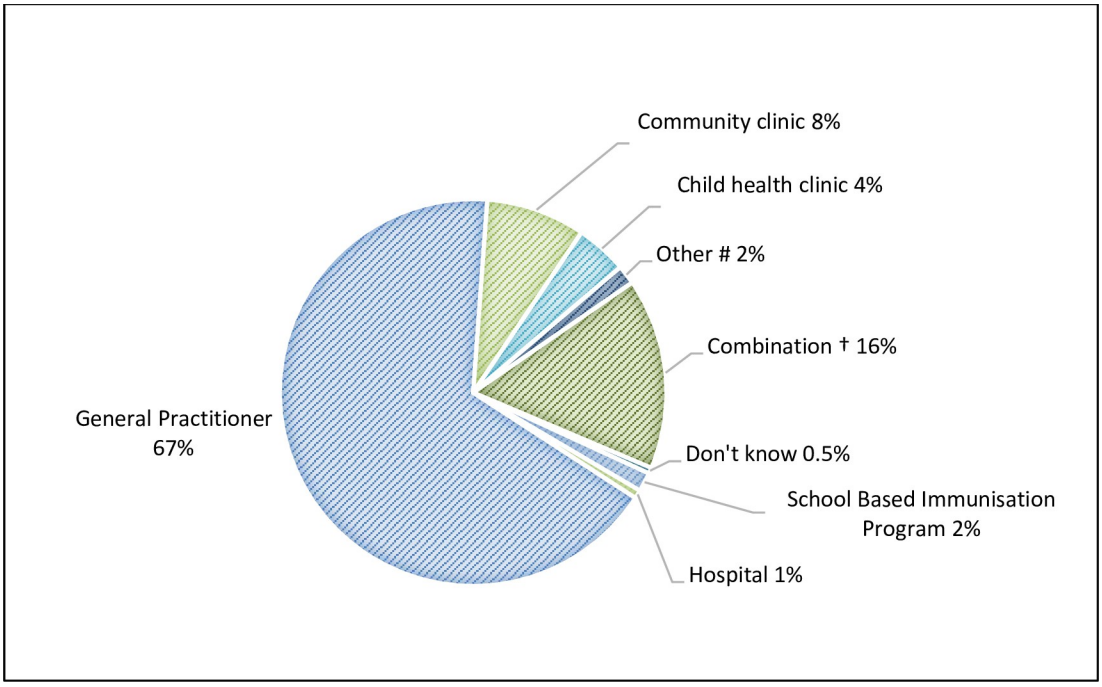

Fig 4. Children's immunisation providers (N = 530). These data exclude parents who did not vaccinate (n = 9; weighted data). Parents could only nominate one place. #: other were vaccinations administered by Aboriginal Health Service home visit (n = 4) and pharmacy (n = 4); † any combination of either family medical practitioner, community clinic or child health clinic.

https://doi.org/10.1371/journal.pone.0230425.g004

Cost and satisfaction with service. A small percentage of vaccinating parents (n = 72, 13.6%) recalled paying for the service to see their immunisation provider, such as medical practice, to obtain their child's most recent vaccination, with a further 8% (n = 42) unable to recall. There was high satisfaction with the experience with 93.8% rating it as good or excellent and less than two percent of vaccinating parents (1.6%, n = 8) rating their child's most recent vaccination service as fair or poor.

Sources of information on places to receive immunisations. A quarter (25.7%, n = 137) of vaccinating parents thought there was insufficient information on where they could obtain a vaccination for their child, with a further 6.9% undecided. Parents obtained information on the location of immunisation services from a variety of sources (S2 Fig). The major sources were medical practice (53.1%), news media (newspaper, radio or internet) (20%) and friends or other parents (12%).

Discussion

For parents, vaccination decision making on behalf of their children can be a complex process. Awareness of the schedule and current recommendations forms a considerable part of this process and a cue to further action. Our study found only low to moderate awareness towards influenza vaccine recommendations for children.

Our finding of modest parental awareness of the influenza vaccination recommendation for children <5 years is lower than another Australian study [13] where 20% of parents incorrectly believed it is not recommended in this age group, with another 30% unsure. This Australian study reports the level of parent's awareness towards the influenza vaccine recommendations for children from a community sample. Although, a recent study also found moderate awareness of the recommendation in parents of children with SRMCs [17], a much

higher proportion of those who were aware of the recommendation were likely to receive it, even in the absence of a healthcare professional's recommendation.

In our study, the strongest characteristic associated with awareness of the recommendation for children <5 was awareness of the recommendation for children with SRMC. However, given the change in effect size from the crude to final model, it is likely that some of the effect of 'awareness of the SRMC recommendation' was influenced by other variables. Being born in the UK/Ireland was also associated with lack of awareness with the difference in effect size between the crude and final adjusted model indicating little influence from other variables in the model. We also found a positive effect for residing in a metropolitan area that remained consistent, with little fluctuation in OR from the crude analysis to the final adjusted model indicating little influence from other variables in the model. The reason why residing in a metropolitan area showed such a strong effect is unclear. Research has previously identified regional GPs (non-metro) to be less likely to discuss non-funded immunisations. [32] While it is possible that this may indicate variability in access to GPs and medical care or an inadequate approach to influenza campaign messaging in general for regional areas, it may also be reflective of the health promotion messages and health education in regional areas more generally. The negative effect of not being employed also remained constant as did having trade level qualifications. It is possible that the type and amount of workforce participation mediate exposure to vaccination messages in general.

Our model exploring awareness of the recommendation for children with SRMC revealed the strongest characteristics associated with awareness was awareness of the recommendation for children <5 and being born outside Australia. Being a female participant was also associated with awareness of this recommendation and could reflect the fact that mothers are more likely to the primary carer of children with SRMC. The contrasting awareness towards the recommendations based on country of birth is interesting and possibly reflects policies towards recommendations in other countries. To further examine this and to test for the effect between 'Aware of influenza recommendation. . .' and other model variables, we included the related awareness variable last in each of the models and found it had only slight effect on other variables. For awareness of the recommendation (children < 5 years) the significance of immunisation provider diminished. It is possible that this had more to do with smaller numbers receiving vaccines at a community clinic (compared to GP) whilst influence of country of birth increased, with reduction in the boundaries and point estimate for those from UK/Ireland. Whilst for awareness of the recommendation for children with SRMC, the inverse is true with parents from Australia less likely to be aware of this recommendation.

Immunisation service use

Our study showed a similar pattern of immunisation service use to that reported previously [33] with 66.7–82.9% of our sample receiving children's vaccinations from their family GP. Our finding that the most influential factor for a child's future influenza vaccination, nominated by parents, was a GP recommendation, is consistent with previous research that found a key facilitator for hospitalised children or children with SRMC was healthcare provider (HCP) recommendation. [12, 17, 20–24, 34] However, little has focused specifically on the cues to action towards influenza vaccination for children in general.

Influenza vaccine access

Our study identified that access to vaccines may be problematic for particular groups of parents. More specifically, we found that parents who delayed or excluded vaccines reported finding vaccination services difficult to access. Additionally, that two in five parents would be

willing for their child to receive the influenza vaccine from a pharmacy is also worth highlighting. Although Australian pharmacists began administering the influenza vaccine from 2014 (with variation across jurisdictions), only some states have recently endorsed delivery to children as young as 10 years of age. [35, 36] In contrast, pharmacists in several countries including Argentina, the United Kingdom (UK), Canada, Portugal, New Zealand and the USA (United States of America) have been administering the influenza vaccine for almost a decade. [37–39] With Canada, Argentina, the UK and several states in the USA also endorsing pharmacist administration to young children, with deviation in the minimum age requirement across countries. [37–39] In order to improve access, alternative delivery sites should be given consideration. Although generally Australian children do not start schooling until 5 years of age, one delivery option could be school-based influenza vaccination programs, such as those implemented in the UK and the USA [40, 41], delivery in childcare or pre-school programs or broader access through community clinics at extended times which would improve access overall, particularly during the peak influenza vaccination season.

Community awareness of influenza vaccine

It is important to place community awareness within the context of recent Australian influenza vaccination events (Fig 1). In South Australia, at the time of this study the influenza vaccine was recommended but not funded for all children aged >6 months to < 5 years, although will be funded from 2020 as part of the NIP. [19] Our finding that a key motivator for 38.1% of parents was access to the vaccine at no cost is lower than other Australian studies reporting 48–55% of parents would be motivated by a free annual vaccine [13, 42] and this variance may be attributable to between study differences in the way data were obtained. These same studies also report stronger parental support towards a free influenza vaccine, than the actual cost being a financial barrier. [13, 42] The implications of a recommended but non-funded vaccine are well documented, with increased parental support for vaccines included on the NIP. [42, 43] This is also true of providers, with enhanced support for government funded vaccines and lower perceptions of disease severity towards non-funded vaccines previously noted.[32] Government funding implies to parents and providers alike that the vaccine is a priority, thereby influencing the decision-making process. Consideration of the implications of vaccine funding is therefore essential in the context of planning vaccination programs.

Parental vaccine concerns

A third of parents (32.8%) reported belief in the vaccine's safety and being beneficial to the child as a motivator to future vaccine receipt. Concerns about vaccine safety has remained a barrier to influenza vaccination in children complicated by the serious adverse events in 2010. [43, 44] Yet even prior to this, parental belief in the vaccine's safety was shown to be associated with support for vaccination. [42] More recent studies have also found belief in the vaccine's safety to be positively associated with vaccine uptake [12] but also suggest that negative publicity has lingered, complicated by parental knowledge towards the vaccine itself with a perception that the vaccine has not been around long enough, qualified by ensuring the safety of the vaccine. [45] Current data is encouraging however, as despite a 2017 poll indicating just 12% of parents believed the vaccine was safe this increased to 61% when the same poll was undertaken in 2018.[13, 46] This may have been influenced by 2017 being a high burden influenza season, with a number of deaths reported throughout Australia. [47]

Despite high recognition as to the importance of vaccines among parents in our study, a considerable number had vaccine concerns according to the Vaccine Communication Framework.[31] Parents who delayed or excluded vaccines placed lower importance on

immunisation and doubted the necessity of vaccination to protect children. Worryingly, comparable proportions of parents who were highly concerned towards vaccinations also held these beliefs. Also consistent with recent literature were vaccine safety concerns [48–51] however, the high number of parents citing 'free-riding' logic as a reason not to vaccinate is also of concern and is higher than other recent Australian studies [15, 48, 49] and may indicate a need to address both the importance and benefits of vaccinations for these parents. The fact that parents who reportedly had no hesitations to vaccinate answered one or more questions about vaccination beliefs in an opposing way suggests that decision-making is complex and integrates many external factors. Understanding all the barriers to vaccination is important and while scales to determine the extent of parental hesitancy exist [52] establishing a tool on which to measure and categorise the broader spectrum of hesitancy is needed. Addressing parent's vaccination concerns especially among those who are more hesitant is critical and requires an understanding of individual concerns, and provider communication, as highlighted previously [53], remains a key determinant of vaccine hesitancy. Moreover, GPs as primary health care providers play a key role in the immunisation landscape and have a pivotal role in providing recommendations for key targeted groups and new vaccines. [54–56] Given the high engagement of GPs in vaccination delivery, they remain in a key position of influence to support vaccine decision making, and communication resources such as SKAI—Sharing Knowledge About Immunisation [57] have been developed to assist in this process.

Previously much attention has focused on influenza recommendations for the elderly and the adult SRMC population with little attention paid to the awareness of influenza vaccination for children with SRMCs and children in general. The success of public health interventions rests of the swell of community attitudes towards such interventions and policies, the balance of perceived threat and risk of the intervention. Prior to this stage, however the community needs to be aware that a potential problem exists and be supplied with cues to action. A lack of awareness on the part of parents or HCPs may translate to missed opportunities for influenza decision making. Social norms may also influence community awareness, which has previously been highlighted in relation to children's' influenza vaccination [25, 42] and may warrant further examination.

The strength of this study is the unique perspective on awareness of influenza vaccine recommendations, with participants randomly sampled with weighting applied to improve the generalisability of the data. As a cross-sectional study however, it has some limitations. Although the study was conducted prior to implementation of state funded vaccine programs in Australia, our findings are still relevant to improving uptake of funded programs and have relevance to countries that recommend but do not fund influenza vaccine. Our sample was limited to those who spoke English and therefore the sample of non-English speaking parents was small. This is relevant considering that ethnicity has been identified as a significant factor in vaccination status [58, 59], with not speaking a country's dominant language previously highlighted as a barrier for influenza vaccination. [60, 61] Accordingly, eliciting the views of non-English-speaking households is important to improving uptake in these groups. As the Health Monitor used the EWP, people without a number listed would have been omitted from the sampling frame. This is relevant considering that mobile-only households have increased in South Australia from 5.2% in 2006 to 27.6% in 2013; while national estimates suggest that in 2016, 31% of Australian adults were mobile-only.[62, 63] The use of EWP increases the risk of non-coverage bias and may limit generalisation of findings to the wider South Australian population, with mobile-only households reported to be more likely to contain younger people, unemployed people, renters, and be of lower socio-economic status. [64] However, there is also evidence that when taking into account living arrangements 'parents and children' and 'single parent' households comprise lower proportions of mobile only households, 22% and

33% respectively, compared to people living in shared households (54%), boarders (41%) and living alone (37%), suggesting parents may be less likely to be omitted compared to other populations. [65] Possible confounders such as a child or parent history of a SRMC and vaccination status, ages and number of children in the household were also not collected. While this is a limitation, the purpose of this study was not to determine associations for specific groups but overall awareness within the 'parent' community. This is important given parents are influenced by social interactions, values, beliefs and comparison to others when considering childhood vaccinations. [66] Thus, although healthcare provider messages are key, vaccine decision making happens in conjunction with the indirect messaging from those around you, thereby adding another layer of vaccine messaging within the community.

The study also did not identify Aboriginal and Torres Strait Islander People which is important given Aboriginal and Torres Strait Islander children are recommended to receive the vaccine from 6-months of age and Aboriginal and Torres Strait Islander people of all ages are currently funded on the NIP. This area requires further study, although high coverage (60%) has been identified in the Northern Territory. [14] Even though parents were only from South Australia, limited information exists in Australia on parental awareness of influenza vaccination recommendations for children in the community and patterns of immunisation service use. Lessons learnt from this study could be applied to other jurisdictions around Australia, given the current models for influenza vaccine delivery are similar.

Conclusions

Parents display low awareness of influenza vaccination recommendations for children, with lower awareness based on place of residence, country of birth, workforce engagement and education level. Developing targeted communication strategies and resources and comprehensive media advertising could help to establish broader community awareness of recommendations for children aged < 5 years and children of all ages with SRMCs. Improving HCP knowledge of recommendations in rural communities as well as equitable assess to vaccines could improve influenza vaccine uptake in these regions. Health care professionals, particularly GPs and paediatric specialists should be encouraged to discuss influenza vaccine with parents at every opportunity.

Supporting information

S1 Table. Multivariable results for the effect of characteristics on awareness of the influenza vaccine recommendation for children aged < 5 years crude versus each additional block of variables (N = 539).
(PDF)

S2 Table. Multivariable results for the effect of characteristics on awareness of the influenza vaccine recommendation for children with SRMC crude versus each additional block of variables (N = 539).
(PDF)

S3 Table. Participants' vaccination beliefs by level of concern towards vaccination (N = 539).
(PDF)

S4 Table. Reason for choice of children's immunisation provider (N = 530).
(PDF)

S1 Fig. Number of responses to vaccination belief questions that indicate views opposing vaccination/hesitancy by parent reported level of concern towards vaccination in general (N = 539).
(PDF)

S2 Fig. Source of information on location of immunisation services (N = 530).
(PDF)

S1 File. Health Monitor questions 2016.
(PDF)

Acknowledgments

The authors would like to thank Professor Katina D'Onise and Dr Rebecca Nolan (SA Health) for their assistance with obtaining Health Monitor data.

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Supervision: Nigel W. Crawford, Helen S. Marshall.

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Writing – review & editing: Jane Tuckerman, Nigel W. Crawford, Helen S. Marshall.

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S1 Table. Multivariable results for the effect of characteristics on awareness of the influenza vaccine recommendation for children aged < 5 years crude versus each additional block of variables (N=539)

Characteristic		Level	Number of parents	crude			model 1			model 2			model 3			Adjusted Model all covariates		
				OR	95 % CI	p value	OR	95 % CI	p value	OR	95 % CI	p value	OR	95 % CI	p value	OR	95 % CI	p value
Demographic	Age (yrs)	-	539	0.99	(0.94-1.03)	0.562	0.99	(0.95-1.03)	0.749	0.99	(0.95-1.04)	0.699	1.00	(0.96-1.05)	0.985	0.99	(0.94-1.05)	0.787
	Gender	Female	288	0.98	(0.48-2.01)	0.957	1.35	(0.59-1.03)	0.481	1.33	(0.57-3.08)	0.505	1.49	(0.62-3.58)	0.369	1.00	(0.38-2.62)	0.998
	Residence location	Metropolitan (vs Regional)	418	2.03	(1.01-4.10)	0.047	2.33	(1.08-1.03)	0.032	2.35	(1.08-5.13)	0.031	2.51	(1.12-5.62)	0.025	2.91	(1.19-7.09)	0.019
	Country of birth	Australia	436	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-
		UK/Ireland	33	0.27	(0.07-1.10)	0.067	0.37	(0.10-1.03)	0.135	0.39	(0.10-1.59)	0.191	0.38	(0.08-1.73)	0.210	0.19	(0.04-0.85)	0.030
		Other	70	1.36	(0.47-3.91)	0.566	1.34	(0.43-1.03)	0.612	1.41	(0.45-4.45)	0.558	1.23	(0.38-4.03)	0.732	0.48	(0.12-1.99)	0.313
	Household speaking language	Non-English (vs English)	44	1.64	(0.39-7.00)	0.502	1.01	(0.18-1.03)	0.994	1.06	(0.18-6.12)	0.949	1.26	(0.20-8.06)	0.807	2.83	(0.48-16.61)	0.250
	Highest educational level	High school or less	148	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-
		Trade Certificate	173	0.29	(0.12-0.73)	0.008	0.28	(0.11-1.03)	0.005	0.29	(0.11-0.71)	0.007	0.30	(0.12-0.76)	0.011	0.25	(0.09-0.71)	0.010
		Bachelor or higher	219	0.64	(0.26-1.55)	0.321	0.49	(0.21-1.03)	0.106	0.49	(0.21-1.16)	0.105	0.51	(0.21-1.22)	0.128	0.55	(0.21-1.45)	0.230
	Employment type	Full time	292	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-
		Part time/casual	166	1.02	(0.45-2.31)	0.958	0.84	(0.35-1.03)	0.685	0.87	(0.35-2.11)	0.750	0.79	(0.32-1.95)	0.613	0.63	(0.26-1.56)	0.319
		Not working	82	0.16	(0.06-0.42)	<0.001	0.12	(0.04-1.03)	<0.001	0.11	(0.03-0.38)	<0.001	0.09	(0.02-0.33)	<0.001	0.13	(0.04-0.47)	0.002
Parental attitudes to immunisation	Vaccines are necessary to protect my children	Disagree*	9	ref	-	-				ref	-	-	ref	-	-	ref	-	-
		Neutral	29	0.56	(0.07-4.51)	0.588				0.79	(0.07-9.40)	0.849	1.42	(0.12-17.25)	0.785	1.00	(0.11-9.14)	0.997
		Agree**	502	0.45	(0.13-1.57)	0.211				0.37	(0.07-1.98)	0.244	0.39	(0.07-2.21)	0.288	0.51	(0.14-1.85)	0.305
	Belief that "immunisation is important to my everyday life"	No/ low importance#	15	ref	-	-				ref	-	-	ref	-	-	ref	-	-
		Neutral	13	0.35	(0.03-3.75)	0.388				1.03	(0.05-23.14)	0.984	0.50	(0.01-18.53)	0.709	1.62	(0.08-31.57)	0.749
		Important##	511	0.58	(0.09-3.82)	0.568				1.43	(0.13-16.31)	0.771	0.82	(0.06-11.44)	0.882	1.10	(0.13-9.45)	0.930
Health service use	Immunisation service provider	GP	355	ref	-	-							ref	-	-	ref	-	-
		Community clinic	44	0.29	(0.09-0.94)	0.040							0.24	(0.07-0.87)	0.030	0.27	(0.05-1.48)	0.132
		Child health clinic	23	0.96	(0.19-4.92)	0.960							0.88	(0.20-3.99)	0.873	0.47	(0.09-2.61)	0.389
		Combination†	85	0.70	(0.26-1.86)	0.471							0.58	(0.22-1.51)	0.263	0.44	(0.18-1.06)	0.067
		Other††	23	0.53	(0.10-2.78)	0.450							0.51	(0.13-1.98)	0.331	0.19	(0.05-0.80)	0.024
		Don't vaccinate	9	1.29	(0.21-8.08)	0.782							0.32	(0.03-3.91)	0.375	0.92	(0.12-7.05)	0.933
	Youngest child has SRMC	Yes	26	0.48	(0.13-1.77)	0.271							1.23	(0.33-4.61)	0.763	0.95	(0.20-4.59)	0.949
Aware of influenza recommendation for children with SRMC		Yes	277	6.421	(2.73-15.11)	<0.001										10.46	(4.44-24.63)	<0.001

Footnote: SRMC: Special Risk Medical Conditions; Disagree* included disagree/ strongly disagree; Agree** included agree/ strongly agree; No/ low importance# included responses 'Not at all/ somewhat important'; ## included Important/ Very important; † included a combination of providers (from MP or clinics); ††other were school (n= 9), hospital (n=4), chemist (n=4), Aboriginal Health Service (n=4) and 'Could not recall' (n=2).

S2 Table. Multivariable results for the effect of characteristics on awareness of the influenza vaccine recommendation for children with SRMC crude versus each additional block of variables (N=539)

Characteristic		Level	Number of parents	crude			model 1			model 2			model 3			Adjusted Model all covariates		
				OR	95 % CI	p value	OR	95 % CI	p value	OR	95 % CI	p value	OR	95 % CI	p value	OR	95 % CI	p value
Demographic	Age (yrs)	-	539	1.01	(0.97-1.05)	0.513	1.02	(0.98-1.05)	0.398	1.02	(0.98-1.05)	0.388	1.01	(0.97-1.05)	0.580	1.02	(0.97-1.06)	0.460
	Gender	Female	288	1.78	(0.95-3.34)	0.071	2.22	(1.02-4.84)	0.045	2.15	(0.99-4.68)	0.053	2.39	(1.09-5.25)	0.030	2.47	(0.97-6.31)	0.058
	Residence location	Metropolitan (vs Regional)	418	1.12	(0.60-2.10)	0.712	1.14	(0.57-2.27)	0.713	1.14	(0.57-2.28)	0.720	1.14	(0.54-2.39)	0.735	0.77	(0.34-1.76)	0.535
	Country of birth	Australia	436	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-
		UK/Ireland	33	3.72	(1.03-13.48)	0.046	4.06	(0.98-16.81)	0.053	4.34	(1.05-17.97)	0.043	4.76	(1.15-19.64)	0.031	7.63	(1.86-31.31)	0.005
		Other	70	1.48	(0.51-4.28)	0.469	3.43	(1.06-11.10)	0.040	3.41	(1.05-11.05)	0.041	3.77	(1.15-12.41)	0.029	3.93	(0.94-16.42)	0.060
	Household speaking language	Non-English (vs English)	44	0.85	(0.20-3.57)	0.827	0.38	(0.06-2.20)	0.279	0.42	(0.07-2.52)	0.342	0.31	(0.05-2.03)	0.224	0.28	(0.04-1.89)	0.190
	Highest educational level	High school or less	148	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-
		Trade Certificate	173	0.88	(0.38-2.03)	0.770	0.82	(0.36-1.86)	0.628	0.87	(0.37-2.01)	0.738	0.97	(0.43-2.19)	0.937	1.64	(0.69-3.89)	0.266
		Bachelor or higher	219	0.77	(0.33-1.77)	0.535	0.62	(0.26-1.44)	0.265	0.63	(0.27-1.48)	0.291	0.69	(0.30-1.63)	0.402	0.89	(0.36-2.19)	0.808
	Employment type	Full time	292	ref	-	-	ref	-	-	ref	-	-	ref	-	-	ref	-	-
		Part time/casual	166	1.65	(0.82-3.34)	0.162	1.07	(0.48-2.38)	0.872	1.13	(0.51-2.54)	0.762	1.22	(0.56-2.68)	0.613	1.37	(0.59-3.19)	0.460
		Not working	82	0.89	(0.36-2.18)	0.797	0.47	(0.17-1.31)	0.149	0.48	(0.17-1.36)	0.168	0.41	(0.16-1.07)	0.068	0.85	(0.31-2.33)	0.748
Parental attitudes to immunisation	Vaccines are necessary to protect my children	Disagree*	9	ref	-	-				ref	-	-	ref	-	-	ref	-	-
		Neutral	29	1.40	(0.14-13.98)	0.775				0.60	(0.04-8.00)	0.697	1.22	(0.07-21.83)	0.894	1.13	(0.12-10.88)	0.917
		Agree**	502	0.92	(0.27-3.16)	0.895				0.52	(0.08-3.58)	0.506	0.47	(0.06-3.45)	0.457	0.63	(0.15-2.66)	0.531
	Belief that "immunisation is important to my everyday life"	No/ low importance[#]	15	ref	-	-				ref	-	-	ref	-	-	ref	-	-
		Neutral	13	0.71	(0.07-7.52)	0.773				0.83	(0.03-27.00)	0.918	0.21	(0.00-9.18)	0.420	0.15	(0.01-2.30)	0.173
		Important[##]	511	1.28	(0.19-8.40)	0.798				1.98	(0.08-46.73)	0.673	0.84	(0.03-20.55)	0.917	0.88	(0.09-8.77)	0.912
Health service use	Immunisation service provider	GP	355	ref	-	-							ref	-	-	ref	-	-
		Community clinic	44	0.65	(0.24-1.79)	0.408							0.51	(0.14-1.85)	0.307	0.85	(0.18-4.10)	0.843
		Child health clinic	23	2.37	(0.66-8.56)	0.187							2.28	(0.59-8.81)	0.233	2.55	(0.77-8.48)	0.128
		Combination†	85	1.20	(0.52-2.78)	0.669							1.14	(0.46-2.82)	0.777	1.48	(0.62-3.51)	0.373
		Other††	23	4.32	(1.24-15.06)	0.022							7.60	(1.95-29.56)	0.003	13.40	(2.93-61.23)	0.001
		Don't vaccinate	9	0.76	(0.12-4.67)	0.763							0.19	(0.01-3.67)	0.268	0.23	(0.02-2.23)	0.203
	Youngest child has SRMC	Yes	26	0.92	(0.26-3.27)	0.899							0.85	(0.22-3.31)	0.810	0.74	(0.15-3.65)	0.713
Aware of influenza recommendation for children <5 years		Yes	177	6.420956	(2.73-15.11)	<0.001										10.21735	(4.39-23.77)	<0.001

Footnote: SRMC: Special Risk Medical Conditions; Disagree* included disagree/ strongly disagree; Agree** included agree/ strongly agree; No/ low importance# included responses 'Not at all/ somewhat important'; ## included Important/ Very important; † included a combination of providers (from MP or clinics); ††other were school (n= 9), hospital (n=4), chemist (n=4), Aboriginal Health Service (n=4) and 'Could not recall' (n=2).

S4 Table. Participants' vaccination beliefs by level of concern towards vaccination (N= 539)

Vaccination belief	Level of concern	Agree/ strongly agree		Neither disagree/ agree		Disagree/ strongly disagree	
		n	(%) 95% CI	n	(%) 95% CI	n	(%) 95% CI
Immunisation is important to my everyday life#	**Overall**	**511**	**94.8 (90.8-97.1)**	**15**	**2.7 (1.3-5.8)**	**13**	**2.5 (1.0-6.0)**
	No or minor concern*	485	97.5 (94.3-98.9)	13	2.5 (1.1-5.7)	0	0.0 (-)
	High level of concern*	16	72.2 (30.2-94.0)	0	0.0 (-)	6	27.8 (6.0-69.8)
	Delay or exclude vaccines	10	52.1 (23.5-79.4)	2	10.9 (1.5-49.2)	7	37.0 (13.2-69.4)
Vaccines are necessary to protect my children	**Overall**	**502**	**93.1 (88.8-95.8)**	**9**	**1.6 (0.6-3.9)**	**29**	**5.3 (2.9-9.4)**
	No or minor concern*	481	96.6 (93.1-98.3)	2	0.3 (0.1-1.5)	15	3.1 (1.4-6.6)
	High level of concern*	13	59.3 (21.9-88.4)	3	12.9 (1.7-56.2)	6	27.8 (6.0-69.8)
	Delay or exclude vaccines	8	41.7 (16.9-71.6)	4	21.3 (6.2-52.6)	7	37.0 (13.2-69.4)
As other children are vaccinated, it isn't necessary to vaccinate my children	**Overall**	**65**	**12.1 (8.0-17.8)**	**7**	**1.3 (0.5-3.4)**	**467**	**86.6 (80.8-90.8)**
	No or minor concern*	54	10.9 (6.9-16.9)	3	0.6 (0.1-2.7)	441	88.4 (82.4-92.6)
	High level of concern*	2	11.4 (2.1-43.9)	1	5.2 (0.6-32.1)	18	83.3 (51.1-96.0)
	Delay or exclude vaccines	8	42.8 (17.2-72.9)	3	14.8 (3.1-48.3)	8	42.4 (17.2-72.3)
Serious side effects are too common for me to accept	**Overall**	**46**	**8.5 (5.4-13.0)**	**14**	**2.5 (1.3-4.9)**	**480**	**89.0 (84.2-92.4)**
	No or minor concern*	28	5.6 (3.1-10.0)	12	2.4 (1.2-5.0)	458	92.0 (87.4-95.0)
	High level of concern*	6	26.7 (6.9-64.2)	1	2.8 (0.3-19.9)	15	70.5 (33.7-91.8)
	Delay or exclude vaccines	12	61.2 (31.0-84.7)	1	5.1 (0.7-30.0)	7	33.7 (12.1-65.1)
Vaccination services for my children are difficult to access	**Overall**	**17**	**3.1 (1.5-6.4)**	**9**	**1.6 (0.6-4.4)**	**514**	**95.3 (91.6-97.4)**
	No or minor concern*	12	2.5 (1.0-6.1)	6	1.2 (0.3-3.8)	480	96.4 (92.6-98.3)
	High level of concern*	1	2.8 (0.3-19.9)	3	12.9 (1.7-56.2)	18	84.3 (44.7-97.3)
	Delay or exclude vaccines	4	19.9 (5.6-51.2)	0	0.0 (-)	16	80.1 (48.8-94.4)

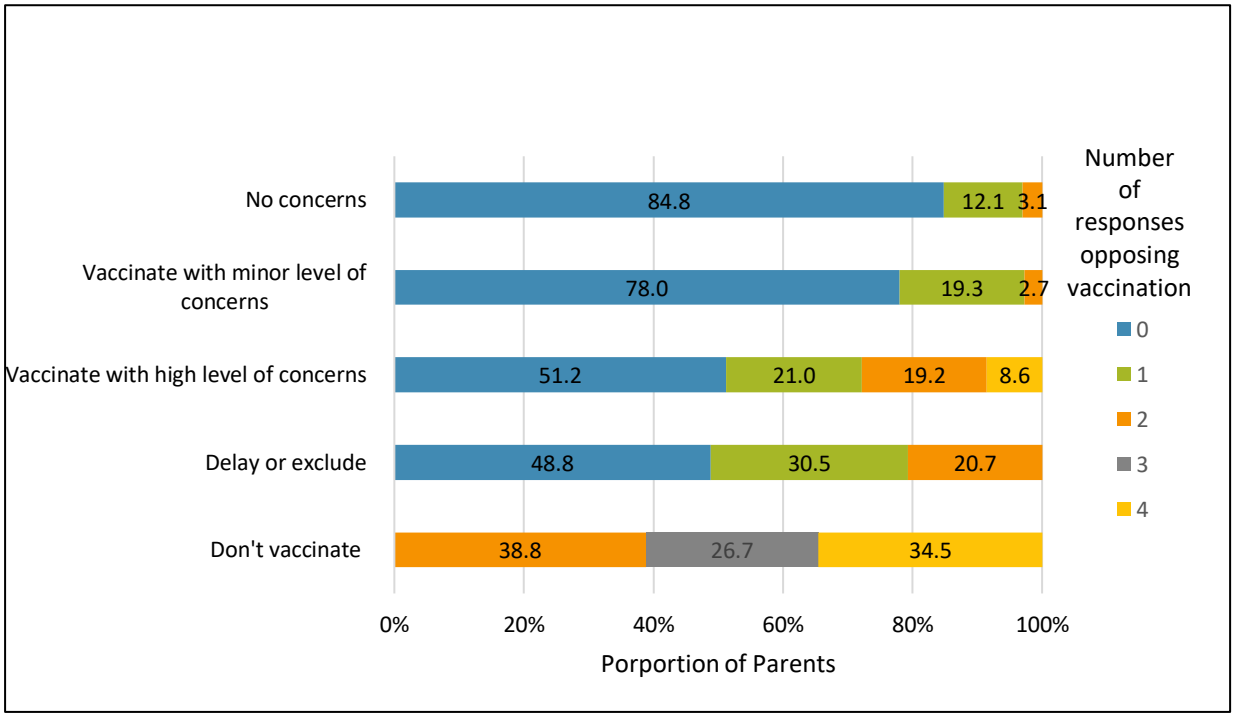
Footnote: * child receives all vaccines; # Participants were asked to rate the importance of immunisation to their everyday life on a Likert scale however responses were important/very important (agree/strongly agree), neutral and not at all or somewhat important (disagree/strongly disagree).

S5 Table. ***Reason for Choice of Children's Immunisation Provider (N=530)***

Reason for Choice of Immunisation Provider	n	% (95% CI)
Close to my home/easy to get to	251	47.4 (39.6 -55.3)
They have our medical records	161	30.3 (23.5 -38.1)
Trustworthy	136	25.7 (18.6 -34.4)
Medical doctor provides the service	86	16.2 (11.6 -22.1)
Can make an appointment	34	6.4 (4.0 -10.1)
No waiting times	31	5.8 (2.9 -11.3)
Opening hours	18	3.5 (1.4 -8.5)
Free of charge	17	3.3 (1.4 -7.2)
Other††	12	2.3 (1.0 -5.1)
Unaware of other options	12	2.3 (1.1 -4.8)
Only option- rural	10	1.9 (0.9 -3.9)
Staff rapport	10	1.9 (0.7 -5.2)
Vaccine availability	7	1.4 (0.5 -3.6)
No sick people in waiting area	3	0.6 (0.1 -2.6)
Experienced staff/technique	2	0.4 (0.1 -1.4)
Don't know	2	0.4 (0.0 -2.5)

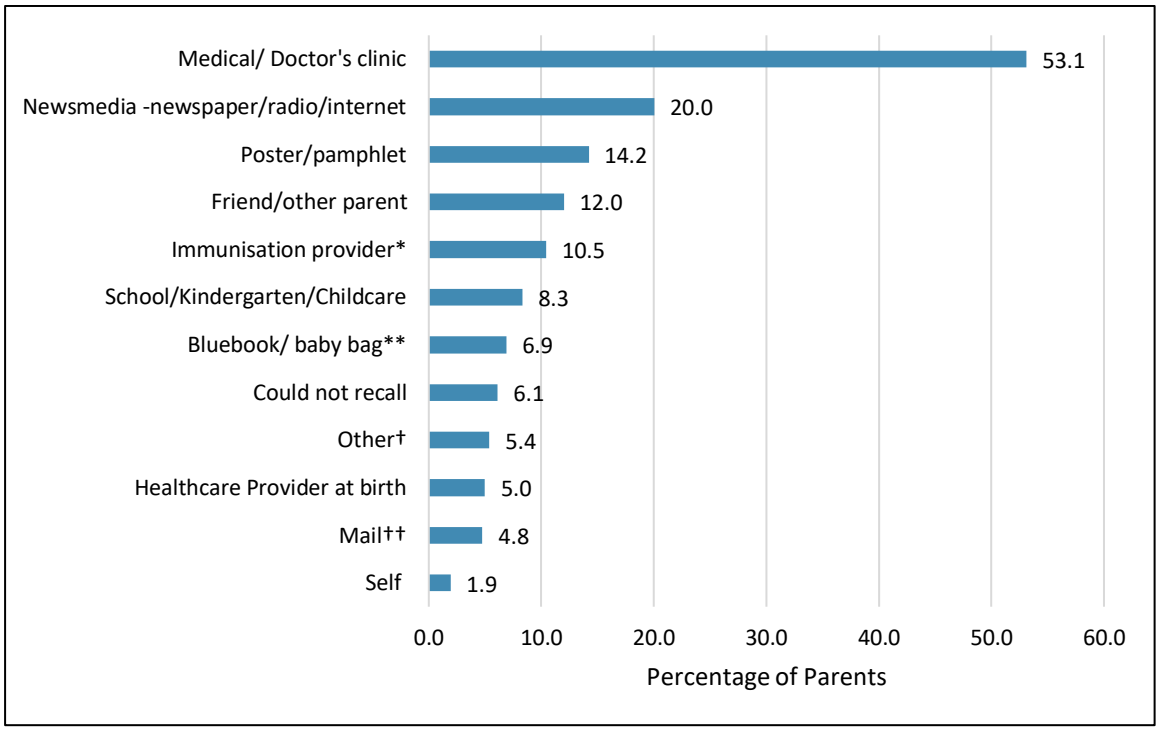
Footnote: Multiple response. These data excluded parents who did not vaccinate (n=9; weighted data); ††: other reasons were 'as listed in blue (baby) book' n=1, 'depends on the situation' n=1, 'word of mouth' n=3, child not yet vaccinated n=2, told to go there n=2 and other health service provided there n=3.

S3 Fig. Number of responses to vaccination belief questions that indicate views and beliefs opposing vaccination by parent reported level of concern towards vaccination in general (N=539)



Footnote: Questions included, 'How important do you think immunisation is to your everyday life?'; ' Vaccines are necessary to protect my child/children'; 'Because other children are vaccinated, it isn't necessary to have my child/children vaccinated'; 'Serious side effects are too common for me to accept'

S6 *Fig. Source of information on location of Immunisation Services (N=530)*



Footnote: Multiple response. *Community Immunisation Clinic, Child Health Clinic or hospital; ** Bluebook is a record book given to new parents at birth to record important health information and milestones; the baby bag is provided to parents at their first antenatal appointment and again at the child's birth; † other included work n=5, Centrelink n=17, email n=4, pharmacy/ drug store n=1, don't receive n=1; †† A number of parents reported the source of information as 'mail' (postal) however, as no further explanation was provided, we assume (but cannot be certain) that parents were referring to information received from Medicare after the baby was registered.

S7. Health Monitor Questions 2016

Demographic variables

A.1	How old are you?
A.2	Which age group are you in? Would it be…
A.3	Sex
A.4	Including yourself how many people aged 18 or over live in this household?
A.5	What is the Postcode of the house?
A.6	What town or suburb do you live in?
Z.1	Which of the following best describes your current marital status?
Z.2	What is your work status?
Z.3	Do you receive any of the following pension benefits?
Z.4	In which country were you born?
Z.5	What year did you arrive in Australia?
Z.6	Are you of Aboriginal or Torres Strait Islander origin?
Z.7	What is the main language you speak at home?
Z.8	Which best describes the highest educational qualification you have obtained?
Z.9	The next question is about housing. Is this dwelling…
Z.10	Household income…

Immunisation variables

B.4	On a scale of 1-5 how important do you think immunisation is to your everyday life?
B.16	Did you know that children with high risk medical conditions are recommended to receive a free flu vaccine each year?
B.17	Does your child have any of these high-risk medical conditions?
B.18	Did your child with a medical condition receive a flu vaccine this year?
B.19	Did you know that all children from 6 months of age to less than 5 years are recommended to receive the seasonal influenza vaccine?
B.20	What would be the most influential for you in deciding to have your child receive a flu vaccine?
B.21	Vaccines are necessary to protect my child/children (Likert scale)
B.22	Because other children are vaccinated, it isn't necessary to have my child/children vaccinated (Likert scale)
B.23	Serious side effects are too common for me to accept (Likert scale)
B.24	It is difficult to access vaccination services for my child/children (Likert scale)
B.25	Which of the following best describes your beliefs about vaccination?
B.26	Where do you choose to go to have your child vaccinated?
B.27	Do you have any difficulties in getting there?
B.28	What are some of those difficulties?
B.29	Why do you choose to go there over other clinics?
B.30	Do you think there is sufficient information in the community about where you can go to get vaccinated?
B.31	Where do you receive your information on where to go to get vaccinated?
B.32	How would you rate your experience of the most recent vaccination service your child received? (Likert scale)
B.33	Why was your recent vaccination experience poor?
B.34	Although vaccines provided under the National Immunisation Program are free, did you have to pay for the service at your most recent vaccination?
B.35	Adults are now allowed to get their flu vaccine from a pharmacy. If a pharmacist was allowed to vaccinate your child, would you take them there?

CHAPTER 6 POLICY AND PRACTICE - MEDICAL PROFESSIONALS' INFLUENZA VACCINATION PRACTICES

6.1 LITERATURE REVIEW

Medical care for children with SRMCs often involves medical professionals in the form of general practitioners and paediatric specialists, in primary and tertiary care settings respectively. It is thought that medical practitioners are in a key position to be able to advise and educate parents on the increased risk for influenza in children with SRMC and the importance of vaccination. (167)

6.1.1. Practice and Provider Barriers and Facilitators

Determining the barriers and enablers to recommendation implementation is necessary to develop strategies to improve the translation of recommendations into practice. Barriers to the implementation of clinical recommendations in general, have been examined previously. A systematic meta-review identified four factors influencing the implementation of clinical guidelines in general among health professionals: characteristics of the guidelines (resource requirements), characteristics of the professionals (awareness/ knowledge), patient characteristics (significant medical comorbidities) and environmental characteristics (e.g. lack of peer support).(168) In the Netherlands, a witness seminar, a form of qualitative research, explored the decision-making process of the implementation of systematic prevention programmes over the last 30 years, finding that major difficulties arise when introducing clinical guidelines into routine daily practice and that even if doctors are aware of recommendations, altering well established patterns of care is difficult. It found logistical and financial support were key facilitators. (169) In addition to this, scientific evidence was an important prerequisite; however this did not automatically translate to practice.(169)

Despite poor uptake data from several countries suggesting medical professionals' practices are not in line with recommendations, relatively few studies have examined the barriers towards vaccination for children with SRMCs at the provider level. A cross sectional survey of family practitioners and paediatricians (n=383) in the USA found low awareness of influenza severity, its complications, contraindications to vaccination and dosage.(73) Of note, almost 20% of physicians recommended vaccination <10% of the time, even to children with SRMCs, with a quarter of respondents thinking that none or <10% of children with SRMCs actually received influenza vaccination in their practice.(73) Rickert *et al*., used a cross-sectional survey to evaluate physicians perspectives on influenza vaccination in children with asthma or other cardiopulmonary conditions in four medical specialities: general paediatrics, family practice, allergy/immunology and paediatric pulmonary and found the single biggest deterrent amongst providers was involvement of another physician in the child's care.(74) The study also found the greatest barriers encountered to be confusion over responsibility for vaccination (74) and that strategies to identify children were only used by 50-60% of providers and reminders were only used by 20-30%.(74) These are higher than the proportions reported by O'Leary et al., who examined the self-reported practices of paediatricians and family physicians in the USA and found only a minority (38% and 28% respectively) of both groups reported using computerised methods to identify children with conditions at increased risk. Written, telephone or email reminders were only used by 43% of paediatricians and significantly less by family physicians (22%).

Data on the delivery practices and attitudes towards influenza vaccination specifically from the GPs and paediatric specialists who care for children with SRMCs in Australia is lacking. Zwar *et al* who explored the barriers towards influenza vaccination of people

aged 18- 65 years through focus groups with GPs and practice nurses found several practice and GP related barriers. (170) A lack of practice nurses to assist the GP workload, lack of systems to help identify/recall patients at increased risk being aged 18- 65 years, and a lack of knowledge of indicators for influenza vaccination, complexity of consultations with patients with chronic (increased risk) conditions and uncertainty of the evidence to support vaccination in patients at increased risk aged 18- 65 years, were all identified as barriers to vaccination. (170)

This chapter aims to answer the final three thesis research questions:

- What is known about the influenza vaccine recommendation practices among the treating GPs and paediatric specialists of children with SRMCs?
- What are the most important influencers driving adherence to recommendations?
- What are the experiences and challenges of general practitioners and paediatric specialists when delivering the influenza vaccine recommendation to parents of children with SRMC?

The next two sections report the results and data obtained from a cross-sectional survey and 26 semi structured interviews with medical practitioners.

6.2 INFLUENZA VACCINATION RECOMMENDATION: POLICY AND PRACTICES

Influenza vaccination practices and characteristics associated with a vaccine recommendation were evaluated in a cross-sectional survey with medical practitioners known to be caring for children with SRMC. Purposive sampling (171) was used to select participants, whereby parents of children with SRMC identified their child's current primary care provider and specialist. This ensured the sample was made up of medical practitioners actively involved in the care of children with SRMC from both tertiary and primary care settings, with data collected using a questionnaire from March to September 2018.

Medical practitioners who returned surveys comprised more than half of our total cohort of children with SRMC in our original study (Project 2). Characteristics associated with providing a recommendation were explored using univariable and multivariable analyses. The frequency with which medical practitioners 'always' recommended the vaccine was modest (38.4%), and this was associated with confidence in understanding all the conditions considered 'medically at risk' and perceived ownership of the responsibility to provide the recommendation. The resulting publication entitled "Seasonal influenza vaccination recommendations for children with special risk medical conditions: does policy meet practice?", has been submitted to the Journal of Paediatrics and Child Health. (https://onlinelibrary.wiley.com/journal/14401754)

This is the first study to examine the attitudes and challenges faced by medical practitioners caring for children with SRMC to deliver the influenza vaccine recommendations. Several attitudinal and structural barriers were identified that could be addressed to improve uptake. Although HCP provider recommendation is long

established as critical to vaccination receipt, understanding the context and logistical challenges affords an important understanding that may assist the implementation of an intervention, to improve influenza vaccine uptake.

6.2.2. Statement of Authorship

Statement of Authorship

Title of Paper	Seasonal influenza vaccination recommendations for children with special risk medical conditions: does policy meet practice?
Publication Status	☑ Published ☐ Accepted for Publication ☐ Submitted for Publication ☐ Unpublished and Unsubmitted w ork w ritten in manuscript style
Publication Details	Tuckerman J, Crawford NW, Marshall HS. Seasonal influenza vaccination recommendations for children with special risk medical conditions: does policy meet practice? Journal of Paediatrics and Child Health

Principal Author

Name of Principal Author (Candidate)	Jane Tuckerman
Contribution to the Paper	JT contributed to the study design, collected and analysed the data, prepared the first draft of the manuscript.
Overall percentage (%)	80%
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: 30/July / 2020

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	Nigel W Crawford
Contribution to the Paper	NC contributed to the study design, statistical analysis interpretation and critical review of the manuscript.
Signature	Date: 30/7/20

Name of Co-Author	Helen Marshall
Contribution to the Paper	HM contributed to study design, statistical analysis interpretation and critical review of the manuscript.
Signature	Date: 27 July 2020

6.2.3. Publication

Journal of Paediatrics and Child Health

doi:10.1111/jpc.14943

ORIGINAL ARTICLE

Seasonal influenza vaccination for children with special risk medical conditions: Does policy meet practice?

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Aim: Ensuring children with special risk medical conditions (SRMC) are protected from influenza is important. The study objective was to describe influenza vaccination practices of medical professionals caring for children with SRMC and explore characteristics associated with a vaccine recommendation.

Methods: Design: Cross-sectional survey. Setting/Participants: Treating paediatric specialists and general practitioners of children with confirmed SRMCs. Postal questionnaire administered from March to September 2018 (option for online response). Characteristics associated with providing a recommendation were explored using univariable and multivariable analyses.

Results: Overall response rate of 24.8% with the sample representative of the eligible population in terms of practice location and years practicing medicine. There was a higher response from females and sub-specialists. Of the 198 completed survey responders, 97.8% were aware of the recommendation, yet only 38.4% reported they 'always' routinely recommended influenza vaccine and fewer (19.5%) were very confident in understanding all 'medically at risk' conditions. Medical professionals were more likely to provide a recommendation always or mostly, if they received annual influenza vaccination themselves (adjusted odds ratio (aOR) 3.96, confidence interval (CI) 1.12–14.03), had confidence in understanding all 'medically at risk' conditions (aOR 1.82, CI 1.04–3.17) and perceived ownership of the responsibility to provide the recommendation (aOR 7.35, CI 1.67–32.26). Regional practising medical professionals were less likely to provide a recommendation (aOR 0.25 CI 0.10–0.70).

Conclusions: We need to improve medical professionals' knowledge through reminders and access to consistent and concise information about what constitutes a SRMC. Increasing medical professionals' engagement in the influenza vaccination programme could also provide a sense of responsibility fostering provider endorsement.

Key words: immunisation; infectious disease; influenza.

What is already known on this topic

1 Influenza vaccination rates in children at increased risk are suboptimal.
2 A medical professional recommendation greatly influences vaccine receipt.
3 General practitioners and paediatric specialists play a crucial role in the knowledge exchange concerning influenza vaccination for children with special risk medical conditions (SRMC).

What this paper adds

1 The number of general practitioners and paediatric specialists providing a recommendation for the influenza vaccine to parents of children with SRMC is modest.
2 A sense of responsibility, knowledge and confidence of determining 'at risk' conditions are key drivers towards providing a recommendation.
3 Medical professionals caring for children with SRMC require education to address a knowledge gap and access to concise information about what constitutes a SRMC.

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Conflict of interest: J Tuckerman and NW Crawford report no conflict. HS Marshall is an investigator on clinical trials of investigational vaccines sponsored by Industry. Her institution receives funding from Industry (GSK, Pfizer, Novavax) for Investigator led research. She does not receive any personal payments from Industry.

Accepted for publication 16 March 2020.

Indisputably, vaccination is one of the most important preventive measures, contributing globally to a decrease in the spread of serious infectious diseases and death.[1] General practitioners (GPs) play a major role in the Australian immunisation landscape: 11% of children's (<15 years) GP encounters are for immunisation, second only to acute respiratory infections (16%). In Australia, the majority of children's vaccinations are administered in general practice.[2,3] While 82.9% of children have at least one appointment with a GP annually,[3] for children also under the care of a paediatric specialist, delineating who should provide preventive health care can be challenging, depending on

health-care provider knowledge, practical limitations and parental preference.

Influenza is a serious respiratory disease, with the potential for significant complications including death; children are particularly vulnerable.[4] The 2019 influenza season started early with high notification rates, an unpreceded number of influenza-related hospitalisations and several deaths in young children.[5] Despite a funded recommendation for all individuals aged ≥6 months with a special risk medical condition (SRMC) to receive the influenza vaccine, coverage in Australian children with SRMC remains sub-optimal.[6–9]

The constant, key influence to vaccination in SRMC children is a recommendation from a medical professional,[7,10] considered most influential when delivered by the child's paediatric specialist.[7–9] However, data on the delivery practices and attitudes towards influenza vaccination in the context of Australian GPs and paediatric specialists who care for these children is scarce and there is likely to be a significant policy-practice gap.

The aim of this study was to describe, in a group of medical professionals caring for children with SRMCs, the frequency of influenza vaccine recommendation and explore characteristics associated with that recommendation. Additionally, we aimed to establish provider responsibility, medical professionals' confidence in understanding the conditions 'medically at risk' and their beliefs regarding influenza vaccination.

Methods

Study design

Observational cross-sectional study design consistent with STROBE recommendations.[11]

Study recruitment

Purposive sampling was used to select participants, enabling a homogenous sample of medical professionals actively involved in the care of children with SRMC from both tertiary and primary care settings. Medical professionals were identified as the children's treating paediatric specialists and GPs by the parents of children with confirmed SRMCs. The children were recruited as part of a separate cross-sectional study examining influenza vaccine coverage in children with SRMCs. Parents or guardians of children with SRMC attending outpatient clinics or inpatients at the Women's and Children's Hospital (WCH) were recruited using convenience sampling. Paediatric specialists worked either privately or at the WCH, the major provider of tertiary paediatric health-care services in South Australia. We identified the child's current nominated GP, specified either by name or medical practice. The WCH has a specialist immunisation service including a dedicated immunisation nurse and more recently an immunisation clinic (established in 2015).

Medical professional survey design

The postal survey (31 questions) was administered from March to September 2018. The survey collected data on demographics, experience, individual influenza vaccination behaviour and knowledge of influenza disease. Questions related to influenza vaccine attitudes, understanding of the official recommendations and practice. Additional questions asked participants to elaborate on barriers to recommending the vaccine and future educational resources. A personalised invitation letter was mailed to participants along with the questionnaire and reply-paid envelope. There was an option to complete the questionnaire online, accessible through a web link which was provided. A second mail-out was posted 6 weeks after the first, with a third and final contact made via email to all specialists with an email address and all GPs for whom we were able to contact via their medical practice email address.

Statistical analysis

We estimated that a sample size of 217 participants would allow us to determine the proportion of medical professionals providing an influenza vaccine recommendation to children with SRMC and to determine characteristics associated with vaccine recommendation with a ±5% precision at a 95% confidence level. Respondent attitudes to possible barriers to recommending the vaccine were assessed with a 5-point Likert scale from 'strongly agree' to 'strongly disagree', with agreement representing a positive belief. Negatively worded items were reworded and reverse scored. As appropriate, Likert scale responses were dichotomized based on distribution of responses.

Data were analysed using descriptive and inferential statistics; responses from open-ended questions were coded with content analysis. Concepts contributing to provider recommendation were investigated. Characteristics associated with routinely recommending the influenza vaccine always or mostly were explored using multivariable regression. Odds ratios (OR) and adjusted OR (aOR) were presented with 95% confidence intervals (CI). Stata (version 14.1) was used for all statistical analyses (StataCorp, College Station, Texas, USA). The study was approved by the Women's and Children's Health Network Human Research Ethics Committee.

Results

Study population

In total, 215 surveys were returned (Fig. 1). These returned surveys were the medical professionals of more than half of our total cohort of children with SRMC (n = 410) in our original study. The response rate was highest for specialists 27 of 48 (56%), with a lower rate from GPs 188 of 820 (21.3%), providing an overall response rate of 24.8%. A total of 198 surveys were completed, 18.2% (n = 38) online and 80.8% (n = 160) hard copy. As no differences between groups on any variables were identified, data were combined.

Description of study sample

Participant characteristics are summarised in Table 1. While the sample was representative of the eligible population in terms of practice location and years practicing medicine, there was a higher response from females, and sub-specialists. In all those with complete data (n = 198), there were equal proportions of males and females. Of paediatricians with complete data (n = 23), 10 were general paediatricians and 13 were subspecialist paediatricians.

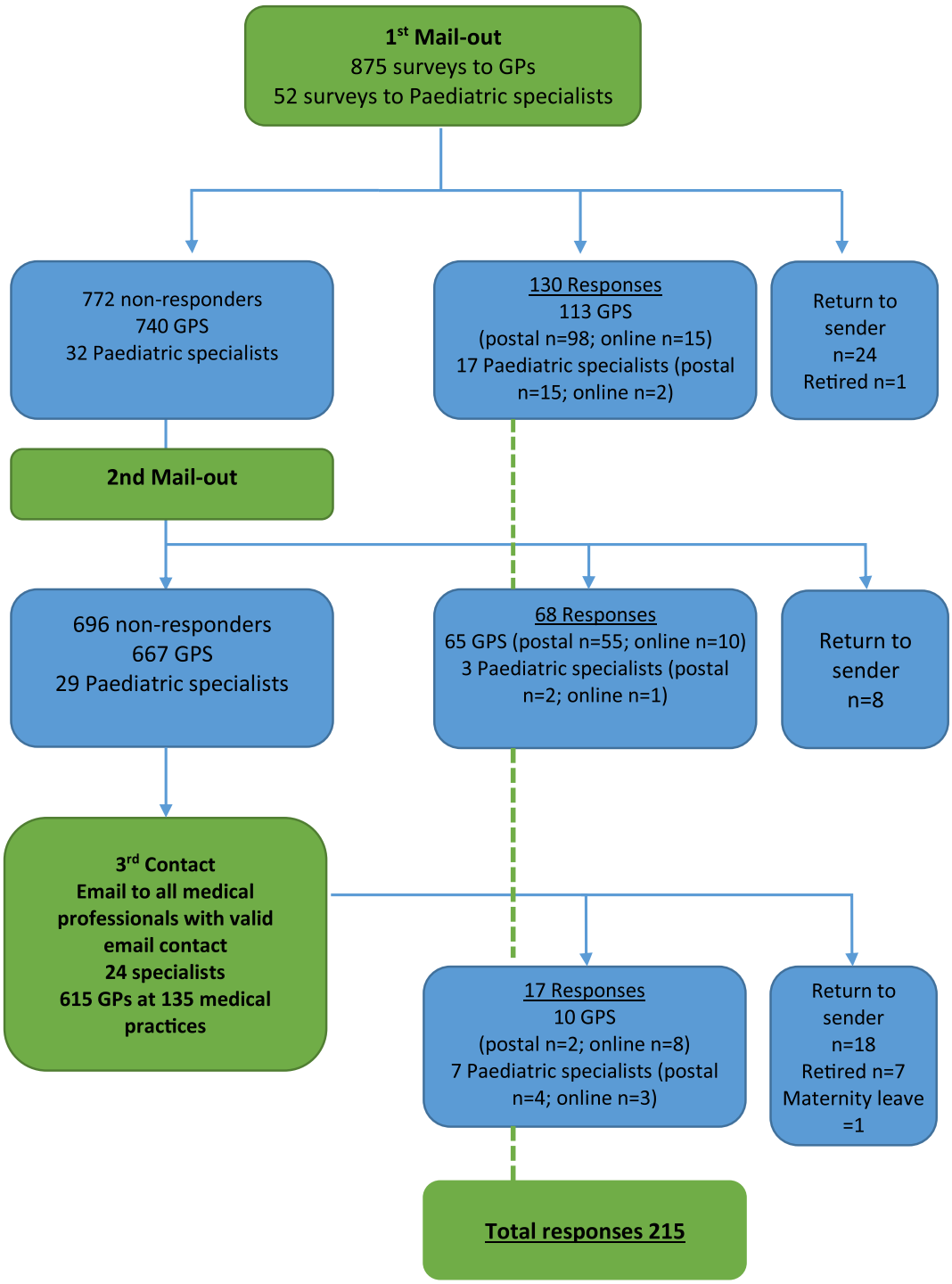

Fig. 1 Participant recruitment.

Medical professionals' vaccination, knowledge and perceptions of influenza disease

Overall 97.5% of medical professionals had previously received the influenza vaccine, with 90.9% reporting annual receipt (GPs 89%; specialists 100%, n = 23). The most influential driver to ever receiving the vaccine was self-protection (67%), followed by protecting patients (23%) and increased risk as a health-care professional (16%). Most medical professionals (90.9%) agreed/strongly agreed that healthcare workers in a hospital should be obliged to be vaccinated against

Table 1 Demographics of survey participants

Level	Eligible sample (*n* = 868†), *n* (%)	Returned surveys (*n* = 215), *n* (%)	Complete surveys (*n* = 198‡), *n* (%)
Gender			
Male	509 (58.6)	107 (49.8)	99 (50)
Female	359 (41.4)	108 (50.2)	99 (50)
Practice location			
Metro	675 (77.8)	161 (74.9)	148 (74.7)
Regional	193 (22.4)	54 (25.1)	50 (25.3)
Time practicing medicine, years			
<5	9 (1.0)	8 (3.7)	7 (3.5)
6–10	92 (10.6)	22 (10.2)	21 (10.6)
11–15	104 (12.0)	23 (10.7)	22 (11.1)
16+	663 (76.4)	162 (75.3)	148 (74.7)
Specialty of medical practitioner			
General practice (*n* = 820)	820 (94.5)	188 (87.4)	175 (88.4)
Subspecialist (*n* = 48)§§	48 (5.5)	27 (12.6)	23 (11.6)
General paediatrics	14	11	10
Cardiology	3	1	1
Endocrinology	4	2	2
ENT	3	1	1
Gastroenterology	4	2	1
Metabolic	2	2	2
Nephrology	3	1	1
Neurology	4	3	2
Orthopaedics	1	1	—
Paediatric surgery	1	—	—
Pulmonary medicine	5	2	2
Rheumatology	2	—	—
Urology	2	1	1
Work status			
Part time	—	81 (37.7)	74 (37.4)
Full time	—	134 (62.3)	120 (62.6)
Survey method			
Online	—	39 (18.1)	38 (19.2)
Postal	—	176 (81.9)	160 (80.8)

†Excludes surveys returned to sender, retired or on maternity leave. ‡Participants with missing data were excluded listwise from the dataset with the exception of those who were missing data for the variables, 'A recommendation is the responsibility of a child's specialist' (*n* = 4), "The 'at risk' medical conditions are well defined " (*n* = 2) and 'A universal recommendation for all children is justified' (*n* = 4). Denominators are clearly indicated where these data are presented. §Subspecialist categories presented by number only. Gender and time practicing medicine for the eligible sample derived from the Australian Health Practitioner Regulation Agency (Ahpra); practice location derived from practice address.
ENT, Ear Nose Throat.

influenza. Only 39.9% strongly agreed that influenza is serious compared to 84.3% who strongly agreed that influenza is serious for children with SRMC ($P < 0.0001$).

There was high awareness (98%) that children aged >6 months with SRMCs are recommended to receive the influenza vaccine (Table 2). Fewer medical professionals indicated (19.2%) they were very confident in understanding all the conditions considered 'medically at risk', with 28.3% being only somewhat confident or lower. Medical professionals expressed a need for concise information to define the qualifying medical conditions, with options for online formats to be available (Table 3).

Medical professionals' views

There was a high level of confidence in influenza vaccine: 97.9 and 91.4% of medical professionals, agreeed/strongly agreeedng it was both safe and effective, respectively. While only 68.9% regarded the wording of the recommendations for the 'at risk' medical conditions as well defined, there was only moderate support for a universal recommendation for all children (62.9%). Overall a higher proportion of medical professionals (*n* = 194) perceived providing a recommendation to be the responsibility of a GP compared to the responsibility of a specialist (92.8 vs. 84.5%). Medical professionals were divided on whether an incentive payment should be provided for vaccinating children

Table 2 Medical practitioners caring for children with special risk medical conditions (SRMCs) knowledge and practices towards influenza vaccination (n = 198)

Influenza vaccination knowledge or practice	Frequency/ Level	*n* (%)
Awareness of recommended for children aged >6 months with SRMCs to receive the influenza vaccine	Yes	194 (97.8)
	No	4 (2.0)
Discuss influenza infection with parents of children with SRMCs	Always	72 (36.4)
	Mostly	96 (48.5)
	Sometimes	27 (13.6)
	Never	3 (1.5)
Level of confidence in understanding all the conditions considered 'medically at risk' for influenza	Very	38 (19.2)
	Confident	104 (52.5)
	Somewhat	43 (21.7)
	A little	8 (4.0)
	None	5 (2.5)
Routinely recommend influenza vaccination to parents of children with SRMCs	Always	76 (38.4)
	Mostly	92 (46.5)
	Sometimes	28 (14.1)
	Never	2 (1.0)

Table 3 Suggested topics and format of future educational resources

Format
- Online webinars/modules (interactive)
- Email
- Online/Electronic printable leaflet
- Brochures/Poster displays
- Local face-to-face (including regional)
- Stickers for medical record books
- CPD events
- School education and parent groups
- You tube videos
- An app

Topics
- Succinct summary of recommendations (who, where and how)
- Benefits
- Complications/Sequelae
- Reminder lists of who/when to offer
- Numbers of deaths + hospitalizations (e.g. relative to meningococcal infections)
- Concise/better explanation of qualifying medical conditions (at risk)
- Vaccine efficacy/safety adjuvants preservatives etc.

with SRMCs, with 25.8% opposed, 32.8% in favour of a payment and 41.1% reporting no view.

Influenza immunisation practices

Whilst 84.9% of medical professionals reported discussing influenza disease with parents, the remainder reported only sometimes (13.6%) or never (1.5%) having such discussions (Table 2). Only 38.4% reported 'always' providing a recommendation for the influenza vaccine. Participants' level of confidence in understanding the 'at risk' conditions was associated with providing a vaccine recommendation to parents and only 66.2% reported prioritising influenza vaccination (Table 4). In total, only 37.4% of medical professionalss reported having a recall or reminder system for children with SRMC, with an additional 13.7% unsure.

Characteristics associated with routinely recommending the influenza vaccine

In the adjusted model (Table 5), medical professionals were more likely to provide a recommendation always or mostly if they received the vaccine themselves yearly (aOR 3.96, CI 1.12–14.03), had confidence in understanding all qualifying 'medically at risk' conditions (aOR 1.82, CI 1.04–3.17) and perceived ownership towards providing a recommendation (aOR 7.35, CI 1.67–32.26). Those practising in a regional location were less likely to provide a recommendation (aOR 0.25, CI 0.10–0.70).

Discussion

This study found that although GPs and paediatric specialists perceive influenza to be a serious infection in children with SRMC, a considerable sub-group do not recommend the influenza vaccine regularly to these children. Medical professionals indicate only moderate confidence in understanding the conditions 'medically at risk' and in endorsing the current 'at risk' groups as being well defined. Additionally, it remains unclear to GPs and specialists who owns responsibility for providing the recommendation.

Characteristics associated with providing the recommendation were a sense of responsibility, practicing medicine in a metropolitan area and receiving the vaccine annually themselves. From the crude to adjusted model, the effect of 'sense of responsibility' attenuated slightly with the influence of other variables, whilst the positive effect for practicing medicine in a metropolitan area remained relatively consistent. The reason for the difference between practicing locations is unclear. Regional GPs may require greater influenza resources, but it may also suggest that children with SRMC living in regional areas who are under the care of a sub-specialist may be less engaged with local primary health-care providers, so the requirement for providing a recommendation is not as clear. Previous research identifies differences in regional areas, with fewer GPs discussing non-funded immunisations and parents not as aware of current children's influenza recommendations. [38].

In the multivariable model, understanding all the conditions considered 'medically at risk' was associated with providing a recommendation. This may suggest medical pofessionals' knowledge and confidence of 'at risk' conditions could be key drivers towards providing a recommendation. Previous studies also indicate that in addition to a lack of confidence towards general vaccine related knowledge and strong support for more vaccine education, paediatricians want more education and clearer influenza vaccine recommendations.[12,13] In addition to provider education, serious consideration is also required regarding what type of structural remedies could result in high uptake. Hospital changes could promote and normalise vaccination as part of SRMC care and help to ensure specialists provide

Table 4 Medical practitioners caring for children with SRMCs beliefs towards influenza vaccination (*n* = 198)

Belief	Routinely recommend influenza vaccination for children with SRMCs	Strongly disagree/ Disagree, *n* (%)	No view either way, *n* (%)	Strongly agree/ Agree, *n* (%)
Consultation time sufficient to discuss influenza vaccination	Overall	33 (16.7)	31 (15.7)	134 (67.7)
	Always	12 (15.8)	6 (7.9)	58 (76.3)
	Mostly	13 (14.1)	21 (22.8)	58 (63.0)
	Sometimes/Never	8 (26.7)	4 (13.3)	18 (60.0)
Influenza vaccination is a clinical priority	Overall	30 (15.2)	37 (18.7)	131 (66.2)
	Always	6 (7.9)	6 (7.9)	64 (84.2)
	Mostly	15 (16.3)	26 (28.3)	151 (55.4)
	Sometimes/Never	9 (30.0)	5 (16.7)	96 (53.3)
Complexity of a childs medical condition does not limit discussing vaccination	Overall	32 (16.2)	26 (13.1)	140 (70.7)
	Always	9 (11.8)	4 (5.3)	63 (82.9)
	Mostly	14 (15.2)	19 (20.7)	59 (64.1)
	Sometimes/Never	9 (30.0)	3 (10.0)	18 (60.0)
Providing a recommendation not limited by certainty, that 'at risk' condition qualifies	Overall	23 (11.6)	33 (16.7)	142 (71.7)
	Always	4 (5.3)	5 (6.6)	67 (88.2)
	Mostly	14.0 (15.2)	18 (19.6)	60 (65.2)
	Sometimes/Never	5.0 (16.7)	10 (33.3)	15 (50.0)
I feel equipped to respond to parents questions, even if a childs medical care involves a specialist	Overall	25 (12.6)	37 (18.7)	136 (68.7)
	Always	6 (7.9)	8 (10.5)	62 (81.6)
	Mostly	11 (12.0)	23 (25.0)	58 (63.0)
	Sometimes/Never	8 (26.7)	6 (20.0)	16 (53.3)

Table 5 Multivariable regression for the effect of characteristics on routinely recommending the influenza vaccine mostly or always (*n* = 198)

		Crude			Adjusted model†		
Characteristic	Level	OR	(95% CI)	*P* value	aOR	(95% CI)	*P* value
Demographic variables							
Regional (vs. metro)		0.32	(0.14–0.73)	0.007	0.26	(0.10–0.70)	0.007
Full time (vs. part time)		1.60	(0.71–3.59)	0.257	1.87	(0.74–4.72)	0.185
HCP type	GP	Reference		—	Reference		—
	Sub specialist	1.63	(0.36–7.43)	0.531	1.39	(0.23–8.54)	0.72
Time practicing medicine, years	<16	Reference		—	Reference		—
	16+	1.14	(0.47–2.79)	0.769	0.78	(0.26–2.34)	0.652
Receives vaccine yearly	Yes	3.41	(1.16–10.01)	0.026	3.96	(1.12–14.03)	0.033
Views and beliefs towards influenza and influenza vaccination							
Influenza vaccine is effective	Yes	1.50	(0.40–5.69)	0.551	0.88	(0.19–4.07)	0.865
Influenza vaccine is safe	Yes	1.96	(0.20–19.57)	0.565	2.47	(0.18–33.04)	0.496
Consultation time sufficient to discuss influenza vaccination		1.41	(0.62–3.22)	0.418	1.59	(0.58–4.42)	0.370
Influenza vaccination is a clinical priority		2.06	(0.91–4.62)	0.081	1.15	(0.41–3.22)	0.795
I feel equipped to respond to parents questions		2.06	(0.91–4.65)	0.083	1.09	(0.37–3.16)	0.878
Confidence in understanding all of the conditions considered 'medically at risk'		2.26	(1.46–3.50)	<0.001	1.82	(1.04–3.17)	0.036
A recommendation is my responsibility		10.47	(3.05–35.98)	<0.001	7.35	(1.67–32.26)	0.008

†Adjusted for all other variables. aOR, adjusted odds ratio; CI, confidence interval; HCP, health care professional; OR, odds ratio.

recommendations to parents. Discussion of influenza vaccination in patient groups during hospital staff meetings or the establishment of registers of children with SMRC and use of messaging software, currently used for appointment reminders, could assist in improving uptake. Alternatively, structural remedies at the practice level incorporating the use of electronic medical record systems that continue to prompt at each visit and encourage an ongoing conversation have demonstrated effectiveness.[14,15]

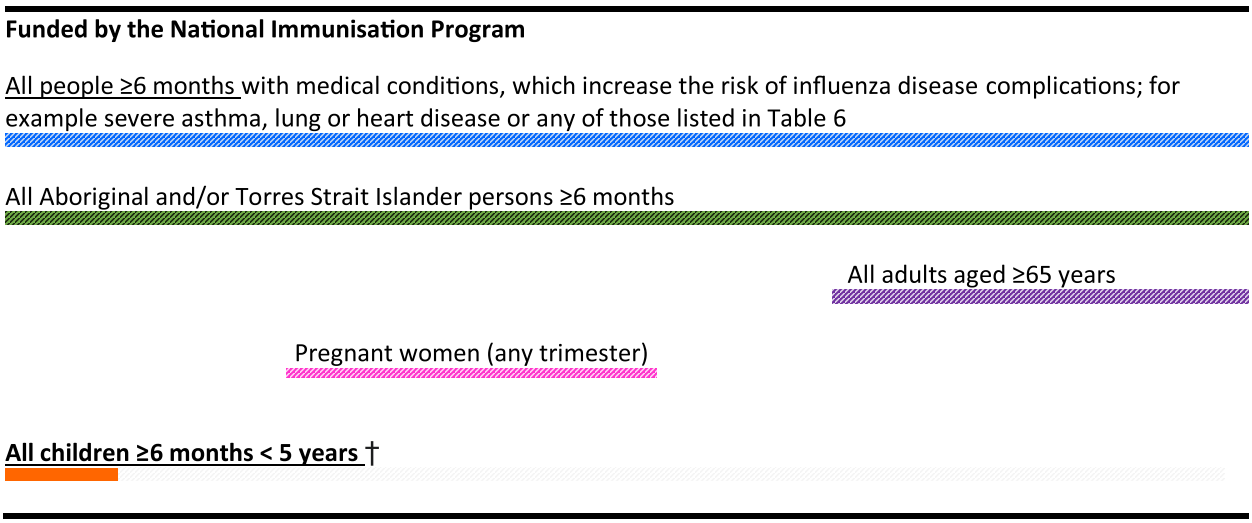

Fig. 2 Eligibility for funded influenza vaccines for 2020.

Table 6 Medical conditions associated with an increased risk of influenza disease complications and for which individuals are eligible for free vaccination under the National Immunisation Program (Reproduced from Australian Technical Advisory Group on Immunisation[20])

Category	Vaccination strongly recommended for individuals with the following conditions
Cardiac disease	Cyanotic congenital heart disease, congestive heart failure, coronary artery disease
Chronic respiratory conditions	Severe asthma, cystic fibrosis, bronchiectasis, suppurative lung disease, chronic obstructive pulmonary disease, chronic emphysema
Chronic neurological conditions	Hereditary and degenerative CNS diseases, seizure disorders, spinal cord injuries, neuromuscular disorders
Immunocompromising conditions	Immunocompromised due to disease or treatment, asplenia or splenic dysfunction, HIV infection
Diabetes and other metabolic disorders	Type 1 or 2 diabetes, chronic metabolic disorders
Renal disease	Chronic renal failure
Haematological disorders	Haemoglobinopathies
Long-term aspirin therapy in children aged 6 months to 10 years	These children are at increased risk of Reye syndrome following influenza infection

HIV, human immunodeficiency virus.

Nationally, increasing the capability of the Australian Immunisation Register to capture risk status could provide another mechanism for recommendations to reach parents and help establish accurate coverage information for this priority target group, which is missing on a large scale globally.[16]

This study identifies that detailed awareness of the recommendation is an important knowledge gap, which may result in hesitancy to recommend the vaccine. Regardless of risk status, the vaccine is recommended for all people >6 months who would like to be protected against influenza.[17] If medical professionals have difficulty in determining whether a child identifies at risk according to the National Health and Medical Research Council recommendations, it is unlikely that the vast majority of parents would make this distinction individually without medical guidance.

In Australia, the influenza vaccine is currently only funded under the NIP for those in specific recognised risk groups >6 months of age, all Aboriginal and Torres Strait Islander persons, those with medical conditions, the elderly and pregnant women eligible (Fig. 2). Since 2018, all Australian states have funded universal influenza vaccination for all children <5 years of age, and the influenza vaccine will be funded on the NIP for children aged <5 years from 2020, alleviating the challenge to identify young children with SRMC. However, this still leaves Australian children and adolescents with SRMC aged ≥5 years in a targeted programme. Elsewhere universal childhood influenza vaccination programmes have increased coverage in children with SRMC.[18]

Australian studies suggest a recommendation to be highly influential when delivered by a specialist,[7–9] yet we found some specialists did not perceive providing a recommendation to be their role. Another study[13] of paediatricians found 16.8% disagreed administering influenza vaccination was their role. Conversely, a study exploring the reasoning behind decisions to immunise young children against influenza from primary care providers found discussions surrounding influenza vaccination to be opportunistic, with deferment to paediatricians regarding children with SRMC.[19] Whilst vaccine administration may be impractical in some circumstances, fostering a greater collaborative partnership could assist all medical professionals treating children with SRMC to take joint ownership for providing the recommendation, with repeated consistent messaging reinforcing its importance to parents.

The ATAGI is currently working on consistency in identifying categories of 'at risk' groups identified in the Australian Immunisation Handbook,[17] including specific medical conditions and the increasing use of immunosuppressive therapies in these patient groups. (Personal communication, N Crawford) This will need to be communicated to all stakeholders involved in the provision of influenza vaccination. The 2019 ATAGI statement on seasonal influenza recommends vaccination for people with any of the medical conditions listed in Table 6.[20] Additionally, the Guidelines for preventive activities in general practice (Red Book)[21] published by the RACGP should include the most recent influenza vaccination recommendations to ensure messages are within reach of the broadest audience of GPs and therefore remain consistent with ATAGI and specialists.

This is the first study to provide the unique perspective of Australian medical professionals linked to a child with a SRMC, ensuring we captured GPs and paediatric specialists at the core of primary health prevention for these children. Our study is not without limitations, particularly the low response rate despite the use of reminders[22], and although paediatric specialists had a higher response rate, most respondents were GPs. This likely represents the workload of Australian GPs and paediatric specialists and is consistent with other surveys.[23,24]

Conclusion

We need to improve medical professionals' knowledge through reminders and access to consistent and concise information about what constitutes a SRMC. Increasing medical professionals' engagement in the influenza vaccination programme could also provide a sense of responsibility fostering provider endorsement.

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6.3 CHALLENGES TO PROVIDING A RECOMMENDATION

The experiences and challenges faced by medical practitioners to deliver the influenza vaccine recommendation and vaccine to children with SRMC were examined using semi-structured one-to-one interviews with medical professionals working in hospitals and community medical practices in (predominately) South Australia. Participants were identified from respondents who completed a separate quantitative survey on the same topic (Section 6.2). The initial survey participants, paediatric specialists and general practitioners, were the treating medical professionals of children with known SRMCs. The original survey with medical practitioners was anonymous but respondents were asked to provide their contact details if they were willing to participate in a one-to-one interview. Interviews were undertaken between June and December 2018.

Twenty-six medical professionals participated in the study: 21 GPs and 5 paediatric specialists. Thematic analysis and inductive coding were used to examine data. Identified themes, grouped by COM-B category, included: Capability - communication and knowledge and Motivation - clinical prioritisation, responsibility/professional role and recommendation as standard practice. However, much discussion was focused on barriers and potential drivers that fall under Opportunity - such as communication resources, social acceptance and normalisation and consistent messaging, with systems to identify children, prompt clinicians and remind parents reported as the most urgently required.

The resulting publication entitled “Influenza vaccination: a qualitative study of practice level barriers from medical practitioners caring for children with special risk medical conditions”, has been submitted to the “Vaccine” journal.

The study offered a unique perspective through interviewing a group of medical practitioners known to be involved in the care of children with SMRC. The absence of structural systems supporting the recommendation to be implemented was an important finding. At the practice level, several structural solutions to these identified barriers are required to increase influenza vaccine coverage for children with SRMC, along with improving collaboration and communication between tertiary and primary care providers.

6.3.4. Statement of Authorship

Statement of Authorship

Title of Paper	Influenza vaccination: a qualitative study of practice level barriers from medical practitioners caring for children with special risk medical conditions.
Publication Status	☐ Published ☐ Accepted for Publication ☑ Submitted for Publication ☐ Unpublished and Unsubmitted w ork w ritten in manuscript style
Publication Details	Tuckerman J, Kaufman J, Danchin M, Marshall HS. Influenza vaccination: a qualitative study of practice level barriers from medical practitioners caring for children with special risk medical conditions

Principal Author

Name of Principal Author (Candidate)	Jane Tuckerman		
Contribution to the Paper	JT contributed to the study design, collected and analysed the data, prepared the first draft of the manuscript.		
Overall percentage (%)	80%		
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	30/7/2020

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	Jessica Kaufman		
Contribution to the Paper	JK contributed to study design, coding interviews, data interpretation and critical review of the manuscript.		
Signature		Date	30/7/20

Name of Co-Author	Margie Danchin		
Contribution to the Paper	MD contributed to study design, data interpretation and critical review of the manuscript.		
Signature		Date	30/7/20

Name of Co-Author	Helen Marshall		
Contribution to the Paper	HM contributed to study design, data interpretation and critical review of the manuscript.		
Signature		Date	27 July 2020

6.3.5. Publication

Title: Influenza vaccination: a qualitative study of practice level barriers from medical practitioners caring for children with special risk medical conditions

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Abstract

Background: Understanding the influenza vaccination practices of general practitioners (GP) and paediatric specialists caring for children with special risk medical conditions (SRMC) is imperative for designing interventions to improve uptake. This study aimed to identify the vaccination decision making, provider practices and perceived barriers and facilitators to recommending or delivering influenza vaccine at the tertiary and primary care levels.

Methods: Medical practitioners from a single tertiary hospital and the child's nominated and treating GP were interviewed to explore influenza vaccination practices and challenges for children with confirmed SRMCs. Interviews were digitally recorded and transcribed verbatim and thematic analysis was used to inductively code these data. Resulting themes were then mapped across the COM-B ('capability', 'opportunity', 'motivation' and 'behaviour') theoretical framework for understanding barriers and potential interventions.

Results: Twenty-six medical practitioners (21 GPs and 5 specialists) completed semi-structured interviews. Identified themes were grouped by COM-B category. The main barriers and potential drivers for vaccination were grouped under Opportunity: such as structural barriers to influenza recommendation, including lack of processes to support the identification of children with SRMC and limited use of systems to prompt providers and remind parents, as well as lack of communication resources, social acceptance and normalisation and consistent messaging. Other identified barriers included Capability: provider communication and knowledge gaps to implement the recommendation and

Motivation: provider clinical prioritisation and responsibility towards providing a recommendation.

Conclusions: The main drivers for under vaccination of children with SRMC were structural barriers to influenza recommendation, including lack of processes to identify children with SRMC, limited use of reminder systems and unclear delineation of role responsibility between specialists and GPs. Interventions to increase influenza vaccine coverage for children with SRMC will require addressing practice level structural barriers and improving collaboration.

Introduction

In Australia, influenza vaccination is recommended for all people aged >6 months with special risk medical conditions (SRMC) as defined in the Australian Immunisation Handbook, such as specific respiratory and cardiac diseases and neurological disorders. (1) Despite being funded on the National Immunisation Program (NIP) since 2010, influenza vaccine coverage for children with SRMCs remains suboptimal, between 26 to 44%. (2-5)

Medical practitioners are considered crucial to achieving optimum influenza vaccine coverage for children with SRMCs (2, 5-7), but their willingness and capacity to provide the recommendation to parents limits implementation and uptake. Few studies have examined attitudes and delivery practices towards influenza vaccination from the perspective of Australian general practitioners (GPs) (family physicians) and hospital paediatric specialists who care for children with SRMCs. Additionally, little is documented about the interface and collaboration between GPs and specialists who care for these children in the context of influenza immunisation.

The majority of Australian childhood vaccinations are delivered in family medical practices.(8) However, some children with SRMCs are managed predominately by hospital paediatric specialists and infrequently visit a GP.(2) Consequently, responsibility for provision of an influenza recommendation remains unclear. Studies suggest that the single biggest deterrent amongst physicians is the involvement of another physician in the child's care, which generates confusion over responsibility for vaccination. (9)

Addressing the drivers of low influenza vaccination coverage for children with SRMC requires the use of interventions based on theory to identify the barriers and facilitators.(10) An implementation science framework enables the systematic assessment and development of such an intervention. The Behaviour Change Wheel, incorporating the COM-B Model, is a comprehensive theoretical model that provides a structure to understand the fundamental factors to guide evidence-based intervention design.(11) The COM-B explanatory model of behaviour asserts that 'Capability', 'Opportunity' and 'Motivation' factors influence Behaviour.(11) Using the Behaviour Change Wheel, each of these behavioural drivers can be mapped to potential intervention functions and subsequent policy domains.(11)

The primary aim of this study was to use the COM-B model to categorise influenza vaccination decision making, provider practices and perceived barriers and facilitators at the practice level from the perspective of medical practitioners who care for children with SRMCs. A secondary aim was to identify potential interventions to address the identified gaps.

Participants and Methods

Study design

In this qualitative study, semi-structured interviews were conducted with medical practitioners involved in the care of children with SRMCs. This approach enabled a detailed exploration of medical practitioners' decision making, practices and views related to influenza vaccination. The study protocol was approved by the Women's and Children's Health Network, Human Research Ethics Committee.

Setting and participants

The study was undertaken with GPs and hospital paediatric specialists identified by parents as the treating doctors for a group of children (N=410) with confirmed SRMC who attended the Women's and Children's Hospital (WCH) Adelaide. The children's specialities are detailed in Supplemental file 1. Participants self-identified following completion of a survey examining the frequency and responsibility towards influenza vaccine recommendation, confidence in understanding the conditions 'medically at risk' and provider beliefs towards influenza vaccination.(12) The survey was anonymous, but respondents could provide their details if they were willing to participate in a one-to-one interview. Written informed consent was collected from each participant prior to interview.

Data collection

Interviews were conducted between June and December 2018. The interview guide was informed by the core constructs of COM-B (11) and was developed by two investigators (JT & HM). It also incorporated elements of Ajzen's Theory of Planned Behaviour (13), such as the intensity of social pressure the medical professional perceives to provide a recommendation, and normalisation process theory (14), such as cognitive participation and collective action. An interview script was used for all participants and all interviews were conducted by JT via phone for participant convenience. Data collection ceased when saturation was reached and was defined as no additional unique responses.

Data analysis

All interviews were digitally recorded and transcribed verbatim. Two authors (JT and JK) inductively coded data using thematic analysis in NVivo 12. After initial coding of all data, the framework was reviewed by all authors (HM, MD, JK and JT). The author

group revisited the coding process to discuss themes as they emerged. Inductively derived themes were deductively mapped across the COM-B, according to sub-category (Table 1), enabling conceptualisation of barriers to inform interventions.

Results

Twenty-six medical practitioners were interviewed: 21 GPs and 5 paediatric hospital specialists (Table 2). Interviews lasted from 9 to 57 minutes (median: 19.5 minutes). Eighteen themes were identified and categorised according to COM-B (Figure 1 and Table 3). Recognising that some factors could be both barriers and facilitators, and that themes could overlap categories, we retained themes in clusters to facilitate understanding and interaction between components.

Capability - Physical (skills)

Influenza vaccine communication with parents

Influenza vaccine discussions with parents was predominately verbal and opportunistic, with variation in the approach used. Medical practitioners talked about the need to discuss a variety of opposing views towards influenza with parents, such as it not being as "*severe*", the "*concept that flu is actually not a problem*" (GP #11 – Metro). Views were entwined with perceived previous exposure, severity, complacency towards the vaccine and the need for more needles. While many recommended it for all children, some GPs planned conversations based on previous vaccination history and encounters.

Specialists tended to simply provide a recommendation and not engage in in-depth discussions about influenza vaccination, while GPs used a variety of communication styles to try to engage with hesitant parents. Most GPs accepted that conversations needed to move at the parent's pace and that some would not be persuaded. To

preserve the doctor-patient relationship, some GPs brought it up subtly at repeated encounters for those requiring more guidance to reach a decision. In contrast, others emphasized disease risks (or severity) or graphic analogies in order to counter people's concerns, as they felt it was the best way to engage with these parents.

> *"Tell me the last time you were nearly in a near fatal car accident? Do you still wear a seat belt? When was the last time your house nearly burned down? Do you still insure it?"* GP #11 – Metro

GPs attempted to counteract facts or dispel concerns and felt that this was part of their role but were limited by the consultation time. Approaching more challenging conversations was time consuming, particularly ensuring vaccine messages were understood by parents, and some felt the conversations '*rarely got anywhere'*. Advocating for the influenza vaccine was often seen as a hard sell against more high-profile diseases, such as meningococcal, that are represented in the media and portrayed as more serious. Many felt that medical practitioners required upskilling as much as parents and identified a need for "*GPs to be educated in a coordinated way*" (GP #11 – Metro).

Capability - Psychological (knowledge)

Knowledge of influenza vaccine recommendations

While most participants were aware of the recommendation, one questioned the existence that there was even a recommendation at all, *"I mean, I don't know. Is there actually a guideline about this?"* (GP #17 – Regional). Some GPs felt it was challenging to implement the recommendation and determine who qualifies, particularly in a fast-paced clinical environment. A few openly acknowledged immunising everyone, avoiding the need to delineate who was eligible. Additionally, medical practitioners identified a lack of

parental awareness of the recommendation as a barrier, suggesting that most parents probably hadn't considered the need for the vaccine, which they perceived to be interrelated with the general health of the child.

> *"… maybe some of them think, well, my asthma's not that bad, I don't qualify GP" #21 – Metro*

Professional boundaries

Many GPs talked about the difficulty and confusion as to whether it was the role of the primary care provider or tertiary level specialist to provide the recommendation. They used terms such as "*black hole*" and need to draw a clear "*line in the sand*". Discussion on GP and specialist roles for influenza vaccination was entwined with responsibility and professional role towards influenza vaccination. Many acknowledged the need for clearer professional guidance for whom should provide the recommendation, so it doesn't get missed.

Opportunity –Physical (environment)

Communication and education resources

Few GPs or specialists reported using communication resources when recommending the vaccine. Some directed parents with concerns to websites, but many expressed a need for resources that go beyond simply saying the vaccine was '*safe'* and '*effective'*. They suggested improvements in the way communication is directed to patients and the public. Many felt the message should focus as much on who should get the vaccine as why it was important. One GP referenced the detailed resources available for zoster and meningococcal, including the website, bulletins, and wondered why there was an absence of such resources for influenza. Others highlighted the general absence of

information in the public about the actual complications of influenza in children. Both GPs and specialists wanted detailed information on vaccine development, why it's recommended, the side-effect profile and the complications of influenza in children, particularly in a format to provide to families. The nature of clinic resources was also discussed, such having them singled sided and in a format that could be stuck on computers, particularly to provide a visual cue of all the medically at-risk groups.

Systems

Functioning reminder or prompting systems were perceived as one of the key facilitators to improving influenza vaccine coverage for children with SRMC, and the lack of systems was viewed as a barrier. As one GP said, influenza vaccination was "*generally left up to either the parent or to the doctor to remember*" (GP #5 – Regional). Discussion focused on the need for a system to achieve the "*comprehensive identification of these children*" and then the "*actual proactive recruitment of them to come in*" (GP #8 – Metro). It was seen as highly beneficial to have this group already identified at the clinical encounter, thereby alerting and prompting treating doctors to provide the recommendation. This was viewed as particularly important in a busy consultation when vaccination may be missed, in conjunction with low parental awareness of the recommendation. While one GP detailed how their practice had already implemented such a system through the practice's clinical software, the lack of systems was more commonly discussed.

Despite written communication resources being infrequently used (e.g., SMS or reminder letters), most participants could see benefit in an annual 'prompt' for parents to get their child the vaccine. Still, both groups expressed uncertainty over how to implement identification or reminder systems into clinical practice. Setting up a reminder

system was seen as multilayered with several obstacles, including identifying children, particularity in the absence of electronic medical records. Many GPs perceived the process of using a reminder system and the requirement for initial consent to be placed on the system as a major stumbling block.

Recommendation as standard practice

Participants used words like, "*absolutely*" and "*definitely*" with high frequency to describe whether the influenza vaccine should be a part of disease management for children with SRMC. Most specialists considered providing the recommendation to be standard practice but stated that achieving this beyond a verbal recommendation was difficult. Conversely, many GPs talked about the use of care plans and the need for these to incorporate annual recommendation. Mostly, however, these care plans related solely to asthma and beyond asthma there was a sense of decreased urgency as specialists were perceived to already have disease management 'in hand'.

Most GPs felt that specialists providing an initial recommendation or discussion of the vaccine at SRMC diagnosis would be beneficial for the parents and help balance clarity over the role responsibility, removing assumptions about what had or had not been discussed. Additionally, many participants saw the initial diagnosis period as a time when parents are most receptive to information but remained uncertain on how best to achieve this. However, as one specialist pointed out this was also a time when parents could be overwhelmed with medical information and terminology.

Vaccination inconvenience

Several GPs considered the inconvenience for parents in recalling them for, yet another appointment. Acknowledging the time for these additional appointments on top of a

program of medical appointments and treatments and the difficulty of juggling multiple children within a family.

Barriers to opportunity

In many cases, the absence of systems meant provision of a recommendation or the vaccine followed an opportunistic pattern. Not all children necessarily attended frequently or at the time of year when the vaccine was being offered leaving "*less opportunity to think of it and bring it up*" (GP #9 – Regional). There was acknowledgement that opportunities were missed due to competing clinical priorities, such as acute infection or just forgetting "*because there's always other stuff*" (GP #5 – Regional). Many GPs were mindful to maximise opportunities for this cohort of children within general practice and much discussion revolved around recognising both the children and opportunities when they presented. Conversely, 'specialists' were perceived as having greater engagement with these children at intervals when they were well, and a few GPs discussed the need for greater availability of the vaccine in the tertiary care environment, which was also echoed by specialists.

Cost

Cost emerged as a theme throughout discussions. Participants identified the perceived financial burden of lost parental work hours and paying to see the GP to obtain the vaccine and acknowledged how this could quickly add up for a family even if one member was covered under the NIP. Interestingly, one GP thought that the availability of a free vaccine, coupled with low cost and widespread availability through pharmacies, invalidated the seriousness of influenza disease and the vaccine. They felt that higher cost vaccines presented more appeal to parents.

Opportunity - Social (societal influences)

Social acceptance & normalisation

While not restricted to children with SRMC, some discussions focused on the need to improve social acceptance of the influenza vaccine and normalise it as part of our everyday culture. Most participants came from workplaces where it was considered a normal occurrence to get the vaccine. Many participants perceived extending the program to "*everyone, not necessarily an isolated group*" (GP#12 – Regional) would contribute to normalisation, "*that thing that you do at the start of the flu season*" (GP #10 – Metro). The potential for greater social acceptance and normalisation was perceived as being closely tied with state-based funding of the program. Some considered it odd that funding of a population-wide recommendation for all children stopped at 5 years of age and started again at 65 years of age. Conversely, the need for a population-wide program was also balanced by the need to incorporate and normalise into the treating model of care, similar to the way the elderly perceives the vaccine as a normal part of their 'healthy living'.

Professional collaboration

Virtually all participants discussed GP-specialist interaction, with these types of encounters being "*very occasional*" Rather than a routine culture of communication between tertiary and primary care, the interaction participants described generally pertained to specific patients, events or circumstances, such as checking it was ok to give the vaccine. Some GPs acknowledged that some background written communication about influenza vaccination did occur, but they "*wouldn't be any more or less likely to do it"* (GP #10 – Metro) because the specialist had mentioned it. Many GPs could see the need for better and more coordinated communication regarding vaccination in general – not just for influenza vaccine.

Media messaging

Some participants perceived a need for greater involvement of the media and advertising placement for maximum target group exposure. In addition to commercial television, participants suggested web/YouTube videos, targeted local social media and the potential to increase motivation using vaccine ambassadors. One participant saw a need for more transparent evidence on the disease severity and efficacy of the vaccine to be discussed in the public domain. There was also a need for consistent messaging, so "*everybody they're seeing is giving them the same message*" (GP #2 – Metro), from the specialist through to the government advertising and websites.

Motivation - Reflective (beliefs)

Responsibility

In terms of delivering the vaccine, nearly all GPs felt a strong sense of responsibility for this, seeing vaccine delivery as part of their role as primary healthcare providers. *"I mean it's our responsibility [as GPs] to give it, and we're all happy to give it.*" (GP#6 – Regional) Conversely, specialist's responsibility aligned with providing the recommendation, "*…we're happy to make recommendations, but I think it's appropriate that they [GPs] actually do it.*" (Specialist #4) While it was evident that some GPs wanted the recommendation to come from the tertiary level of care, others had no hesitation and believed they should provide the recommendation and deliver the vaccine. In general, this discussion was as much about encouraging all medical practitioners to capitalise on available recommendation opportunities as it was everyone's professional responsibility or role.

Opinions towards different vaccines

Many participants viewed all NIP vaccines across the population spectrum similarly and reported giving them according to current guidelines. Most providers believed parents held positive views towards vaccination reporting that they were generally, "*more proactive*" and "*well informed*" when it came to vaccinations. In contrast, it was perceived that parents who held negative views towards vaccination were related to the disorder itself, with parents of children with allergy or lowered immune conditions or conditions for which less medical support were available seen as more questioning and having greater vaccine concerns.

Prior experience of influenza and perceived severity

Most GPs described limited firsthand experience with treating paediatric patients with severe influenza, using language such as, "*from time to time*" and "*a couple*' when describing the frequency. Mostly their very unwell patients would go straight to hospital and not see GPs until after discharge.

Overall, children in general were considered more susceptible to severe influenza disease, but GPs and specialists discussed the associated risks of children with SRMC not receiving the influenza vaccine in more detail. While acutely aware that an underlying disorder could deteriorate, many medical practitioners also mentioned "*pneumonias and complications*", "*the risk of hospitalization*", requirement for "*high-level hospital care*" and the possibility of death when talking about possible sequalae. Respondents perceived children with SMRC to be a "*more vulnerable population*" and considered the need for time off school and length of hospital stay.

Vaccine efficacy & safety

Some participants had concerns about vaccine efficacy but were no less likely to provide it. Most medical practitioners did not hold concerns about vaccine safety, though they acknowledged that the influenza vaccine does carry the risk of potential rare side effects. However, some participants did have safety concerns and brought up the serious adverse events that occurred in 2010. (15, 16) They were divided regarding their perceptions of parents' memory of the events. These discussions also raised the role of poor commercial media reporting.

Many participants were familiar with encountering parents who held the popular belief that the flu vaccine gives you the '*flu*'. While some discussion focused on the perceived risks of the vaccine from parents, this was not at the forefront of discussions. As one specialist illustrated, this was often in the process of seeking greater clarity and reassurance rather than opposing the vaccine.

Motivation - Automatic (emotions and habits)

Clinical prioritisation

Delivery of the recommendation did not comprise a routine part of care and was often only brought up if the patient presented for another reason. Understandably, medical practitioners reported being more motivated to address children's more immediate clinical concerns. In a time-limited engagement with parents providing the recommendation was frequently deprioritised.

Discussion

Our study highlights many themes at both the tertiary and primary care level in the provision of influenza vaccination for children with SRMC. The main drivers for under

vaccination of children with SRMC were structural barriers to influenza recommendation, including lack of processes to support the identification of children with SRMC and limited use of systems to prompt providers and remind parents. Additionally, there was confusion regarding the responsibility to provide a recommendation between GPs and specialists (Motivation) and the need for additional, well defined resources to support vaccine discussions (Capability).

The absence of structural reminder systems to identify eligible SRMC and support the provision of a flu vaccine recommendation is an important finding of this study. In the USA, studies examining family practitioners and paediatricians suggest that strategies to identify children with SRMCs and reminder systems are underutilised. (9, 17) The capacity to correctly identify SRMC children either at the tertiary or primary care level is imperative to improve coverage. In a paper-based system this is a time-consuming exercise; yet even with an electronic medical record, accurate identification requires medical coding that aligns with the recommendations. Furthermore, the Australian Immunisation Register (AIR) does not record at risk status, limiting the ability to track coverage and assist clinicians at the point of care, with the additional issue of low reporting to AIR previously identified. (18) In an increasingly digital world, health systems need to keep pace in order to support healthcare care staff to provide quality care. Without such identification, it is challenging to implement the structural supports, such as prompts, that are needed within the clinical encounter to increase the clinician's capacity to engage in conversations regarding influenza. This is important, given routinisation is identified as playing a considerable role in driving change to healthcare professionals' behaviour (19, 20).

Our finding that GPs look to specialists for confirmation and reassurance before recommending the vaccine is consistent with other findings in the Australian context (21) alongside widespread lack of influenza vaccine recommendation from healthcare providers. (21-26) GPs communicated a strong sense of responsibility to deliver vaccinations in their professional role as primary care providers but may not be willing to interfere with the disease management for which another medical practitioner is seen as providing primary care. (9) A Victorian study found that GPs deflected responsibility to the child's specialist when influenza vaccine decision making involved a child considered medically at-risk. (21) Successful communication was systematically absent in the relationship between GPs and specialists. As was collaboration that incorporated parents. Written communication between tertiary and primary care could decrease ambiguity towards the vaccine (27-29) but given the influenza vaccine is funded and has been recommended for this group for some time, both providers should be giving a recommendation.(1) Although few medical practitioners lacked motivation towards influenza vaccination, some voiced safety concerns, consistent with recent findings.(15, 16, 21) With low awareness of influenza severity, its complications, and vaccine contraindications identified amongst family practitioners and paediatricians in the USA, with 20% of physicians seldom recommending the vaccine. (17)

At the tertiary level, most hospital departments maintain a patient list which could be adapted and utilised by the hospital to develop a database of children considered medically at-risk. Given the identified need to support vaccination for these children more generally (30) a tertiary located database could also serve as central communication point for all parties (specialists, GPs, parents), generating annual reminders to parents, providing prompts for specialists and communication reminders with children's referring GPs. While prompts have been shown to increase provider

recommendation and contribute to routinisation by specialists (23, 31, 32) consideration is required towards access within the hospital environment to address' parental opportunity barriers (2) such as multiple appointments and preference for the whole family to be vaccinated at once.

Improving GP self-efficacy is likely to entail changes to internal systems such as modifications to practice software that could be supported by policy, overcoming barriers to opportunity, such as the use of recall and providing clinic times that most suit families and young people, and normalisation and incorporation of influenza messaging into routine disease management at the primary care level. With all of these needing to be implemented a milieu, where influenza vaccination is seen as the norm by all groups. Across both levels of care, the need for more comprehensive communication resources warrants further research.

Multicomponent interventions are widely regarded as the most effective in changing behaviour (33, 34) with interventions that contribute to normative restructuring of practice shown to offer the most success for professional behaviour change. (35) Improving the capacity for both GPs and specialists to engage with parents regarding influenza vaccination is crucial given provider recommendation is identified to improve uptake for targeted groups, particularly children with SRMC and will be especially relevant in the context of the COVID-19 pandemic. (2, 5-7, 36-39)

The strengths of this study are the unique perspective offered through interviewing a group of medical practitioners known to be involved in the care of children with SMRC. Notably, we included medical practitioners from both metropolitan and regional areas. However, limited numbers of specialists participated, and the interviews of specialists

were considerably shorter and lacked the richness provided by GPs. This may be an important finding in itself; possibly indicating lower specialist engagement and ownership of this issue. Reasons for non-response to participate in an interview from survey respondents were not sought, and it is possible that participants had higher level of interest in influenza or research. While the study included medical practitioners from predominately South Australia, the broad spectrum of participants and the structural similarity of the primary/tertiary care interface would be comparable to other Australian jurisdictions.

Conclusions

Using a theory driven approach we identified several themes to explain the challenges of delivery of influenza vaccination from the perspective of primary and tertiary care medical practitioners caring for children with SMRC. Central themes revolved around responsibility, systems, and barriers to opportunity. These data can used to develop interventions at both the tertiary and primary care levels to improve influenza vaccination coverage for this medically vulnerable group of children.

Acknowledgements

Helen Marshall acknowledges NHMRC Fellowship APP1155066 funding.

Conflict of Interest

JT, JK and MD report no conflict. HM is an investigator on clinical trials of investigational vaccines sponsored by Industry. Her institution receives funding from Industry (GSK, Pfizer, Novavax) for Investigator led research. She does not receive any personal payments from Industry.

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Table 1: Sources of behaviour according to the COM-B

Source of Behaviour		Example
Category	**Sub-category**	
Capability	Physical	Skills, abilities or proficiencies required to perform the task or health behaviour. E.g., skills to engage in vaccine discussions with parents.
	Psychological	The capacity to engage in the necessary thought processes - comprehension, knowledge, memory. E.g., forgetting to perform a task.
Opportunity	Physical	The opportunity afforded by the environment to perform the behaviour. E.g., prompts for doctors to provide a vaccine recommendation.
	Social	Societal influences that dictate the way that we think about things. E.g., people around us are receiving the vaccine.
Motivation	Reflective	Driven by beliefs about what is good and bad, conscious intentions, decisions and plans. E.g., belief that providing the vaccine to children with SRMC would be the right thing.
	Automatic	Driven by emotional responses, desires, impulses and habits resulting from associative learning and physiological states. E.g., Having habits and work patterns to provide influenza recommendations without having to think.

Table 2: Participant demographics by specialty

Characteristic		General Practitioners	Paediatrics Sub Specialists
Number of participants		n=21	n=5
Median interview duration (minutes)		20 (range 10-57)	15 (range 7-29)
Years practicing medicine median		15 (5-41)	45 (38-46)
Gender	Female	14	-
	Male	7	5
Practicing location	Metro	14	5
	Regional/rural	7	-
Subspecialty (paediatricians)			Respiratory (n=2) Paediatrics (n=1) Gastro (n=1) Metabolic (n=1)

Table 3: Factors related to influenza vaccination in medical practitioners who care for children with special risk medical conditions, mapped to subcategories of the COM-B

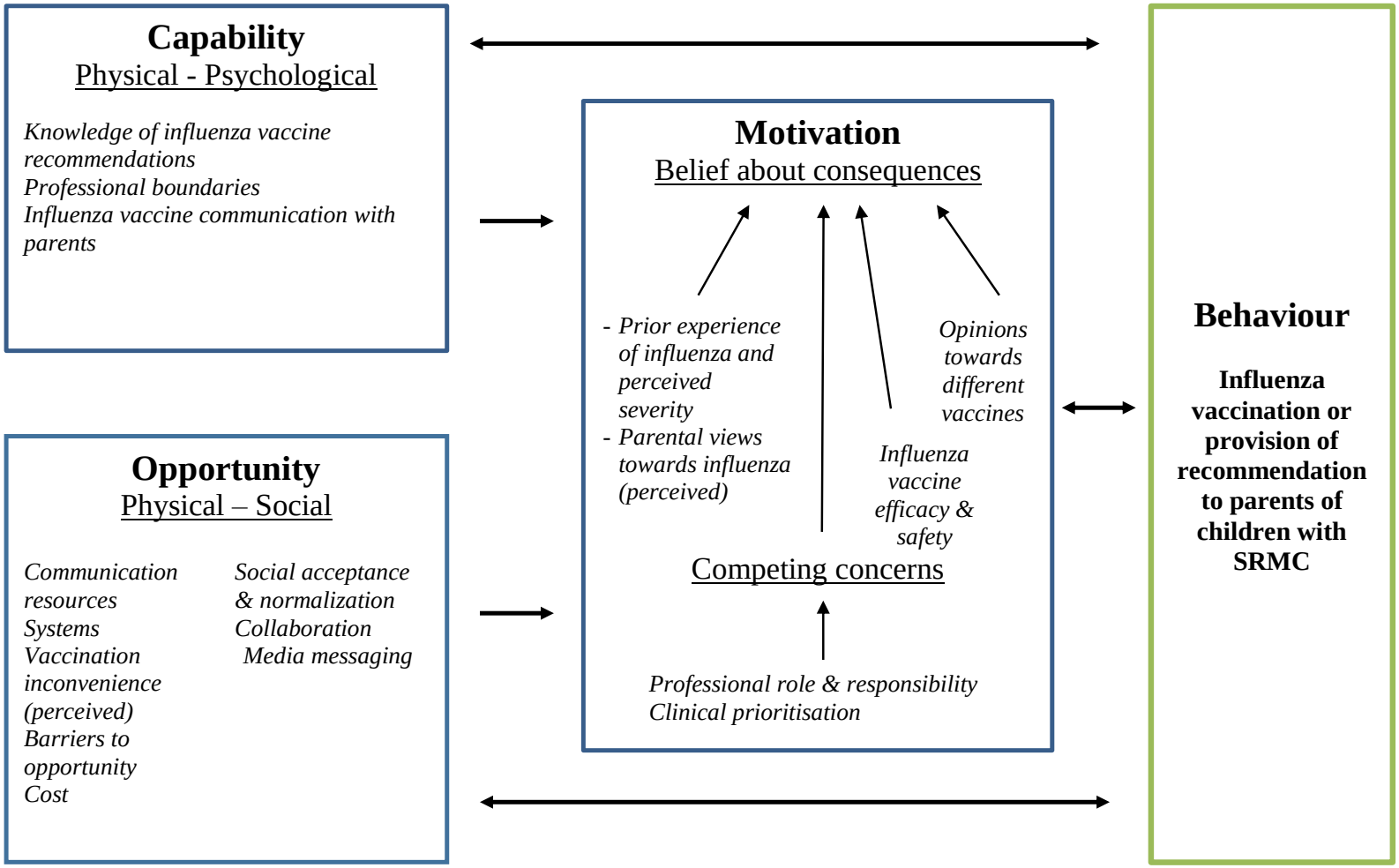
Capability	Opportunity	Motivation
Physical (skills)	**Physical (environment)**	**Reflective (beliefs)**
<u>Influenza vaccine communication with parents</u> - communication skills and styles used with parents - limited communication skills to deal with the range of concerns raised by parents towards the vaccine. - communication styles to address deal with parents with vaccine concerns in general parents	<u>Communication resources</u> - need, format and content <u>Systems</u> - lack of systems - types of systems required - identification of children with SRMC - limited use of reminder systems - scare use of provider prompts at the clinical encounter - consent requirement for reminders <u>Recommendation as standard practice</u> - frequency of recommending the vaccine as part of routine disease management - timing for first recommendation at diagnosis as a perceived facilitator <u>Vaccination inconvenience (perceived)</u> - recall of parents, to ask them to come in for another appt, especially if the child is otherwise well. - need for additional appt on top of an already full schedule of medical appts - time taken for appt in the context of busy homes/families. <u>Barriers to opportunity</u>	<u>Responsibility</u> - responsibility between specialists and GPs towards vaccine recommendation and vaccine delivery <u>Opinions towards different vaccines</u> - consistent views towards all vaccines recommended across all population groups on the NIP - views of parents of children with SRMC to view vaccination (perceived) <u>Prior experience of influenza and perceived severity</u> - limited current experience with treating paediatric patients with severe influenza - high awareness of the potential severity of influenza disease - high awareness of the risk of children with SRMC not receiving the influenza vaccine <u>Vaccine efficacy & safety</u> - limited concerns about safety, although acknowledgement

Capability	Opportunity	Motivation
Physical (skills)	**Physical (environment)**	**Reflective (beliefs)**
	- frequency of appointments: children may not see GP very often, perceived to have more contact with specialist. - timing of appointments (not in season): children may not see GP or specialist at times when influenza vaccine is provided, or contact may be when unwell, i.e. acute infection. - recognising opportunities when they present, i.e. contact for other reasons. memory, forgetfulness (capability) Cost (perceived) - financial burden of GP appointment, especially for families. Recognising GP gap payment. - perceived value of vaccine lowered, given extensive availability and low cost.	towards the risk of potential rare side effects - recollection of serious adverse events in 2010.

Capability	Opportunity	Motivation
Psychological (knowledge)	**Social (societal influences)**	**Automatic (emotions)**
Knowledge of influenza vaccine recommendations - lack of knowledge to implement the recommendation and classifying 'at risk' i.e. determining who is medically at risk Professional boundaries - lack of knowledge as to	Social acceptance & normalization - participant's workplace culture towards the influenza vaccine - perceived value of expanding influenza program to improving social acceptance and normalisation - perceived negative messaging generated through recommending the vaccine to select/ isolated groups or age brackets	Clinical prioritisation - need to always consider the clinical needs of the patient and available time.

Capability	Opportunity	Motivation
Psychological (knowledge)	**Social (societal influences)**	**Automatic (emotions)**
who's professional role it is to provide the recommendation.	- requirement to normalise into the treating model of care, like the way the elderly perceives the vaccine as a normal part of their 'healthy living'. <u>Professional collaboration</u> - limited coordinated communication between care providers regarding the vaccine <u>Media messaging</u> - poor media messaging and role of the media - need for greater targeted media, including vaccine ambassadors - requirement for consistent messaging and transparent evidence	

Figure 1: Factors related to influenza vaccination in medical practitioners who care for children with special risk medical conditions, real and perceived.



CHAPTER 7 KNOWLEDGE TRANSLATION, GAPS AND FUTURE RESEARCH

The studies presented within this thesis provide a valuable contribution to the influenza vaccination landscape not only for children with SRMC but children in general. Data collected as part of a number of these studies has directly informed both an NHMRC Research Grant and a successful 2020 Women's and Children's Hospital Foundation Grant. The focus of both these grants was the development, implementation and evaluation of interventions that aimed to increase influenza vaccine coverage for children with SRMC. The following commentary of the knowledge translation, gaps and future research in this chapter is broken into the themes used throughout this thesis.

Impact: risk identification and understanding of severity

The results from the systematic review are significant and timely given influenza vaccination recommendations for children with medical conditions are now implemented or being considered in many countries. Quantifying and categorising the increased risk faced by these children will benefit not only clinicians but could also serve to strengthen recommendations. The review has provided estimates and data on bacterial pneumonia, ICU admission, mechanical ventilation, death, neurological outcomes, and hospital resource use.

These review findings equip clinicians with evidence to more effectively communicate influenza risk in real terms. My findings will contribute to enabling more focused and detailed discussions between health care providers and parents during the vaccine decision making process. However, the review evidence showing an increase in the probability of death or requirement for mechanical ventilation was inconsistent. This

finding supports the need for further research using large datasets to evaluate the impact of influenza complications and associated morbidity from influenza in SRMC children. The systematic review also found the severity and complications associated with influenza infection for children with SRMC has not been particularly well documented and inadequate reporting restricted thorough study quality assessment. The level of GRADE evidence was low for all outcomes.

Research focused on influenza vaccination in children with SRMC remains in its infancy and this was no more evident than when reviewing and synthesising study data, exacerbated by a lack of adherence to standardised reporting guidelines for observational studies in epidemiology, such as the STROBE (172) guidelines. Notably, data collection should extend to potentially modifiable factors such as age appropriate influenza vaccination status and use of antivirals. Data encompassing multiple influenza seasons that could detect the nuances of difference between groups would assist to progress further policy and clinical practice for this vulnerable group. The strengths of linked administrative data are well-characterised (173) and could offer several advantages such as larger sample sizes data collection over several years with the ability to overcome seasonal variation and capacity to detect rarer / lesser reported differences/ outcomes. However, the use of administrative data has its own limitations such as protracted access that is strictly controlled, missing data and the potential for the way certain variables are recorded in administrative records being different from the purpose of the study.

Coverage and parental recall: coverage and validation

The survey with parents of children with SRMC and subsequent studies, provided a valuable contribution because an understanding of the level of uptake, as well as,

associated characteristics is important in informing interventions aimed at increasing coverage. The results of the study are meaningful for all medical professionals caring for children at increased risk, as well as policy makers highlighting the importance of reviewing the influenza vaccine status of children with SRMC and changes incorporated into the NIP to achieve this. The survey confirmed the importance of recommendations for influenza vaccination being communicated in the context of tertiary care, particularly the reason for their child's increased risk status. While previous studies establish a need for medical practitioner recommendation, understanding this in the Australian context until now has been limited. Our results will enable more appropriately tailored interventions to be developed that directly address the needs of this targeted vaccination group, such as strategies that increase tertiary care provider-parent influenza vaccine communication. The survey also served to highlight the importance of parental influenza vaccination. Targeting household contacts, or the whole family, may be one way to increase coverage, by supporting the child in the family who is medically at risk but also serve to 'cocoon' individual family members at increased risk within the family unit. Particularly as young children are known to be key transmitters of the virus within families.

The results from the second line of enquiry using data from the survey to examine parental-provider confirmation and reporting to AIR are important for all medical professionals caring for children with medical conditions as well as policy makers. Current methods capturing influenza vaccinations of these children need to be improved, and limitations acknowledged of the various methods currently available. Only 30% of influenza vaccines given to study participants (aged <7 years) were reported to AIR (previously ACIR). Reaffirming and convincing immunisation providers of the importance of recording all immunisation encounters to AIR is critical to the future

success of the program, especially now that a funded influenza program will be implemented from 2020. However, this could prove challenging without greater provider engagement. Educating immunisation providers as to the importance of AIR reporting is a critical next step. Integrating and improving GPs knowledge to report influenza vaccination encounters could prove challenging in the context of the current passive reporting and may require incentives or 'nudges'. Measures such as a requirement to report all vaccinations could be considered. Improvements in software or the transition to a whole of life registry may have provided the refocus needed to view the usefulness of the immunisation registry. Software programs are needed that automatically upload to the AIR to additionally improve timeliness of reporting.

Community awareness: community acceptance and knowledge

The use of Health Monitor data provides a valuable perspective on parental knowledge of children's influenza recommendations. Integrating community perspective to vaccination requirements is a value add to programs seeking to elicit behaviour change and is important in informing interventions aimed at increasing coverage in all children. The survey results reinforced the need for medical practitioner recommendation, even for parents in the general community. It is worth noting that the funding landscape of children's influenza vaccination changed throughout the course of this PhD. Children in general (aged ≥6 months to < 5 years) were for a long time recommended but not funded to receive the vaccine; on account of the identified increased risk from influenza in children < 5 years. Up until 2017, only Western Australia had a funded paediatric influenza vaccination program for all children aged 6 months to < 5 years. This changed in 2018 with the introduction of state funded influenza vaccination programs across all remaining jurisdictions, with the exception of the Northern Territory that commenced in 2019.(19) The vaccine is set to be incorporated and funded on the NIP for all children

aged ≥6 months to <5 years as of 2020. Key concepts remain particularly relevant and the study also identified factors that parents considered their greatest influencers to future receipt which will be used to design and implement future communication strategies. Along with the key influencers of receiving a GP recommendation and a funded vaccine was the need for a belief in its benefit. Incorporating this into future program messaging and communication is important as it is likely that increasing parent's knowledge of the vaccine will be required in addition to a funded program. Many parents indicated a willingness for their child to receive the vaccine at a pharmacy. Moving forward, the logistics of administering the vaccine to a large cohort of under-fives each season over a short space of time will present challenges in access across all age groups. Taking the pressure of general practice and expanding the lower age limit at pharmacies and increasing the number of potential immunisation providers for older children (and adults) may be one way to address this and could help to improve access in general practice for young children and those who are medically at risk. However, there is a risk that with different providers administering influenza vaccine the need to record on AIR increases or there is likely to be wastage due to repeat vaccinations. If there is any expansion to include other providers, it is imperative that vaccines administered are recorded on the AIR. Awareness was limited by geographic location and decreased in regional areas. While the low parental awareness of influenza recommendations means any influenza vaccine messaging to regional areas will require due consideration in future campaigns the differential access to health services, and health behaviours based on place of residence require further examination.

The state-wide representative sample of parents meant the study was also ideally positioned to explore parental decision making towards vaccination in general, patterns

of information provision and immunisation service use. This work adds to the increasing body of work supporting a need for consistent provider endorsement and discussion. Parent's vaccination beliefs followed a pattern in line with increasing levels of concern towards vaccination. This is important given that vaccine hesitancy and the threat of a global influenza pandemic have recently been acknowledged by the WHO as two of the top 10 threats to global health. (174) Even amongst the 96.3% of vaccinating parents, 27.8% expressed some concern towards vaccination. Greater support of healthcare workers (HCW), particularly those in engaging preventative health care (such as GPs), is critical to improve awareness and communication of influenza risk messaging. Public health immunisation programs should incorporate education and appropriate messaging for healthcare professionals and the public alike.

Policy and practice: practice level factors used by medical practitioners

The mixed methods study with GPs and specialists who are the treating medical practitioners of children with SRMC provides a valuable contribution through understanding the dynamics of influenza vaccination for these children. Previous research examining the delivery practices and attitudes towards influenza vaccination in the context of Australian GPs and paediatric specialists who care for these children is scarce. The cross-sectional survey results of paediatric specialists and GPs can assist by ensuring influenza vaccination programs incorporate medical education including concise information about what constitutes a SRMC, appropriate messaging and reminders for healthcare professionals. Knowledge in understanding the 'at risk' conditions as well as responsibility for proving a recommendation remains a key challenge. For example, most were aware of the recommendation but were limited in their detailed knowledge and confidence to implement the recommendation in all situations. This is a critical finding, given our study findings with parents highlighting the

expressed need for medical practitioner recommendation particularity in the context of care – be that GP or specialist. Addressing the educational requirements of GPs and specialists along with task sharing responsibility are essential. Support to undertake these tasks is an essential building block to the future of the National Seasonal Influenza Vaccination Program.

Additional exploration through qualitative interviews provided rich detail that illustrated the challenges faced by these care providers. Most clinicians are time pressured and receiving provider education or finding solutions to identify children at increased risk will be challenging. Use of medical software or electronic medical record systems offers one solution, but it's likely to require significant financial input. Another option is to assign a risk status once diagnosed or place on a reminder system following a 1st recommendation or vaccination. However, these are piecemeal approaches in lieu of a transparent systems approach, with clarity over responsibility. A considered systematic approach will have greater sustainability. The addition of an 'at risk' field code to AIR is one solution that has several merits. Identification of those at increased risk would enable more accurate coverage and foster bidirectional preventative care when several care providers are involved in care. However, an intermediary step may still be required, and a tertiary systems approach would enable GPs to deliver vaccination, but the initial vaccination messaging could come from within the context of the tertiary care, such as through the use of SMS messaging. GPs are major stakeholders in the provision of children's immunisations in Australia, while the role of specialists is less well established, particularly for influenza. Forging a new paradigm of care that incorporates both GPs and specialists while challenging, is required.

CHAPTER 8 DEVELOPMENT OF AN INTERVENTION

Effective interventions are needed to drive improvements in influenza vaccine coverage for children with SRMC. In order to address the issue of low influenza vaccine coverage in children with SRMC at the WCH, a 2020 WCH Foundation Grant application was submitted to implement and evaluate an intervention. Intervention development followed the Behaviour Change Wheel (66) and the principles from the Tailoring Immunization Programmes (TIP) guidance produced by the WHO.(175) The TIP Guide provides tools and guidance on 1: Identifying the population; 2: Diagnosing the barriers to vaccination and 3: Designing evidence-informed responses. The Behaviour Change Wheel intervention design method is divided into three phases: 1: understand the behaviour; 2: identify intervention options; 3: identify content and implementation options. (66, 71)

To achieve the first phase of the Behaviour Change Wheel, all factors identified throughout the various projects in this thesis related to influenza vaccination in children with SRMC were mapped (Figure 5) across the COM-B ('capability', 'opportunity', 'motivation' and 'behaviour') Model. (66) Collating the evidence from these integrated sources enabled an understanding of the dynamics in the influenza vaccination pathway. The information generated (as part of this thesis) to identify and diagnose has been important to order to gain an understanding of the situation and the group's knowledge, perceptions and practices.

In the second phase, a table of intervention functions, as per the Behaviour Change Wheel, guided the selection of potential interventions considered effective for each driver of behaviour (Table 3).

Figure 5: Parent, provider and health system level factors mapped to the subcomponents of the COM-B model (66, 176)

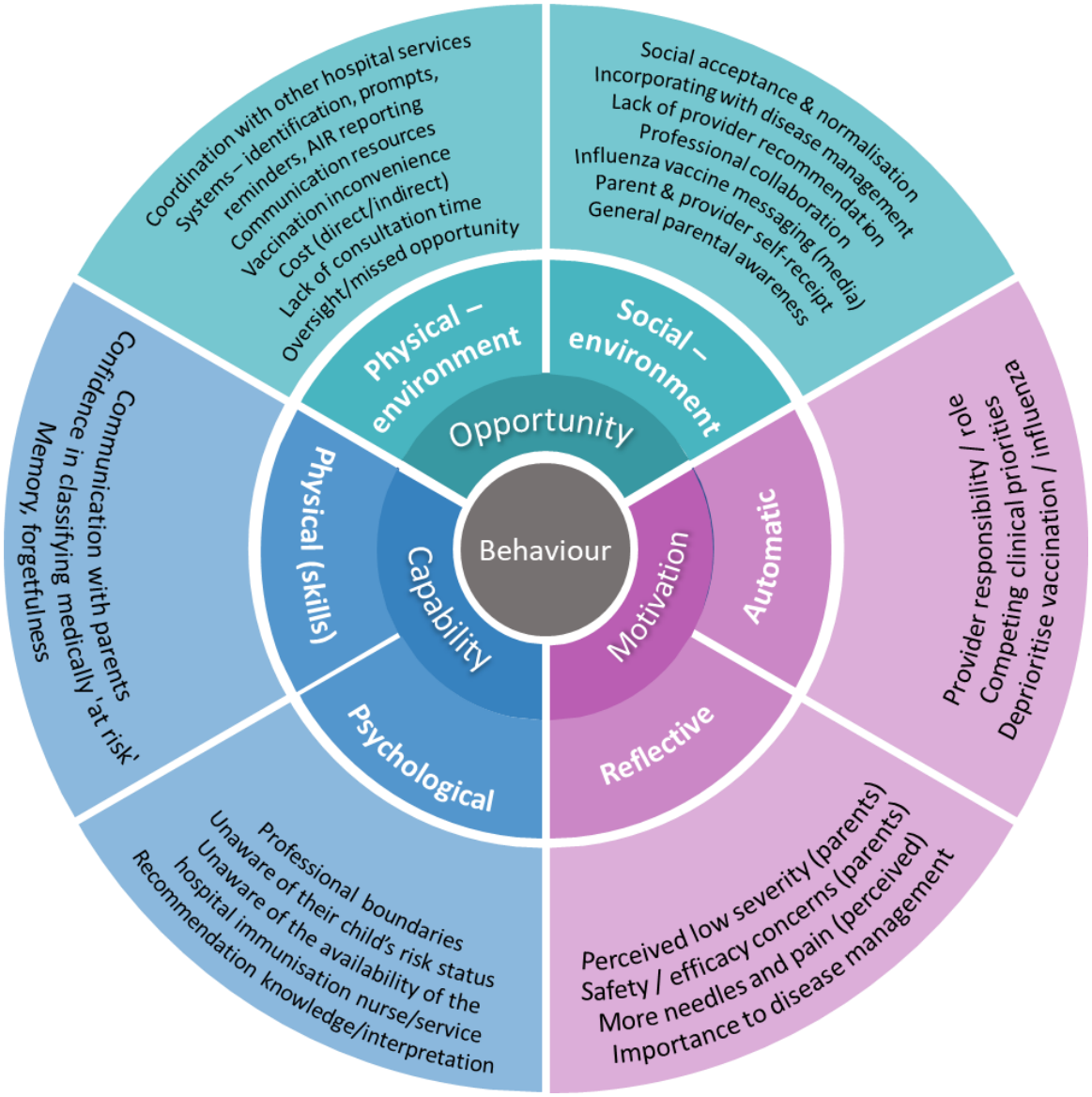


Table 3: Components of the 'COM-B' model of behaviour matched with intervention functions (66)

Drivers of behaviour		Intervention functions: Education	Persuasion	Incentivisation	Coercion	Training	Restriction	Environmental restructuring	Modelling	Enablement
Capability	Physical					✓				✓
	Psychological	✓				✓				✓
Opportunity	Physical						✓	✓		✓
	Social						✓	✓		✓
Motivation	Automatic		✓	✓	✓			✓	✓	✓
	Reflective	✓	✓	✓	✓					

✓ denotes effective interventions

Explanations and further examples of intervention functions are explained in detail in Michie *et al*. and The Behaviour Change Wheel guidebook. (66, 176) In brief, these interventions may include: education: increasing knowledge or understanding; persuasion: using communication to induce positive or negative feelings or stimulate action; incentivisation: creating expectation of reward; coercion: creating expectation of punishment or cost; training: imparting skills; restriction: using rules to reduce the opportunity to engage in the target behaviour (or to increase the target behaviour by reducing the opportunity to engage in competing behaviours); environmental restructuring: changing the physical or social context; modelling: providing an example for people to aspire to or imitate; and enablement: increasing means/reducing barriers to increase capability or opportunity.

This second Behaviour Change Wheel phase was carried out parallel to constructing a summary of the situation according to the TIP principles including the key challenges (Table 4) that should be focused on as well as opportunities (Table 5) at the WCH site. The emphasis placed on tertiary care provider recommendation by parents, lack of recommendation by specialists as well as missed opportunities in general practice through lack of identification were considered key drivers to address and were prioritised to target in our population as part of our intervention.

Table 4: Key Challenges at the Women's and Children's Hospital

Challenges associated with the target group´s knowledge, attitudes and behaviours	Heterogeneous group with divergent medical needs and health service use. Moderate awareness of recommendation (parents). Highly motivated by tertiary care provider recommendation. Specialists have competing priorities which lead to missed opportunities. GPs have high sense of responsibility to provide vaccine.
Challenges related to being able to communicate effectively	Lack of communication resources designed for providers/parents of children in target group. Low provider influenza specific communication skills to deliver influenza vaccine messaging.
Challenges related to creating circumstances that make it easier for the target group to take desired action	Vaccination inconvenience due to multiple medical appointments. Unwilling to attend for more appointments, if otherwise well. Lack of co-ordination with other hospital services. Uncertainty of location of WCH Immunisation Clinic Memory/forgetfulness to remember to get vaccine/ provide recommendation. GPs look to specialists to provide recommendation.

Table 5: Key Opportunities at the Women's and Children's Hospital

Opportunities associated with the target group´s knowledge, attitudes and behaviours	Most parents motivated to protect their children if a tertiary care provider recommends the vaccine.
Opportunities related to being able to communicate effectively	Specialists are keen to engage but require environmental supports.
Opportunities related to creating circumstances that make it easier for the target group to take desired action	WCH supportive of immunisation. Project goals aligns with WCH Strategic Plan 2018-2020 Availability of modernised ICT infrastructure Good relationships exist between health mediators and specialists

In the third Behaviour Change Wheel phase, content and implementation options were identified. The **Flutext-4U** intervention (Table 6) is therefore evidence-based and targeted to the study population. Considering that the intervention would be delivered at a single site, the multimodal intervention (based on research findings presented in this thesis) integrates prompts at to both providers (specialists and GPs) and reminders to parents. Reminders to parents will consider text messaging (SMS) to serve as an intermedium between parents-specialists to moderate coverage. The GP prompts will be in the form of a hospital-based communication to the child's treating primary care provider. The intervention will also target the requirement for environmental/structural supports and the social environment at the site (WCH) to support influenza vaccination.

Table 6: Utilising provider-parent strategies to improve influenza vaccination in children and adolescents with special risk medical conditions: Flutext-4U intervention components by vaccination pathway level

Vaccination Pathway Level	Intervention component
Practice Health Service (WCH)	Identification of children with SRMC at the WCH with a hospital appointment between April and September and: i) previously hospitalised with an ICD-10-coded medical condition listed in the AIH and/or ii) attending specialist clinics managing children with specific special-risk conditions (e.g. oncology, cystic fibrosis, diabetes clinics, etc.), will be identified and enable a tertiary centred vaccination tracking system to be established. Lists of existing and newly identified special -risk children will be provided to the study coordinator, enabling real-time review of AIR records and set up of SMS reminders. (Environmental restructuring) Ensuring ease of access*:* The WCH has committed to ensuring that influenza immunisation will be readily available and provided free upon request (i.e. without a prescription; a standing order) to children with SRMC. (environmental restructuring) – Availability of immunisation-competent staff (Environmental restructuring) – Provision of additional wayfinding and/or signage (Environmental restructuring) – Availability for family members to receive the vaccine at the WCH. (Environmental restructuring/ incentive-isation)
Tertiary Provider (paediatric specialists)	Influenza messaging strategies for clinicians to use with parents. (Training) Provider reminders (e.g. alert stickers) will be attached to medical case notes and/or electronic reminders) prompting providers to discuss influenza immunisation with the parents of children with SRMC attending outpatient clinics and other appointments. (Environmental restructuring)

Vaccination Pathway Level	Intervention component
	Resources will be developed to address answers to common questions and dispels misconceptions and will include departmental in-services and a grand-round presentation to be timed for the Flutext-4U 2020 launch. (Environmental restructuring/ modelling)
Primary Care Provider (GPs)	Provider reminders the tertiary centred vaccination tracking system (based at WCH) will send communication to the child's current health care provider to prompt GPs to advise that child 'X' is medically at risk, and request their assistance in ensuring that the child receives the influenza vaccine. Two-way communication between tertiary care and primary care will be established and encouraged. (Environmental restructuring)
Parent	Text-message reminders will be provided in a non-directive educational approach, between April and June each year, text-message reminders will be sent (on behalf of the Women's & Children's Hospital [WCH] and the study team) to the parents of children with SRMC. Up to three messages, separated by a minimum of two weeks, will be sent with mechanism to rate the user experience incorporated. Text messages will cease once the child is immunised. Text messages will have an appropriate readability statistic score and will comprise: 1. the influenza vaccination message reminder text, 2. an option to reply with the date of vaccination, if the vaccine has been received elsewhere and 3. three short acceptability questions. If the vaccine is administered at the WCH, the acceptability questions will be triggered by clinic staff and sent to the person's mobile while in the hospital. (Environmental restructuring) Parents will be encouraged to engage with their child's specialist, general practitioner or immunisation provider to answer any related questions arising from the influenza vaccination message. (Environmental restructuring)

Footnote: Behaviour Change Wheel intervention functions are denoted in ().

Notably omitted from the intervention frame were the development of GP specific communication resources, due to the complexities involved to include these as part of the submission in such as short space of time, with plans to later develop these.

It is planned that the intervention will be further developed and implemented in conjunction with i) Clinician Reference Group (a multidisciplinary group of key clinical stakeholders), led by a Senior Pediatrician, at the Women's and Children's Hospital; ii) Community Reference Group (incorporating the WCH consumer group) led by the Executive Director, Nursing and Midwifery at the Women's and Children's Hospital and iii) Youth Advisory Group (which will include some children with SRMC who agree to be involved. Once developed, usability of the Flutext-4U toolkit will be further tested through surveys and semi-structured interviews with an independent group of parents of children with SRMC. Following testing, the content will be iteratively modified. Feedback from the WCH, providers and parents will be sought at the intervention to further optimise and develop tools (such as the way alert stickers are used).

The intervention will be implemented in 2020 and evaluated in a randomised controlled trial.

CONCLUSIONS

This thesis compromises four interrelated themes on influenza vaccination in children identified at increased risk. The themes were constructed to resemble the pathway to vaccination including: risk identification and understanding of severity (impact); coverage and parental recall (coverage and validation); community acceptance and knowledge (community awareness) and lastly to practice level factors, such as vaccination practices and influenza specific communication strategies and resources used by medical practitioners both community and tertiary hospital based (policy and practice).

A systematic review found that compared to healthy peers, children with SRMC had higher odds of ICU admission and bacterial pneumonia, less consistent were higher odds for mechanical ventilation and death. Children with SRMC were more likely to experience prolonged hospital length of stay. However, the level of GRADE evidence was low. Well conducted and reported data on the severity and complications associated with influenza infection for children with SRMC are lacking.

Amongst parents of children with confirmed SRMC, verified influenza vaccination at least once in the last two years was moderate however, only a third received the vaccine annually. An array of factors influences influenza vaccination uptake for children with SRMC and characteristics strongly associated with uptake included: receiving a recommendation from a specialist or GP and having a parent receive the influenza vaccine annually. Overall, 78% of parent reported vaccinations were able to be substantiated by a provider with the kappa indicating good to very good agreement for the two study years. Sensitivity of the AIR to reflect a child's influenza immunisation status was low.

Data from the community survey found low awareness of the recommendation for all children (<5 years) to receive influenza vaccine annually with moderate awareness for the recommendation for children with SRMCs. Parental awareness of the recommendation for children was strongly associated with awareness of recommendation for children with SRMC, living in a metropolitan area and being born in Australia. Those who obtained immunisations from a combination of providers showed lower awareness. The most influential cues to future receipt were a general practitioner (GP) recommendation and providing influenza vaccine free for all children. There was support for the vaccine to be administered at community pharmacies. Expansion of the influenza program to all children < 5 years will require due consideration of access issues.

A cross-sectional survey with medical practitioners found high awareness of the recommendation but a significant gap to practice. The number of medical practitioners' reporting high level confidence in understanding all the conditions considered 'medically at risk' was low. Provision of a recommendation was more likely if they received annual influenza vaccination themselves, had confidence in understanding all the conditions considered 'medically at risk' and perceived ownership of the responsibility to provide the recommendation. Those practising in a regional location were less likely to provide a recommendation.

Qualitative interviews with medical practitioners identified several themes under the categories of the COM-B. Motivation: divergent expectations towards the responsibility to provide a recommendation between GPs and specialists with some GPs seeking specialists' endorsement. Opportunity: lack of systems to support the identification of these children, as well as structural supports that would prompt providers and remind

parents; substantial variability in the routine disease management and engagement with health services for these children and a requirement for additional, well defined resources to support discussions on influenza with parents. Capability: specialists and GPs do not have a clear understanding of each other's roles for influenza vaccination of children with SRMC that overlaps with collaboration, which critically affects expectations for delivery of the recommendation in conjunction with opportunity and GPs report varied methods of communication styles when discussing influenza that are dictated by their personal practitioner style.

Importantly, this thesis confirms that annual influenza vaccination uptake in children with SRMC remains low. The major parental driver to influenza vaccine receipt is receiving a recommendation from a medical practitioner, with a preference for this to be delivered in the context of their child's specialist care. GPs and specialists voiced low levels of confidence in understanding the medical at-risk groups in the recommendation, and preferred, in addition to education, strategies utilising systems approaches to address this. Encouraging families to be protected against influenza could be used as a strategy to increase uptake in medically at risk and "cocoon" the medically at-risk individual. Forging a new paradigm of care in which GPs and specialists collaborate in the immunisation space is required, particularly for those at increased risk, and should establish clear roles and responsibilities. Improving influenza recommendation awareness and providing multimodal approaches that address other barriers is likely to positively affect vaccine uptake in children identified at increased risk.

APPENDICES

A. PROSPERO SYSTEMATIC REVIEW PROTOCOL

Influenza complications in children with high risk medical conditions

Jane Tuckerman, Siobhan Misan, Helen Marshall

Citation

Jane Tuckerman, Siobhan Misan, Helen Marshall. Influenza complications in children with high risk medical conditions. PROSPERO 2017 CRD42017074648 Available from: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017074648

Review question

Do children with high risk medical conditions hospitalized with influenza experience higher rates of complications compared to healthy children?

Searches

Proceeding the systematic literature review, predetermined search strategies and applied pre-defined criteria for inclusion or exclusion and data extraction will be defined. A preliminary search of PubMed and EMBASE will be undertaken to identify keywords contained in the title and abstract, and of the index terms used to describe the article.
The final search of the MEDLINE database (using the PubMed platform) will use all identified keywords and keywords relating to outcomes associated with seasonal influenza complications, along with keywords to identify children and conditions associated with a high risk for influenza complications such as chronic disease or illness or high risk medical conditions (HRMC). The search will be adapted for EMBASE and will be similar to that used for MEDLINE.
In addition, the reference lists of full-text articles included will be reviewed to identify any relevant publications.
Studies published in English from 1990 to 28th Feb 2017 will be considered for inclusion in this review.

Types of study to be included

Retrospective cohort or database studies, prospective cohort and cross-sectional studies will be included.

Condition or domain being studied

The focus of this review is on the complications of influenza in children with high risk medical conditions hospitalized with influenza.

Participants/population

Participants of included studies will include: Infants, children and adolescents hospitalized with influenza. Where a study includes a combination of population ages, only studies that report the results for non-adults separately will be included.
Studies with any of the following conditions will be included: respiratory (severe asthma, cystic fibrosis or bronchiectasis), cardiac disorders such as congenital heart disease; neurological conditions such as hereditary and degenerative diseases including multiple sclerosis, seizure disorders such as epilepsy, spinal cord injuries such as spina bifida and neuromuscular disorders, immune-compromising conditions such as those receiving immunosuppressive therapy (e.g. malignancy, transplantation, HIV or chronic steroids), renal conditions, metabolic disorders and diabetes or as defined as high risk by study authors. Studies that do not breakdown hospitalizations by risk group are excluded.

Intervention(s), exposure(s)

Children with high risk medical conditions hospitalized with influenza infection.

Comparator(s)/control

Children without a high risk medical condition hospitalized with influenza infection.

Primary outcome(s)

the probability of pneumonia,
the probability of ICU admission,
the probability of mechanical ventilation,
the probability of a neurological outcome: seizures,
the probability of a neurological outcome: influenza related encephalopathy,
the probability of dying from influenza,
the length of stay in the hospital,
the length of stay in the ICU.

Secondary outcome(s)

None.

Data extraction (selection and coding)

We will use Covidence to manage the search output. Studies will be screened in a two-step process. Initially by one author (JT) based on title and abstract with full-text copies then retrieved and screened by two authors (SM and JT), disagreements will be resolved by a third author (HM).
The following information related to study characteristics will be extracted independently by two authors (JT and SM):design, year of study, country, number of sites, medical risk group, ages of participants, influenza type along with outcome data. Discrepancies will be identified and resolved through discussion with an additional author (HM), where necessary.

Risk of bias (quality) assessment

Included studies will be independently assessed for quality by two reviewers (JLT & SM) using the Quality in Prognosis Studies (QUIPS) tool. This tool, with 3-6 prompting items and considerations examines the potential for bias in the following 6 domains: (1) study participation; (2) study attrition; (3) prognostic factor measurement; (4) outcome measurement; (5) study confounding; and (6) statistical analysis and reporting. Judgments of low, moderate, high risk of bias or unable to determine will be made for each applicable domain. Differences between reviewers will be discussed, and a decision will be made by agreement.
Quality of evidence for each outcome will be assessed by JLT according to the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) framework modified for prognosis reviews.

Strategy for data synthesis

We will pool data, where possible in statistical meta-analysis using RevMan, with weighted mean differences for continuous outcomes and odds ratios for dichotomous outcomes, and calculate 95% confidence intervals for each outcome.
Where statistical pooling is not possible we will provide a narrative synthesis of the findings from the included studies, using tables and figures to present summary data visually for each outcome, as appropriate.

Analysis of subgroups or subsets

Heterogeneity will be assessed statistically using the I-squared statistic. We will classify an I-squared of 50% or above to indicate a substantial level of heterogeneity. If there is sufficient data to permit analyses, we will also explore heterogeneity by subgroup analysis of studies based on laboratory confirmed influenza (LCI), risk of bias and influenza vaccination status.

Contact details for further information

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Organisational affiliation of the review

The University of Adelaide

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Professor Helen Marshall. Robinson Research Institute and Adelaide Medical School, The University of Adelaide and Women's and Children's Health Network

Anticipated or actual start date
10 August 2015

Anticipated completion date
30 November 2017

Funding sources/sponsors
This review was initiated as part of studies towards a Doctor of Philosophy (PhD) undertaken by JLT. JLT's studies are funded by an Australian Government Research Training Program Scholarship (formally Australian Postgraduate Award). HM is supported by NHMRC Fellowship. This review is not sponsored or financed by a third party

Conflicts of interest
None known

Language
English

Country
Australia

Stage of review
Ongoing

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Child, Hospitalization, Humans, Influenza, Human, Risk

Date of registration in PROSPERO
30 August 2017

Date of publication of this version
30 August 2017

Stage of review at time of this submission
The review has not started

Stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	No
Risk of bias (quality) assessment	Yes	No
Data analysis	No	No

Versions

30 August 2017

B. SYSTEMATIC REVIEW SEARCH STRATEGY

Systematic Review Search Strategy

Search terms

Title + keywords relating to outcomes associated with influenza complications and including the following keyword combinations:

((Influenza, Human[majr] OR Influenza[tiab] OR Flu[tiab]) AND (Adolescen*[ALL] OR Teen*[ALL] OR Youth*[ALL] OR Child[MH] OR Child*[ALL] OR Pre school*[ALL] OR Preschool*[ALL] OR Infant[MH] OR Infant*[ALL] OR Paediatric[ALL] OR Pediatric[ALL]) AND (Hospital admission*[ALL] OR Hospitali*[ALL] OR Length of Stay[ALL] OR Death*[ALL] OR Mortality[MH] OR Mortalit*[ALL] OR Fatal*[ALL] OR Pneumonia [ALL] OR Intensive care[ALL] OR ICU[ALL] OR Respiration, Artificial[MH:noexp] OR Artificial Respiration[ALL] OR Mechanical Ventilation[ALL] OR Outcome*[ALL]) AND (cohort studies[mh] OR cohort analys*[tw] OR cohort design*[all] OR cohort evaluation*[tw] OR cohort research[all] OR cohort stud*[tw] OR cohort survey*[tw] OR concurrent stud*[tw] OR concurrent survey*[tw] OR incidence analys*[tw] OR incidence research*[all] OR incidence stud*[tw] OR incidence survey*[tw] OR longitudinal analys*[tw] OR longitudinal design*[all] OR longitudinal evaluation*[tw] OR longitudinal research[all] OR longitudinal studies[tw] OR longitudinal study[tw] OR longitudinal survey*[tw] OR follow up evaluation*[tw] OR followup evaluation*[tw] OR followup stud*[tw] OR follow up stud*[tw] OR followup survey*[tw] OR follow up survey*[tw] OR prospective analys*[tw] OR prospective design*[all] OR prospective evaluation*[tw] OR prospective studies[tw] OR prospective study[tw] OR prospective survey*[tw] OR retrospective analys*[tw] OR retrospective design*[all] OR retrospective evaluation*[tw] OR retrospective research[all] OR retrospective stud*[tw] OR retrospective survey*[tw] OR cross-sectional studies[mh] OR cross sectional analys*[all] OR cross sectional design*[all] OR cross sectional

evaluation*[all] OR cross sectional research[all] OR cross sectional stud*[all] OR cross sectional survey*[all] OR prevalence research[all] OR prevalence stud*[all] OR prevalence survey*[all])) NOT (H1N1[ALL] OR Pandemic*[ALL]) NOT (Animal* NOT(Human OR Humans))

influenza	Children	Outcomes	Conditions	NOT
Influenza, Human[majr] OR Influenza[tiab] OR Flu[tiab]	Adolescen*[ALL] OR Teen*[ALL] OR Youth*[ALL] OR Child[MH] OR Child*[ALL] OR Pre school*[ALL] OR Preschool*[ALL] OR Infant[MH] OR Infant*[ALL] OR Paediatric[ALL] OR Pediatric[ALL]	Hospital admission*[ALL] OR Hospitali*[ALL] OR Length of Stay[ALL] OR Death*[ALL] OR Mortality[MH] OR Mortalit*[ALL] OR Fatal*[ALL] OR Pneumonia [ALL] OR Intensive care[ALL] OR ICU[ALL] OR Respiration, Artificial[MH:noexp] OR Artificial Respiration[ALL] OR Mechanical Ventilation[ALL] OR	Chronic disease*[ALL] OR Chronic Illness*[ALL] OR High risk[ALL] OR Medical condition*[ALL]	H1N1[ALL] OR Pandemic*[ALL]

		Outcome*[ALL]		
Study design				Filters
(cohort studies[mh] OR cohort analys*[tw] OR cohort design*[all] OR cohort evaluation*[tw] OR cohort research[all] OR cohort stud*[tw] OR cohort survey*[tw] OR concurrent stud*[tw] OR concurrent survey*[tw] OR incidence analys*[tw] OR incidence research*[all] OR incidence stud*[tw] OR incidence survey*[tw] OR longitudinal analys*[tw] OR longitudinal design*[all] OR longitudinal evaluation*[tw] OR longitudinal research[all] OR longitudinal studies[tw] OR longitudinal study[tw] OR longitudinal survey*[tw] OR follow up evaluation*[tw] OR followup evaluation*[tw] OR followup stud*[tw] OR follow up stud*[tw] OR followup survey*[tw] OR follow up survey*[tw] OR prospective analys*[tw] OR prospective design*[all] OR prospective evaluation*[tw] OR prospective studies[tw] OR prospective study[tw] OR prospective survey*[tw] OR retrospective analys*[tw] OR retrospective design*[all] OR retrospective evaluation*[tw] OR retrospective research[all] OR retrospective stud*[tw] OR retrospective survey*[tw]) OR (cross-sectional studies[mh] OR cross sectional analys*[all] OR cross sectional design*[all] OR cross sectional evaluation*[all] OR cross sectional research[all] OR cross sectional stud*[all] OR cross sectional survey*[all] OR prevalence research[all] OR prevalence stud*[all] OR prevalence survey*[all])				NOT (Animal* NOT(Human OR Humans))
	heart disease[ALL] OR renal disease[ALL] OR metabolic disorder[ALL] OR			

	diabetes[ALL] OR respiratory disease[ALL] OR cystic fibrosis[ALL] OR asthma[ALL] OR long term aspirin[ALL] OR neurological[ALL] OR neuromuscular[ALL] OR immune condition[ALL] OR immunosuppressive [ALL] OR spleen[ALL] OR HIV[ALL] OR long term steroid[ALL]

C. CHILDREN WITH SPECIAL RISK MEDICAL CONDITIONS QUESTIONNAIRE (PROJECT 2)

Children with High Risk Medical Conditions Questionnaire

Section A – About You

A.1 How old are you?

☐ 18-30 ☐ 31-40 ☐ 41-50 ☐ >50

A.2 What is your postcode? _____

A.3 What is your relationship to your child ?

☐ Mother ☐ Father ☐ Legal Guardian

A.4 What is your current work status?

☐ Full time employed ☐ Part time employment ☐ Casual ☐ Not working

A.5 Were you born in Australia? ☐ Yes ☐ No

A.5.1 If you answered no, which country were you born in?

_____

A.6 Are you of Aboriginal or Torres Strait Islander Origin?

☐ Yes ☐ No

A.7 Is English your first language? ☐ Yes ☐ No

A.7.1 If you answered no, what language do you speak at home? _____

A.8 Which best describes the highest educational qualification you have obtained?

☐ Certificate/Diploma ☐ High school certificate or less

☐ Bachelor Degree ☐ Post graduate certificate/diploma

☐ PhD ☐ Other (please specify)_____

A.9 Does anybody in your household smoke? ☐ Yes ☐ No

A.10 Have your ever been vaccinated against influenza? ☐ Yes ☐ No

A.11 Do you receive the vaccine every year? ☐ Yes ☐ No

Section B – About Your Child

B.1 What is your child's name?

First name		Last name	

B.2 What is your child's gender? ☐ Male ☐ Female

B.3 What is your child's date of birth? [DD/MMM/YYYY]

B.4 How is your child's health generally?

☐ Excellent ☐ Very Good ☐ Good ☐ Fair ☐ Poor ☐ Declined

B.5 Is your child of Aboriginal or Torres Strait Islander Origin? ☐ Yes ☐ No

B.7 Have they ever been hospitalized, for any condition? ☐ Yes ☐ No

B.8 How many visits (on average) per year would you have with your....

(If you see more than one specialist, please answer for each one.)

B8.1GP		B8.3Specialist #2	
B8.2Specialist #1		B8.4Specialist #3	

B.9 Has your child received all their standard/ routine immunisations?

☐ Yes ☐ No

B.9.1 If No what was the reason?

_____

B.10 Has your child's medical condition effected your decisions to get any vaccinations? ☐ Yes ☐ No

B.11Has your child's medical condition effected your decision to get any vaccinations for your other children?

☐ Yes ☐ No ☐ Don't have other children

B.12 What medical conditions has your child been diagnosed with:

_____

_____

Section C – About Influenza

C.1 Has anyone ever talked to you about influenza and your child?

☐ Yes ☐ No

Please answer the next two questions by circling a number on a scale of 1 to 10 that matches your opinion.

C.2 Do you think getting influenza (or flu) can be serious?

Strongly disagree 0 1 2 3 4 5 6 7 8 9 10 Strongly agree

C.3 Do you think getting influenza (or flu) can be serious for children with certain medical conditions?

Strongly disagree 0 1 2 3 4 5 6 7 8 9 10 Strongly agree

C.4 Prior to hearing about this study did you know the flu vaccine is recommended for children aged >6 months with certain medical conditions?

☐ Yes ☐ No

C.5 Do you think that Health Care Workers working in a hospital should have an obligation to be vaccinated against influenza to reduce the risk of spread of infection to their patients?

- Strongly agree ☐
- Agree ☐
- No view either way ☐
- Disagree ☐
- Strongly disagree ☐
- Don't know / can't say ☐
- Refused ☐

Section D – About Influenza Vaccination

D.1 Has your child ever received a seasonal influenza vaccine?

☐ No ☐ Yes ☐ Don't Know

☐ Declined

('yes' proceed; else ↳ go to Section E)

D.2 How old was your child when they first received it? _____

D.2.1 Did they receive two doses (2 needles) in the first year that they received it?

☐ No ☐ Yes ☐ Don't Know

D.4Have they received a seasonal influenza vaccine in the last two years?

☐ No (↳ go to Section E.1.2) ☐ Yes ☐ Don't Know (↳ go to Section E.1.2)

☐ Declined

D.5 Does your child receive the seasonal influenza vaccine every year?

☐ No ☐ Yes ☐ Don't Know

D.6 Who recommended that your child have the vaccine?

- ☐ No One
- ☐ GP
- ☐ Child's Specialist
- ☐ Hospital Nurse
- ☐ Immunisation Provider
- ☐ GP Practice Nurse
- ☐ Family
- ☐ Other (please specify_____

D.7 Has anyone ever recommend that your child **NOT** have the vaccine?

- ☐ No
- ☐ GP
- ☐ Child's Specialist
- ☐ Other HCP
- ☐ Hospital Nurse
- ☐ GP Practice Nurse
- ☐ Immunisation Provider
- ☐ Other (please specify_____

D.8 Has your child received the vaccine this year? (2015)

☐ No ☐ Yes (Go to D.10) ☐ Don't Know

E.2 Has anyone ever recommend that your child **NOT** have the vaccine?

☐ No ☐ Hospital Nurse

☐ GP ☐ GP Practice Nurse

☐ Child's Specialist ☐ Immunisation Provider

☐ Other HCP ☐ Other (please specify_____

(If 'Yes' at E.1 skip to E.4)

E.3 Would your child have received the vaccine had it been recommended for them?

☐ No ☐ Yes ☐ Don't Know

E.4 Do you know the influenza vaccine is free for children with certain medical conditions?

☐ No ☐ Yes ☐ Don't Know

E.5 Do you know where to get it?

☐ No ☐ Yes ☐ Don't Know

E.6 Did you know that there is an immunization nurse at the hospital?

☐ No ☐ Yes ☐ Don't Know

E.7 If there was a prominent immunisation service at the hospital would you go and receive the 'flu vaccine for your child. Would you access this service?

☐ No ☐ Yes ☐ Don't Know

E.8 If not why not?

☐ Live too far away ☐ Prefer to receive vaccinations from GP

☐ Other, please specify

_____

Section F – Your child's healthcare provider's contact details

F.1 May we please have your child's **GP** contact details

GP, clinic, hospital, Council Name	
Address	
Address	
Telephone	

F.2 May we please have your child's medical specialist's contact details ☐ Yes ☐ Declined

F.2.1 **Specialist #1**

Clinic or hospital name	
Address	
Address	
Telephone	

F.2.2 **Specialist #2**

Clinic or hospital name	
Address	
Address	
Telephone	

F.2.3 **Specialist #3**

Clinic or hospital name	
Address	
Address	
Telephone	

G.1 Thank you that concludes the survey. Do you have any additional information that you would like to add?

_____

D. INFLUENZA VACCINATION QUESTIONNAIRE FOR MEDICAL PRACTITIONERS (PROJECT 4)

Influenza Vaccination Questionnaire for Medical Practitioners

About you

A.1 How long have you been practicing medicine? ☐ <5 yrs ☐ 6-10 yrs ☐ 11-15 yrs ☐ 16+ yrs	A.5 What specialty do you work in? _____
A.2 What is your gender? ☐ Female ☐ Male ☐ Other	A.6 Have your ever been vaccinated against influenza? ☐ Yes ☐ No
A.3 What is your current work status? ☐ Full time ☐ Part time ☐ Casual	A.7 Do you receive the vaccine every year? ☐ Yes ☐ No
A.4 Which would best describe your job title? ☐ General Practitioner ☐ Specialist ☐ Other _____	A.8 What is your main reason for wanting to get vaccinated? (Please specify) _____

About Influenza

For the following statements please indicate your response by marking with an 'X' in the table.

	Strongly agree	Agree	No view either way	Disagree	Strongly disagree
B.1 In general, influenza is serious					
B.2 Influenza is serious in children with high risk medical conditions					
B.3 Health Care Workers working in a hospital should have an obligation to be vaccinated against influenza					

Recommending the influenza vaccination

C.1 Prior to this study did you know the flu vaccine is recommended for children aged >6 months with select medical conditions? ☐ Yes ☐ No

C.2 Do you discuss influenza infection with parents of children with high risk medical conditions?
☐ All of the time ☐ Most of the time ☐ Sometimes ☐ Never

C.3 Are you confident you understand all of the conditions considered 'medically at risk' for influenza?
☐ Very confident ☐ Confident ☐ Somewhat confident ☐ A little confident ☐ Not confident at all

C.4 Do you routinely recommend and encourage parents of children with medical conditions to vaccinate their child against seasonal influenza?
☐ All of the time ☐ Most of the time ☐ Sometimes ☐ Never

For the following statements please indicate your response by marking with an 'X' in the table.

	Strongly agree	Agree	No view either way	Disagree	Strongly disagree
C.5 Recommending the influenza vaccine is my responsibility					
C.6 Recommending the influenza vaccine is the responsibility of a child's specialist					
C.7 Recommending the influenza vaccine is the responsibility of a child's GP					

PLEASE TURN OVER...

For the following statements please indicate your response by marking with an 'X' in the table.

	Strongly agree	Agree	No view either way	Disagree	Strongly disagree
C.8 The wording of the recommendations in the NHMRC Australian Immunisation Handbook for influenza for the 'at risk' medical conditions are well defined					
C.9 A recommendation for all children to receive the influenza vaccine is justified.					
C.10 The influenza vaccine is effective					
C.11 The influenza vaccine is safe					
C.12 Consultation time is not sufficient to discuss influenza vaccination					
C.13 Influenza vaccination is a lower priority compared to treating other clinical issues					
C.14 The complexity a child's medical conditions limits discussing influenza vaccination					
C.15 I often do not recommend the influenza vaccine if I'm unsure a medical condition qualifies as 'at risk'					
C.16 I feel equipped to respond to parent's questions particularly when they involve 'other' medical conditions, for which the child is under the care of a specialist.					
C.17 Medical Practitioners should receive an incentive payment to vaccinate children identified at risk of influenza					

C.18 Do you have a reminder/ recall system for medically at risk children to be offered the influenza vaccine? ☐ Yes ☐ No ☐ Unsure

C.19 Do you have any other reasons that restrict your ability to recommend the influenza vaccine for high risk patients that we have not listed?

_____

_____

C.20 If more education about influenza vaccination recommendations was made available. What format would you like to see?

_____

_____

C.21 **Would you agree to be contacted (during business hours) to participate in a further 10-15-minute individual telephone interview to better understand your attitudes towards the influenza vaccine?**

NB: You **DO NOT** need to participate in an interview to return your completed survey.

☐ YES → Please read, complete and return the attached Participant Information Sheet and Consent form along with your completed questionnaire in the reply-paid envelope.

☐ NO → Thank you for your time. Please return the completed questionnaire in the reply-paid envelope.

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