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Originality Statement

'I hereby declare that this submission is my own work and to the best of my knowledge it contains no materials previously published or written by another person, or substantial proportions of material which have been accepted for the award of any other degree or diploma at the Australian National University or any other educational institution, except where due acknowledgment is made in the thesis. Any contribution made to the research by others is explicitly acknowledged in the thesis. I also declare that the intellectual content of this thesis is the product of my own work, except to the extent that assistance from others in the projects' design and conception or in style, presentation or linguistic expression is acknowledged'.

Signed ……..

Date ……..

THESIS ABSTRACT

My field placement for Master of Philosophy in Applied Epidemiology (MAE) program was with the Indigenous Health Division of the Australian Government Department of Health, and it provided opportunities for epidemiological training in a broad range of contexts. I present four projects to fulfil the core requirements of the MAE.

I participated in a retrospective investigation into cases of carbapenemase-producing *Enterobacteriaceae* (CPE) identified over a four year period in the Australian Capital Territory. In this investigation I collected epidemiological evidence and analysed existing environmental and whole-genome sequencing data to identify two small, but prolonged, outbreaks at a tertiary hospital. The investigation revealed that nosocomial transmission of CPE is more extensive than previously understood, and is characterised by lengthy asymptomatic carriage and persistence of CPE in the hospital environment. We used the outbreak data to assess the utility of an interstate CPE prevention and control guideline, and to develop infection control recommendations specifically for the hospital.

I analysed data from the Longitudinal Study of Indigenous Children (LSIC) to identify early life exposures associated with social and emotional wellbeing (SEWB) in Aboriginal and Torres Strait Islander children at school commencement. Large household size and frequent exposure to major life events were weakly associated with poorer mental health and fewer prosocial behaviours; but conversely predicted a greater connection of the child to community, culture and country. Most importantly, I found that mainstream mental health assessment tools do not reflect the positive, holistic concept of SEWB, and I was unable to create a more appropriate index using LSIC data. This study highlighted the need to develop measures that privilege Indigenous ways of being and knowing.

My evaluation of Australia's Enhanced Invasive Pneumococcal Disease Surveillance Program found that this complex system is highly flexible and stable, and is acceptable to users and stakeholders. It has proved very useful for monitoring the national infant vaccination program—informing a change to the recommended vaccine in 2011. The

program is less useful for evaluating targeted vaccination in other high-risk groups and for surveillance of antimicrobial resistance. My key recommendations focussed on collecting complete data for all cases, ensuring stakeholders can easily access useful surveillance data, and improving collection of antimicrobial resistance data.

I conducted the first evaluation of the New Directions: Mothers and Babies Services (NDMBS) program, which aims to increase access to maternal and health child services for Aboriginal and Torres Strait Islander families. I assessed the effect of over $224 million of investment between 2007 and 2015 using data from the Australian Early Development Census. I found that there was little difference in indicators of early child development in the first year of school in areas that were serviced by NDMBS-funded organisations, compared to areas that did not. This may have been due to differences in geographical remoteness between the two exposure groups, but the equivocal findings were more likely due to the evaluation's ecological design and classification error. The project highlighted the importance of developing a program logic model and evaluation plan during the program planning stage, to ensure that data is prospectively collected for use in evaluation.

ACKNOWLEDGEMENTS

Firstly, I am so grateful to my academic supervisor, David Harley. Thanks David for continuing on as my supervisor this year, despite starting a new job interstate. Your common sense, sound advice and good humour kept me on track. You surely should get some sort of prize for responding so quickly to my questions and drafts, and for having the sharpest editor's eye! It was a privilege to have worked under someone with your experience and wisdom.

Thank you to my colleagues at my Department of Health field placement. It was a pleasure to work with such a great team, and I really enjoyed the conversations I've had with you over the last three years. You supported me with kind words, encouragement and food, despite most of what I do being somewhat of a mystery to you all! Thank you to Nick Pascual, for whom nothing was too much trouble.

I feel very fortunate to have been a part of the 2015 MAE cohort, with its breadth and depth of skills and experience. You are a kind, generous and very funny bunch, and it's been a delight to share this journey with you. I am especially grateful to Sam Siripol and Amy Burroughs for all the chats and laughs. Thanks to the other MAE scholars from various cohorts in the Department for support and advice. Thank you also to my former epidemiology tutor and MAE alumni, Kerry-Ann O'Grady, for suggesting that I apply to the program.

To my family and friends: thank you for your understanding and many kindnesses. To my two beautiful MAE babies, Josephine and Susannah: bless you for sleeping occasionally and bringing joy frequently. And finally to Gerrard: thank you for getting us through two babies, three house moves and a renovation; for your unwavering love and belief in me; and for your patience and strength.

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CHAPTER 1 – OVERVIEW OF PLACEMENT AT AUSTRALIAN GOVERNMENT DEPARTMENT OF HEALTH AND SUMMARY OF PROGRAM REQUIREMENTS

Bring us policy approaches that nurture hope and optimism rather than entrench despair…In fast thinking on Indigenous affairs we often hear things like 'We've tried everything and nothing has worked' when actually we haven't tried everything, and we certainly haven't seriously tried a high expectations relationships policy approach.

Dr Chris Sarra

Go to the end of the path until you get to the gate. Go through the gate and head straight out towards the horizon. Keep going towards the horizon. Sit down and have a rest every now and then. But keep on going. Just keep on with it. Keep on going as far as you can. That's how you get there.

Michael Leunig

ABBREVIATIONS

ANFPP	Australian Nurse Family Partnership Program
CaFHS	Child and Family Health Section
CPE	Carbapenemase-producing *Enterobacteriaceae*
IHD	Indigenous Health Division
LSIC	Longitudinal Study of Indigenous Children
MAE	Master of Philosophy in Applied Epidemiology
NDMBS	New Directions: Mothers and Babies Services
OHP	Office of Health Protection
RCT	Randomised controlled trial

About the field placement

I commenced as a Master of Philosophy in Applied Epidemiology (MAE) scholar at the Australian Government Department of Health in the Indigenous Health Division (IHD), Health Programs and Sector Development Branch, Child and Family Health section (CaFHS) on 16 February 2015. This was an excellent placement for me, as my work experience in the last 10 years has been in rural and remote nursing, Aboriginal and Torres Strait Islander ear health and diabetes research, and Aboriginal Health Practitioner pre-registration training. As I took two leaves of absence to have babies, and worked part time for a period, my MAE program was extended by a year.

The Child and Family Health section (CaFHS) is responsible for a range of programs to improve the health and life outcomes for Aboriginal and Torres Strait Islander families, and specifically to halve the gap in child mortality by 2018. These programs include the Australian Nurse Family Partnership Program (ANFPP), a nurse-led home visiting program for mothers of Aboriginal and Torres Strait Islander babies; and the New Directions: Mothers and Babies Services (NDMBS) program, which aims to increase access to maternal and child health services. The section also supports activities that increase understanding of Fetal Alcohol Spectrum Disorders, and leads the Connected Beginnings program, in partnership with the Department of Education and Training, which integrates services for maternal and child health, early childhood and family support within school settings in a number of disadvantaged Aboriginal and Torres Strait Islander communities.

Although a scholar from the 2014 MAE cohort was placed with the Division, I was the first to be placed with CaFHS. Initially, my field supervisor was Dr Annie Dullow, the section Director. With a background in nursing and midwifery, Annie has worked within the Department since 2003 on a range of child and maternal health policies and programs including the National Early Childhood Development Strategy and the National Framework for Protecting Australia's Children. When I returned from maternity leave in 2016, the new Director, Nick Pascual, became my field supervisor. Nick has an extensive history in management in the Department, and as a senior adviser to the Minister for Indigenous Health. In some ways this was a challenging placement, as my colleagues had backgrounds in national policy and programs rather than

epidemiological, public health, or data analysis skills. This meant that I had flexibility in choosing projects, but also that I had to seek support on epidemiological and data analysis matters outside the placement.

Summary of public health experience and impact

Two of my field projects contributed directly to the work of my field placement support organisation. I undertook the first evaluation of the NDMBS program, and analysed data from the Longitudinal Study of Indigenous Children (LSIC) to identify determinants of social and emotional wellbeing for Aboriginal and Torres Strait Islander children.

Due to my epidemiological training and previous work experience, I was able to contribute to policy discussions, review documents, and provide advice to my section colleagues. For example, I provided comments on the draft *National Framework for Health Services for Aboriginal and Torres Strait Islander Children and Families*; the draft child mortality chapter of the Australian Institute of Health and Welfare's analysis of data for the new Closing the Gap targets; and the evaluation strategy for the Connected Beginnings program. During my placement, CaFHS also committed to investing in a randomised controlled trial (RCT) to evaluate the effectiveness of the ANFPP in Brisbane. I have experience in two RCTs in Aboriginal and Torres Strait Islander health, and wrote a course for Menzies School of Health Research on clinical trials, so I provided advice on RCT design and implementation.

In my final weeks on the placement, I prepared and delivered a two hour workshop for my section colleagues. At their request, I presented an overview of the inter-relationships and lifelong impacts of maternal and child health to Aboriginal and Torres Strait Islander health. I also presented short summaries on diabetes and pregnancy, middle ear disease, acute rheumatic fever and rheumatic heart disease, and an interactive session on program logic models and evaluation.

Being placed within the Department facilitated my evaluation of Australia's Enhanced Invasive Pneumococcal Disease Surveillance Program evaluation, including easy access to relevant staff from the Office of Health Protection (OHP) and gaining access to

surveillance data. I was also able to attend fortnightly meetings of the OHP epidemiologists, during which they prepared for their report to Communicable Diseases Network Australia. I drafted and finalised ten International Reports for these meetings. I valued the opportunity to assess reports of communicable disease outbreaks and trends for their relevance to public health and emergency response in Australia.

One of the most rewarding aspects of my training was participating in the investigation of cases of carbapenemase-producing *Enterobacteriaceae* (CPE) with the Departments of Infectious Diseases and Microbiology at the Canberra Hospital. I enjoyed sitting in with the hospital's Infection Prevention and Control Team, observing the daily activities, and learning about these important pathogens and their control. I was able to provide a tangible contribution to the team through the investigation.

It was accepted into the MAE program on my second application. I am so glad I persisted. The MAE has provided the rigorous training, real-life experience and professional network I hoped for. I am looking forward to putting the skills and knowledge I've gained to worthy use, and to calling myself an epidemiologist.

Fulfilment of program requirements

Table 1 Overview of my Masters of Philosophy in Applied Epidemiology program requirements, February 2015 – November 2017

Requirement	Chapter 2	Chapter 3	Chapter 4	Chapter 5	Chapter 6
Analyse a public health dataset			✓	✓	
Design and conduct an epidemiological study		✓			
Evaluate a surveillance system			✓		
Investigate an acute public health problem	✓				
Literature review and critical appraisal		✓	✓		
Oral conference presentation		✓ (Appendix)			
Advanced draft of a paper for peer-reviewed journal	✓	✓ (Appendix)	✓ (Appendix)		
Summary for a lay person				✓	
Teaching requirements					✓

Coursework	**Unit**	**Grade**
	Outbreak Investigation	High Distinction
	Public Health Surveillance	High Distinction
	Analysis of Public Health Data	High Distinction
	Methods in Applied Epidemiological Research	Course requirement satisfied
	Issues in Applied Epidemiology	Course requirement satisfied

CHAPTER 2 – CARBAPENEMASE-PRODUCING *ENTEROBACTERIACEAE* IN THE AUSTRALIAN CAPITAL TERRITORY: OUTBREAK INVESTIGATION AND ASSESSMENT OF INFECTION CONTROL GUIDELINES

When you have eliminated the impossible, whatever remains, however improbable, must be the truth.

Arthur Conan Doyle

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ABBREVIATIONS

CARAlert	National Alert System for Critical Antimicrobial Resistances
CPE	Carbapenemase-producing *Enterobacteriaceae*
ETT	Endotracheal tube
ICU	Intensive Care Unit
MIC	Minimum inhibitory concentration
MOOC	Massive online open course
RACF	Residential aged care facility
SNP	Single nucleotide polymorphism
ST	Sequence type
TCH	The Canberra Hospital
WGS	Whole-genome sequencing

Prologue

I had heard that there was an opportunity to investigate transmission of multi-resistant organisms at the Canberra Hospital (TCH), so I approached the Director of Infectious Diseases, Dr Nick Coatsworth. Nick was kind enough to facilitate my involvement in the investigation of cases of carbapenemase-producing *Enterobacteriaceae* (CPE). I met with Nick, Dr Karina Kennedy (Director of Microbiology), Dr Kathryn Daveson (Infectious Diseases physician), and Wendy Beckingham (Assistant Director of Nursing, Infection Prevention and Control) to discuss the investigation. They wanted to determine if there was transmission of CPE within Canberra hospitals, and also to assess the utility of the Victorian CPE control guideline. This was an exciting project, as the Department of Microbiology had just received the results of whole-genome sequencing (WGS) for four years' worth of stored CPE isolates from patient and environmental samples. The WGS was performed at the Doherty Centre in Melbourne, and I was grateful for Karina and Kathryn's assistance in understanding the sequencing data.

In this chapter, the findings from the projects are presented as two articles that have been prepared for submission to peer-reviewed journals (*Infection Control & Hospital Epidemiology* and *The Medical Journal of Australia*, respectively). They were co-authored with Karina, Kathryn and my academic supervisor, David Harley.

MY ROLE

For this project I

- developed the case definition
- identified cases
- collected clinical and admissions data for cases
- analysed the WGS and admissions data
- developed the transmission maps
- drafted the articles and incorporated edits from co-authors, including the recommendations for CPE infection prevention and control at TCH
- submitted a conference abstract for the outbreak investigation
- presented the findings of the two studies to the TCH Infection Prevention and Control Unit team.

LESSONS LEARNT

It was on this project that I wore out my proverbial epidemiologist's shoe-leather, and learnt about the hard graft of outbreak investigation. Trawling through years' worth of admissions data and hand-written clinical notes for each case took weeks, and looking for patients who could plausibly have been undetected carriers was also very time-consuming.

My understanding of antimicrobial resistance mechanisms and WGS were limited, so I undertook two Massive Open Online Courses (MOOCs) through the Technical University of Denmark and Health Education England. This provided me with the basic knowledge to undertake targeted literature reviews and participate in discussions with my co-investigators.

PUBLIC HEALTH IMPACT

This project provided the TCH Infection Prevention and Control Unit with evidence of significant local transmission of CPE. It also provided the Unit with guidelines for CPE prevention and control that have been tailored to the local context.

The findings will be presented at the Australasian College for Infection Prevention and Control conference in late November 2017.

ACKNOWLEDGEMENTS

Thank you to Kathryn Daveson, who gave guidance, patiently checked my analyses, and encouraged me. I am grateful to Wendy Beckingham and the TCH Infection Prevention and Control Team nurses, who provided vital information on the clinical practice context for the outbreaks, and friendly morning teas. Thank you to Dr Nick Coatsworth, who facilitated my access to TCH systems, provided comments on the articles, and was a constant source of encouragement. I also wish to acknowledge the work of Dr Glen Carter, Senior Project Officer at the Doherty Centre for Applied Microbial Genomics. I am grateful for the practical and technical advice of Dr Norelle Sherry, also at the Doherty Centre.

Two carbapenemase-producing *Enterobacteriaceae* outbreaks at an Australian tertiary hospital

ABSTRACT

OBJECTIVES

Carbapenemase-producing *Enterobacteriaceae* (CPE) pose a serious threat to the effectiveness of last-line antimicrobial agents in Australia. In 2014, two genetically linked cases of CPE were detected at the Canberra Hospital (TCH), prompting an investigation and response that appeared to contain transmission. We report a 2017 retrospective investigation that aimed to identify clusters and transmission mechanisms.

METHODS

Cases of CPE between 2012 and 2016 were identified from the Australian Capital Territory (ACT) Pathology laboratory information system. Whole-genome sequencing was performed retrospectively on 83% of isolates. We investigated two multilocus sequence type clusters using epidemiological, molecular and environmental evidence.

RESULTS

Seventy-two cases were identified, with 90% of isolates containing bla_{IMP} genes. *Enterobacter cloacae* complex and *Citrobacter freundii* were most frequently detected and, based on multi-locus sequence types (STs), were implicated in two outbreaks each spanning over three years. The *E. cloacae* complex ST24 (bla_{IMP}-4) outbreak consisted of seven cases, including the two linked cases identified in 2014. The *C. freundii* ST8 (bla_{IMP}-4) outbreak consisted of ten cases. Both outbreaks most likely originated in the haematology ward and spread via environmental reservoirs and undetected carriers there, in the intensive care unit, and in five other wards.

CONCLUSIONS

Epidemiological and molecular evidence indicate CPE transmission at TCH is more extensive than previously understood. Prevention and control measures must address asymptomatic carriage and persistence in the hospital environment. The value of WGS in CPE outbreak investigation would be increased by using methods that account for gene transfer between *Enterobacteriaceae* species.

INTRODUCTION

Carbapenemases are enzymes capable of hydrolysing the majority of β-lactam antibiotics and most resist inhibition by available β-lactamase inhibitors (1). Since the appearance in the 1990s of carbapenemase genes transferred between gram-negative bacteria (both inter- and intra-species) on mobile plasmids (1), β-lactam antibiotic resistance and nosocomial carbapenemase-producing *Enterobacteriaceae* (CPE) outbreaks are increasingly detected in Australia (2-4). These bacteria are usually resistant to multiple antimicrobial classes, leaving few if any treatment options for CPE infections (5). In Australia, carbapenemases are the most frequently reported antimicrobial resistance mechanism posing a serious threat to the effectiveness of last-line antimicrobial agents (6). Bacteria are predominantly *Enterobacter cloacae* complex, *Escherichia coli* and *Klebsiella pneumoniae*, contain the metallo-β-lactamase gene bla_{IMP}, and are mostly detected in hospitalised patients.

In 2009, the first case of CPE—a returned medical tourist whose urinary catheter specimen grew *Providencia rettgeri* containing $bla_{\text{NDM-1}}$—was identified at The Canberra Hospital (TCH) (7). A handful of apparently sporadic cases were recognised over the next four years. In February 2014, incidental molecular typing and genetic analysis by a research laboratory identified two Intensive Care Unit (ICU) patients with genetically similar isolates of carbapenem-resistant *E. cloacae* complex, highly suggestive of local transmission. This finding prompted an investigation and response from the TCH Infection Prevention and Control Unit team. Carbapenemase-producing *E. cloacae* complex was isolated from the hand hygiene sink in the single room occupied by both patients. The assumption at this time was that local transmission was occurring within the ICU in associated with an environmental reservoir. The room was terminally cleaned, the tap aerator was replaced, and the pipes and sink flushed with sodium hypochlorite. Hand hygiene sinks in the rooms subsequently occupied by the two cases on the haematology and surgical wards were also sampled but no CPE were identified. Investigations showed that nursing staff in ICU had been disposing of body fluids, such as gastric aspirate, and unused liquid antibiotics in the hand hygiene sinks. Staff were educated on the infection control risks and single-use syringes were used for gastric aspiration. All remaining hospitalised patients who had occupied the room in the month before the first case were identified and screened, but no CPE was detected. Environmental screening was extended to all 26 hand hygiene sinks in the ICU, with a

variety of CPE species identified in eight of these. All sinks were cleaned and bleached weekly and then sampled until cleared. An enhanced surveillance program including routine CPE screening (mainly via perianal swabs) of all patients on admission, weekly and at discharge from ICU was introduced and continued for six months. Approximately 70% of patients were screened. During this period, five ICU patients were identified via screening, of whom three were identified on admission to ICU and two on discharge without an admission screen. These were considered sporadic cases without definitive evidence of ongoing local transmission.

Purpose of this study and research objectives

We aimed to provide evidence to assist in the prevention of transmission of CPE at TCH. Our research objectives were to: describe cases of CPE detected through routine testing from 2012 to 2016; identify past outbreaks based on epidemiological and molecular evidence; and investigate possible transmission mechanisms using environmental evidence where available.

Setting

The Canberra Hospital (TCH) is a 600-bed tertiary referral hospital for the Australian Capital Territory (ACT) and surrounding Capital Region of New South Wales (NSW), comprising a population of approximately 600,000. Most subspecialty services are provided at TCH, including adult and neonatal intensive care, with the exception of solid organ and allogeneic stem transplantation, and paediatric cancer and intensive care services. ACT Pathology provides all microbiological services to the two ACT public hospitals (TCH and Calvary Hospital), and some community and private hospital services. Two private pathology laboratories provide the remaining, predominantly community, services in the ACT

Methods

Laboratory methods

A case was defined as a person identified from the ACT Pathology laboratory information system with an *Enterobacteriaceae* spp. possessing a carbapenemase gene

isolated from a clinical or surveillance specimen between 1 January 2012 and 31 December 2016. Methods for identification and genetic characterisation of CPE varied over this time period. *Enterobacteriaceae* spp. from clinical specimens were identified by MALDI-TOF (Bruker Daltronics, Bremen, Germany), followed by susceptibility testing using Vitek® 2 (bioMérieux, Marcy l'Etoile, France). Isolates with a meropenem minimum inhibitory concentration (MIC) greater than 0.25µg/ml were screened for carbapenemase production by either double disk diffusion test, Carba NP or Carbapenem Inactivation Method (8). The genotypes of isolates with a positive carbapenemase screening test and/or those with an MIC>4µg/ml were characterised by one of two commercial assays (AusDiagnostics *Easy*-Plex™ CRE Panel, Sydney; Australia and Cepheid Xpert® Carba-R, Sunnyvale, USA). Surveillance specimens were perianal or rectal swabs directly inoculated onto chromogenic agar (bioMérieux Brilliance), and any organisms grown were identified by MALDI-TOF, with *Enterobacteriaceae* tested as per the clinical specimens.

In October 2016, whole-genome sequencing (WGS) was performed on fifty-nine stored CPE isolates. The analysis was conducted by the Doherty Institute, Melbourne, using Illumina paired-end sequencing on a NextSeq platform. This analysis provided multilocus sequence type (ST), resistance profiles, pairwise core single nucleotide polymorphism (SNP) distances and phylogenetic trees, generated using the Nullarbor pipeline (9).

INVESTIGATION OF CLUSTERS

We investigated two clusters of the same multilocus sequence types to identify epidemiological and environmental links. The first was of seven cases of *E. cloacae* complex with sequence type 24 (ST24) containing $bla_{\text{IMP -4}}$. The second was a cluster of 10 cases of *Citrobacter freundii* ST8, also harbouring $bla_{\text{IMP -4}}$. Clinical data were collected from the ACT Health clinical records information system. We recorded bed locations of patients admitted to TCH in Microsoft Excel (2007) using information from the ACT Health patient administration system. We included all admissions and emergency department presentations at least 12 months before CPE specimen collection, or from January 2012, whichever was earlier.

The most parsimonious transmission map was constructed by following the approach reported by Snitkin and others (10). We also accounted for a number of features of CPE epidemiology, which are listed in Box 1. We considered a link between cases most likely if cases overlapped on the same ward, or if the time between their admissions to the same ward was the shortest, and if the source case was confirmed CPE-positive before isolation of CPE from the putative recipient. Weight was also given to relationships where the pairwise genetic distance between the bacteria isolated from the source and recipient was small. We assumed that bacteria separated by small SNPs were more closely related to each other than to others in the cluster, because their sequences diverged from a common ancestor to the same extent (11). Where a direct epidemiological link between cases could not be found, we looked for potential carriers who shared wards with the source and the recipient.

Box 1 Features of hospital-acquired CPE epidemiology considered in construction of the transmission map.

- Duration of CPE carriage following hospital discharge may be at least 12 months (12)
- Colonisation may be detected well after the transmission event (10)
- Because of undetected colonisation, CPE can be detected in the source case after another case who they infected (10)
- CPE can persist for long periods in ward infrastructure (such as sinks) (3, 13, 14), permitting epidemiological links between sources and recipients whose ward admissions do not overlap
- As targeted CPE surveillance was undertaken in only one ward at TCH in 2014, the possibility of multiple unsampled transmission chains cannot be excluded (15).

ETHICAL REVIEW

The ethical aspects of this research were approved by the ACT Health Human Research Ethics Committee Low Risk Sub-committee (Protocol No. ETHLR.17.042) and by the Australian National University Human Research Ethics Committee (Protocol No. 2017/108).

RESULTS

ALL CPE CASES

Sixty-three people met the case definition. As two or more species containing a carbapenemase-producing gene were isolated from nine of these people, seventy-two isolates were included in the study. The largest number of cases over a three month period was observed from January to March 2015 (Figure 1). Eighty-eight percent of cases were hospital inpatients (Table 2), and most (72%) were detected through clinical isolates—mainly from urine specimens. Case and bacterial characteristics are shown in Table 3.

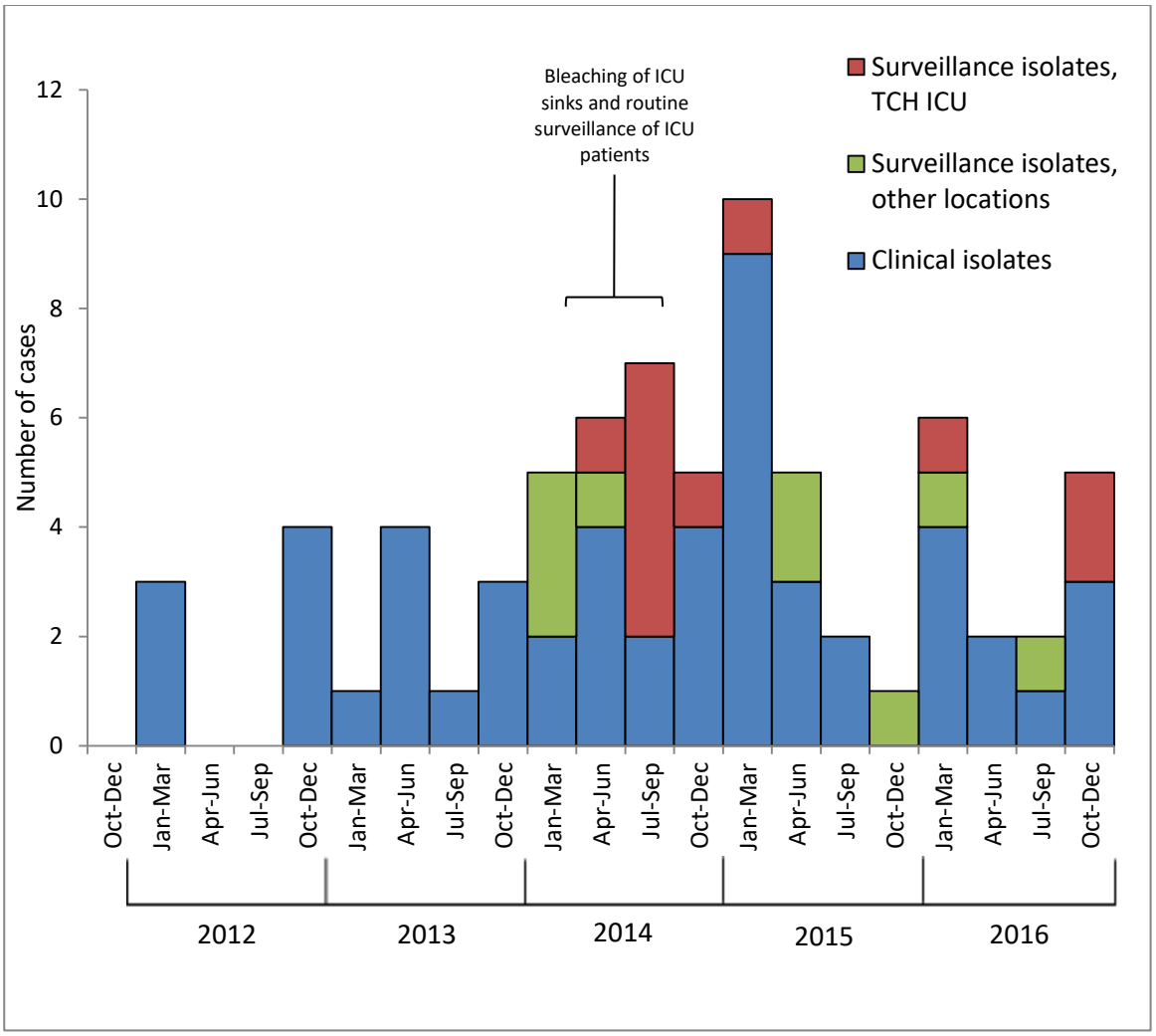

Figure 1 Cases of carbapenemase-producing *Enterobacteriaceae* (CPE) detected by ACT Pathology via surveillance and clinical isolates, 2012-2016.

Table 2 Specimens and admission status of cases of carbapenemase-producing *Enterobacteriaceae* (CPE) detected by ACT Pathology, 2012-2016.

Characteristic		Frequency (n=72)	
Specimen type	urine	25	(35%)
	wound swabs	12	(15%)
	blood	7	(8%)
	sputum	3	(4%)
	other clinical specimens*	5	(8%)
	perianal/rectal surveillance swabs	20	(28%)
Admission status of case at time of specimen collection	TCH inpatient	53	(74%)
	Calvary Public or Calvary Private Hospital inpatient	10	(14%)
	Outpatient of any ACT hospital	7	(10%)
	General practice patient	1	(1%)

* suprapubic catheter site [1], peritoneal swab [1], scrotal wall/groin swab [1], low vaginal swab[1], abdominal drain insertion site[1].

Ninety percent of isolates contained *bla*$_{\text{IMP}}$ genes. Ten species were detected, comprising at least 23 multilocus sequence types—most of which appear only once amongst the sequenced isolates. The most frequently-identified species were *E. cloacae* complex (29%), *C. freundii* (19%), *K. pneumoniae* (13%), *E. coli* (13%) and *Klebsiella oxytoca* (11%). Based on multilocus sequence types and genetic distances, WGS identified two outbreaks.

Median case age was 62 years (range 4 months to 92 years), and a majority were male (57%). Most (79%) were residents of the ACT, and seven percent lived in residential aged care facilities (RACFs). Five had recently received health care internationally (Egypt: *K. pneumoniae* ST383 *bla*$_{\text{OXA-48}}$; Bangladesh: *C. freundii bla*$_{\text{IMP-4}}$; India: *E. coli* ST33 *bla*$_{\text{IMP-4}}$; India: *E. coli bla*$_{\text{NDM}}$; and Vietnam: *E. coli bla*$_{\text{OXA-48}}$) but no other travel histories were recorded. Another case had multiple admissions to hospitals in NSW in the 12 months before her transfer to TCH, where CPE was detected on admission (*K. pneumoniae bla*$_{\text{NDM}}$).

ENVIRONMENTAL INVESTIGATION

The genomes of fourteen environmental CPE isolates collected in 2014 from the ICU were sequenced. All were collected from hand hygiene sinks. Four (isolates E1, E2, E3 and E14) were *E. cloacae* complex ST24 containing *bla*$_{\text{IMP-4}}$ detected between March 2014 and April 2015, and had a similar resistome as seven of the cases. The remainder were *C. freundii* (5 isolates), *K. pneumoniae* (3 isolates) and *K. oxytoca* (2 isolates). Although all of these harboured *bla*$_{\text{IMP-4}}$, none were of the same sequence type as the

Table 3 Selected characteristics of people infected or colonised with carbapenemase-producing *Enterobacteriaceae* (CPE) detected by ACT Pathology, 2012-2016.

Species	Isolates n (%)	Median age (years)	Female n (%)	Detected from clinical isolate n (%)	MLST sequence types detected	No. (%) of isolates carrying gene					
						***bla*$_{IMP-4}$**	***bla*$_{IMP-38}$**	***bla*$_{OXA-48}$**	***bla*$_{NDM-1}$**	***bla*$_{NDM-5}$**	***bla*$_{NDM}$***
Enterobacter cloacae complex	21 (29%)	63	8 (38%)	15 (71%)	24, 32, 45, 50, 66, 113, 127, 742, 610	20 (95%)	1 (5%)	0	0	0	0
Citrobacter freundii	14 (19%)	65	3 (21%)	10 (71%)	8, 62, 98	14 (100%)	0	0	0	0	0
Klebsiella pneumoniae	9 (13%)	63	5 (56%)	8 (89%)	383, 661, 1308, 1528	7 (78%)	0	1 (11%)	0	0	1 (11%)
Escherichia coli	9 (13%)	54	6 (67%)	5 (56%)	33, 221, 410, 687	6 (67%)	0	1* (11%)	1 (11%)	0	1 (11%)
Klebsiella oxytoca	8 (11%)	62	3 (38%)	7 (88%)	20, 29, 53	8 (100%)	0	0	0	0	0
Serratia marcescens	3 (4%)	59	2 (67%)	1 (33%)	none detected	3 (100%)	0	0	0	0	0
Citrobacter amalonaticus	3 (4%)	78	1 (33%)	2 (67%)	none detected	3 (100%)	0	0	0	0	0
Morganella morganii	3 (4%)	56	2 (67%)	3 (100%)	none detected	2 (67%)	0	0	0	1 (33%)	0
Hafnia alvei	1 (1%)	68	1 (100%)	1 (100%)	none detected	0	0	0	0	0	1 (100%)
Enterobacter aerogenes	1 (1%)	85	0	1 (100%)	none detected	1 (100%)	0	0	0	0	0
All cases	**72**	**62.4 years**	**31 (43%)**	**52 (72%)**	-	**64 (88%)**	**1 (1%)**	**2 (3%)**	**1 (1%)**	**1 (1%)**	**3 (4%)**

* Whole-genome sequencing was not performed on these isolates

CPE detected in any of the cases. None of the samples collected from the haematology or gastroenterology wards yielded CPE. However, *Pseudomonas monteilli* harbouring bla_{IMP} (not sequenced) was detected from a sink in the haematology ward.

ENTEROBACTER CLOACAE COMPLEX ST24 OUTBREAK

Seven cases of *E. cloacae* complex ST24 containing bla_{IMP-4} were detected between March 2012 and May 2015, including the two ICU patients referred to in our Introduction (Patients EC3 and EC4) (Table 4). One (EC7) harboured bla_{IMP-38}, which differs from bla_{IMP-4} by one point mutation (16). Its detection may be a sequencing error, or it may have evolved from bla_{IMP-4} (16). All organisms contained genes for β-lactamases, extended-spectrum β-lactamases, aminoglycoside-modifying enzymes, chloramphenicol transferase, and fluoroquinolone resistance proteins. The mean genetic distance between pairs of *E. cloacae* isolated in these seven cases was 915 SNPs (range 323-1535). As the bacteria in each case were around 185 000 SNPs distant from the reference genome used for SNP analysis (*E. cloacae* subspecies *cloacae* ATCC 13047 chromosome, complete genome), it is likely that the SNPs between our cases are inflated. Extended periods of carriage or environmental contamination may also explain these large SNPs. The distances between these and other sequenced *E. cloacae* ranged from 16 000 to 21 000 SNPs.

Results of the epidemiological investigation suggest that *E. cloacae* complex ST24 originated with Patient EC1 in the haematology ward, although it is possible that there were earlier, undetected cases. The pathogen was most likely transmitted via environmental reservoirs or undetected carriers in ICU and the haematology and renal medicine wards (Figure 2, Figure 3). The *E. cloacae* complex detected from Patient EC1 was between 251 and 425 SNPs distant from the ICU environmental samples (E1, E2, E3 and E14) collected from sinks in the ICU. The organism was possibly transmitted from Patient EC1 to Patient EC2 via Patient M (proposed CPE carrier). Patient M, who had lymphoma, was admitted to the haematology ward and ICU, before admission to the renal medicine ward coincident with Patient EC3 for 17 days before collection of Patient EC2's positive sample. Both Patients M and EC2 were subsequently discharged to RACFs. Patient EC2 was not cleared of CPE at discharge. Patient EC4, a 19-year-old who was treated for road trauma, had no risk factors for CPE other than ICU admission. He was transferred to ICU on hospital admission via the operating theatre to a bed within the four-bed bay occupied by Patient EC1 over 20

months earlier. He remained there for 10 days before being transferred to a single room after detection of CPE. Three of the four *E. cloacae* complex environmental samples (EEC1, EEC2 and EEC4) were collected from sinks in this single room after his admission. Patient EC3 also occupied the room. However, the timing of her CPE specimen collection indicates that she arrived in ICU having been infected on the haematology ward, probably while occupying the two-bed room also occupied by Patient EC1.

Patients EC1 and EC6 were admitted to the same single room in ICU in March 2012 and July 2014 respectively. Although more than three years elapsed between their detection, their isolates shared an identical resistome and had the smallest pairwise genetic distance of the outbreak (323 SNPs). This suggests that Patient EC6 was colonised by the resistant *E. cloacae* complex nearly 10 months before detection. Carbapenemase-producing *C. freundii* and *Serratia marcescens* were also detected Patient EC6 in July 2014.

Table 4 Characteristics of people infected or colonised with carbapenemase-producing *E. cloacae* complex ST24 detected by ACT Pathology, 2012-2016. Asterisks indicate that antimicrobial therapy continued for over one month.

					Selected risk factors in the 12 months prior to detection of CPE							
ID	**Sex**	**Age (yrs)**	**Condition/s**	**Specimen Type**	Days in hospital	ICU admission	Upper or lower endoscopic procedure	Long term vascular catheter	Urinary catheter	Type 2 diabetes	Immuno-compromised /suppressed	Antimicrobial therapy
EC1	male	56	B-cell lymphoma with multi-organ failure, scleroderma	Oropharyngeal issue	16	Y	N	Y	Y	N	Y	Meropenem, piperacillin-tazobactam, vancomycin, linezolid
EC2	male	85	Parkinson's disease, foot cellulitis	Urine, suprapubic catheter site swab	59	N	N	N	Y	N	N	Ceftriaxone, cephazolin, cephalexin
EC3	male	19	Motor vehicle accident: traumatic arm amputation, flail chest, pelvic & clavicle fractures	sputum	6	Y	N	N	Y	N	N	Cephazolin, vancomycin
EC4	female	69	Follicular lymphoma, nephrostomy, hospital-acquired pneumonia with sepsis	urine	22	N	N	N	Y	Y	Y	Vancomycin, gentamicin, ceftriaxone, cephazolin, cephalexin
EC5	female	77	End-stage renal failure on peritoneal dialysis	surveillance swab	46	Y	N	Y	Y	Y	N	Cotrimoxazole*, cephalexin*, piperacillin-tazobactam, vancomycin, gentamicin, ciprofloxacin, clarithromycin, ampicillin, amoxycillin-clavulanate, cefuroxime
EC6	female	61	Severe acquired brain injury, tracheostomy, recurrent UTI, recurrent aspiration pneumonia	surveillance swab	365	Y	Y	N	Y	N	Y	Erythromycin*, trimethoprim*, piperacillin-tazobactam, gentamicin, metronidazole
EC7	female	43	Hodgkin's Lymphoma, Crohn's Disease	surveillance swab	61	Y	N	Y	Y	N	Y	Meropenem, piperacillin-tazobactam, vancomycin
	Median	**61 yrs**		**Median**	**55 days**	**71%**	**14%**	**43%**	**100%**	**29%**	**57%**	

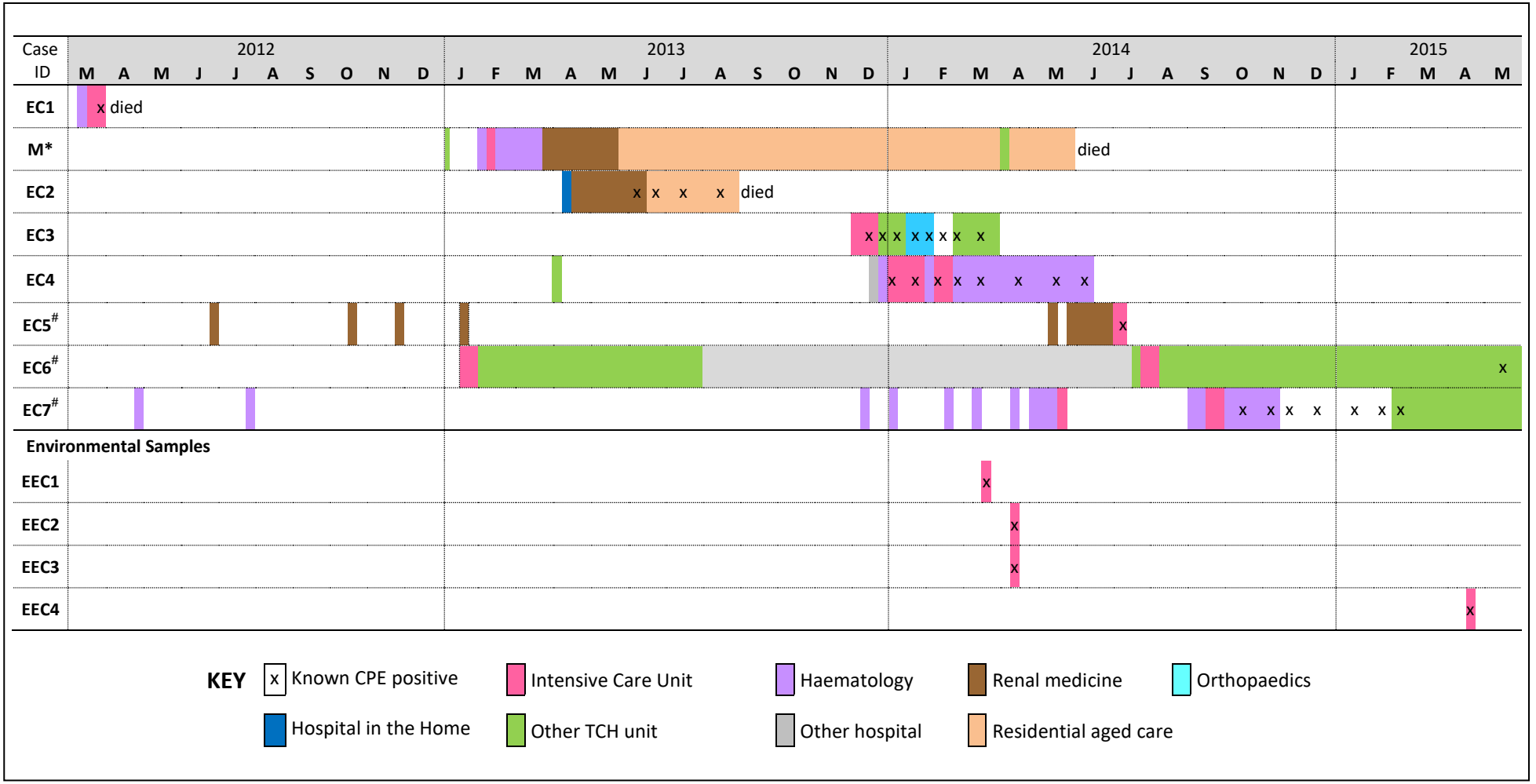

Figure 2 Hospital admission locations of cases of carbapenemase-producing *E. cloacae* complex ST24 (bla_{IMP-4}) detected by ACT Pathology, 2012-2016, and associated environmental samples. *Patient M is a suspected carrier, his CPE status is unknown. #Patients EC5, EC6 and EC7 were detected via surveillance.

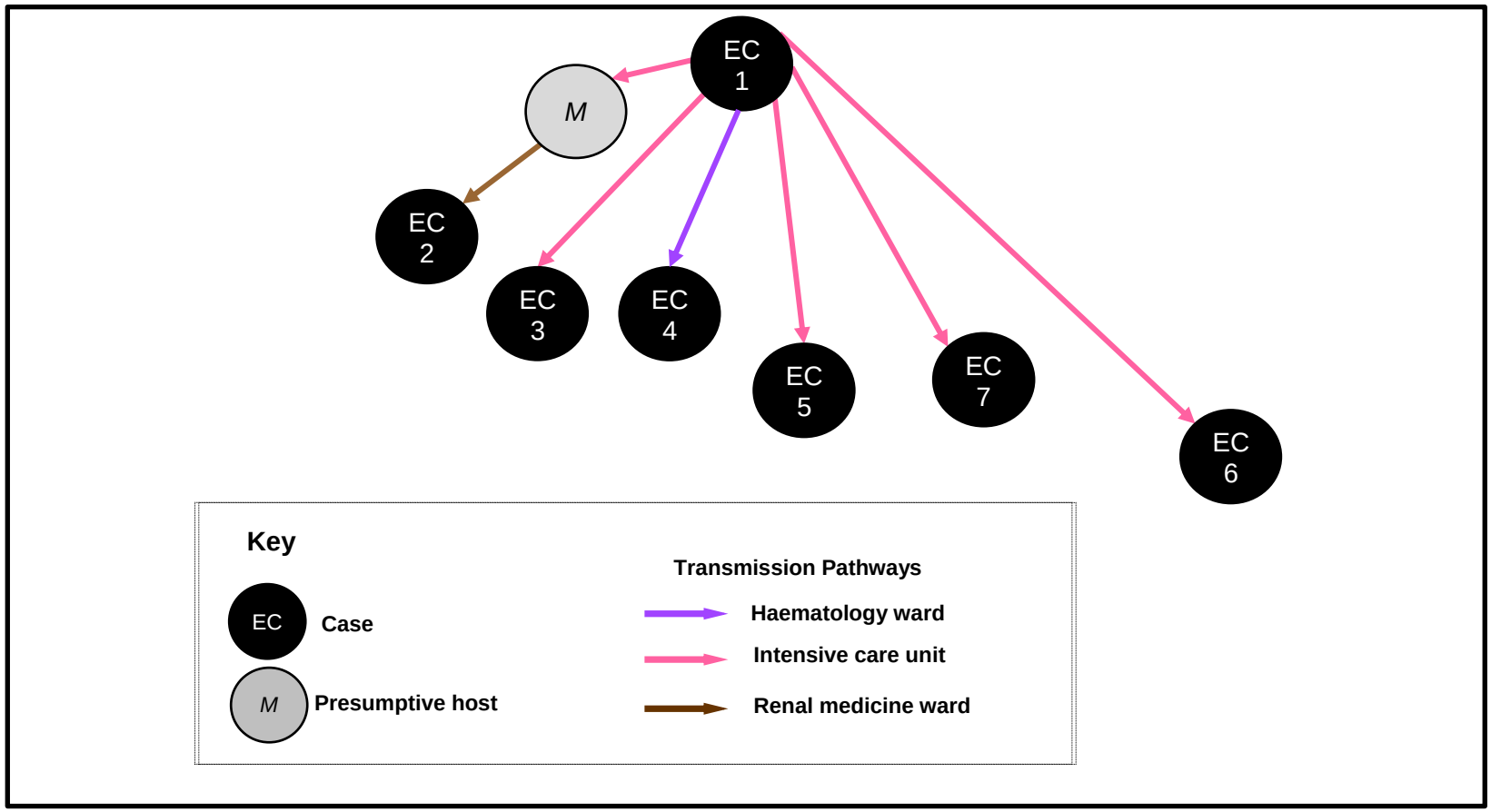

Figure 3 Putative transmission map for the *E. cloacae* ST24 (bla_{IMP-4}) outbreak, the Canberra Hospital, 2012-2016.

CITROBACTER FREUNDII ST8 OUTBREAK

Eight cases of *C. freundii* ST8 containing the carbapenemase gene bla_{IMP-4} were detected between January 2013 and March 2016. A further two cases with bla_{IMP-4} had indeterminate sequence types, because of lack of characterisation of one allele. All other alleles in these cases were identical to ST8. All ten organisms contained genes for β-lactamases, cephalosporinases, and dihydrofolate reductases. The mean genetic distance between outbreak pairs was 122 SNPs (range 37-231). The pairwise distances between these and other sequenced *C. freundii* ranged from 28 000 to 49 000 SNPs.

Cases were mostly male (80%) and had a median age of 69 years (Table 5). Five died in hospital without being cleared of CPE. In the 12 months before CPE detection, four cases had been admitted (on 1 to 5 occasions) to five NSW hospitals, but none had a documented history of international travel in that period. As for the *E. cloacae* complex outbreak, most cases occupied multiple beds and wards during their TCH admissions.

The CPE-positive isolates for the *C. freundii* outbreak were detected between January 2013 and March 2016 (Figure 4). The first, Patient CF1, was admitted to and died in the haematology ward. On epidemiological grounds, we infer that transmission occurred through high risk intermediate carriers (probably Patients G, C, and R) and environmental reservoirs in the haematology ward and ICU (Figure 5). Patient CF4 most likely acquired infection on the orthopaedic ward from Patient CF6, who had been transferred there from the haematology ward. Patient CF3 was briefly admitted to the medical assessment unit and Hospital in the Home (HITH) before outpatient collection of a positive urine specimen. Plausibly she might have acquired the infection in HITH from Patient T who was admitted to ICU concurrently with CF2. There were no environmental samples of *C. freundii* ST8 identified, but samples of three ICU sinks yielded other sequence types (95, 98, and 101) carrying bla_{IMP-4}, one of which was in a room occupied by CF6.

Table 5 Characteristics of people infected with or colonised by carbapenemase-producing *C. freundii* ST8 or similar (genotype bla_{IMP-4}) detected by ACT Pathology, 2012-2016. Asterisks indicate that antimicrobial therapy continued for over one month.

ID	Sex	Age (yrs)	Condition/s	Specimen Type	Selected risk factors in the 12 months prior to detection of CPE							Antimicrobial therapy
					Days in hospital	ICU admission	Upper or lower endoscopy	Long term vascular catheter	Urinary catheter	Type 2 diabetes	Immuno-compromis-ed	
CF1	male	72	Acute myeloid leukaemia, neutropaenic sepsis, leg ulcer	blood	51	N	Y	Y	N	Y	Y	Cotrimoxazole*, piperacillin-tazobactam, flucloxacillin, vancomycin, metronidazole, ciprofloxacin
CF2	male	58	Oesophageal cancer, tracheostomy, percutaneous endoscopic gastrostomy	urine	138	Y	Y	N	Y	N	Y	Cephazolin, metronidazole
CF3	female	61	Extended-spectrum β-lactamase cellulitis, morbid obesity, colostomy	urine	31	N	N	Y	N	Y	N	Ticarcillin-clavulanate, amoxycillin, cephazolin, norfloxacin, cephalexin
CF4	male	77	Hypoplastic myelodysplastic syndrome, pressure injuries, pneumonia with sepsis	wound swab	46	N	N	N	N	Y	N	Piperacillin-tazobactam, gentamicin, amoxycillin-clavulanate
CF5	male	70	Retroperitoneal fibrosis with nephrostomy tube, nephrectomy, vancomycin-resistant *Enterobacter* bacteraemia	urine	93	N	N	N	N	Y	N	Linezolid, teicoplanin, vancomycin, cotrimoxazole, ciprofloxacin, trimethoprim, ceftriaxone, cephazolin, cephalexin, azithromycin
CF6	male	44	Acute myeloid leukaemia	surveillance swab	138	Y	N	Y	N	N	Y	Meropenem (14 days total), cotrimoxazole*, teicoplanin, piperacillin-tazobactam
CF7	male	72	Cerebellar infarction, tracheostomy, percutaneous endoscopic gastrostomy, atrial fibrillation with pacemaker	urine	123	Y	Y	N	Y	Y	N	Piperacillin-tazobactam, cotrimoxazole, cephazolin, cefepime, cefotaxime, cephalexin, roxithromycin, erythromycin, azithromycin, clindamycin, ciprofloxacin
CF8	male	65	Multiple myeloma	surveillance swab	45	Y	N	N	Y	Y	Y	Piperacillin-tazobactam, cotrimoxazole, ceftazidime, cephalexin
CF9	female	68	Neurogenic bladder, rheumatic heart disease, ischaemic heart disease	urine	0	N	Y	N	Y	Y	N	Possibly nitrofurantoin
CF10	male	74	Pneumonia with sepsis, myelodysplastic syndrome, upper gastrointestinal bleed, subdural haematoma, pulmonary fibrosis	surveillance swab	23	Y	Y	N	Y	Y	Y	Piperacillin-tazobactam, doxycycline, ceftriaxone, flucloxacillin, benzyl penicillin, azithromycin, amoxycillin-clavulanate
				Median	**49 days**	**50%**	**50%**	**30%**	**50%**	**80%**	**50%**	

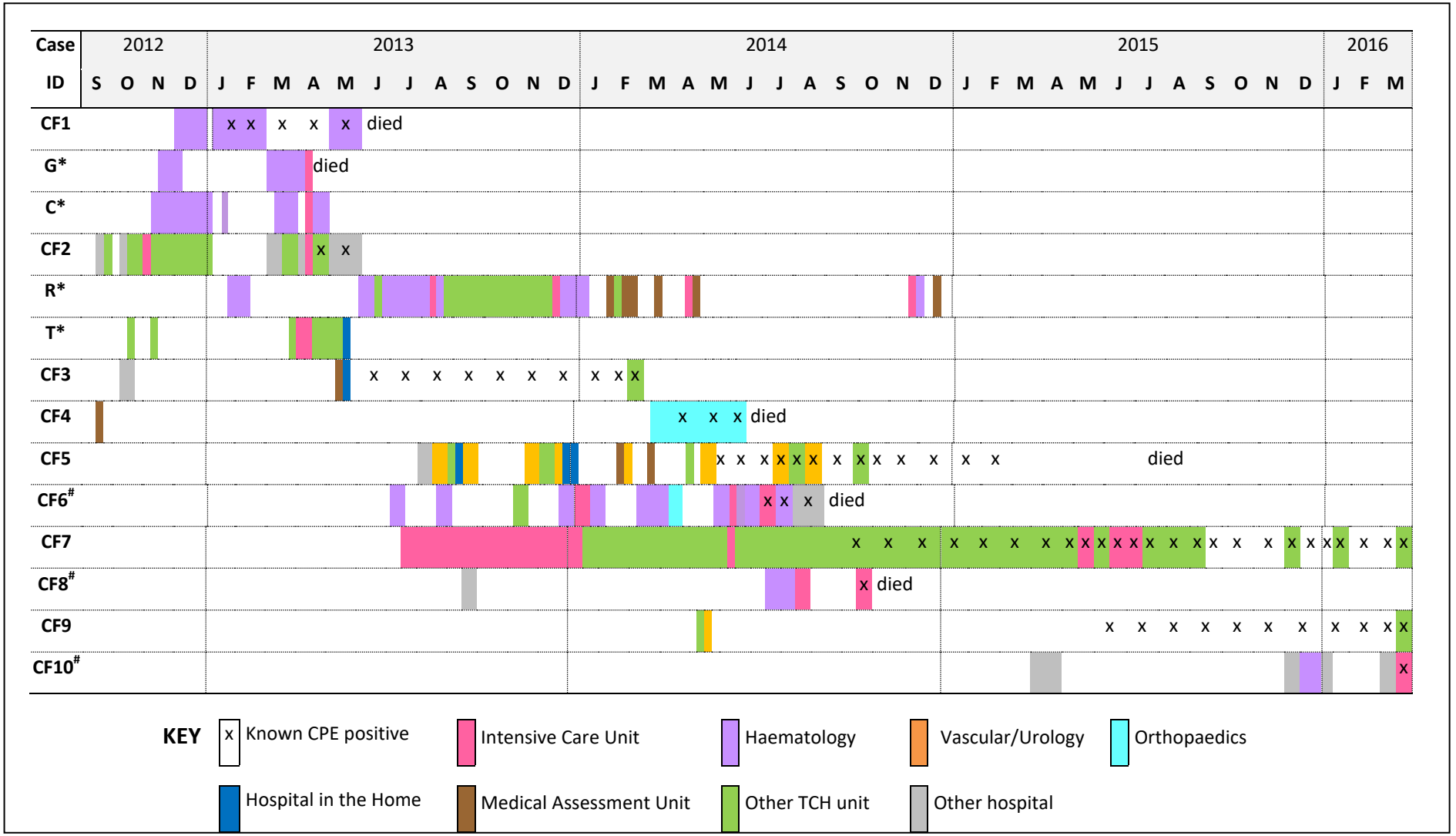

Figure 4 Hospital admission locations of cases of carbapenemase-producing *C. freundii* ST8 or similar (bla_{IMP-4}) detected by ACT Pathology, 2012-2016.

* Patients G, C, R and T are suspected carriers, their CPE status is unknown. #Patients CF6, CF8 and CF10 3 were detected via surveillance.

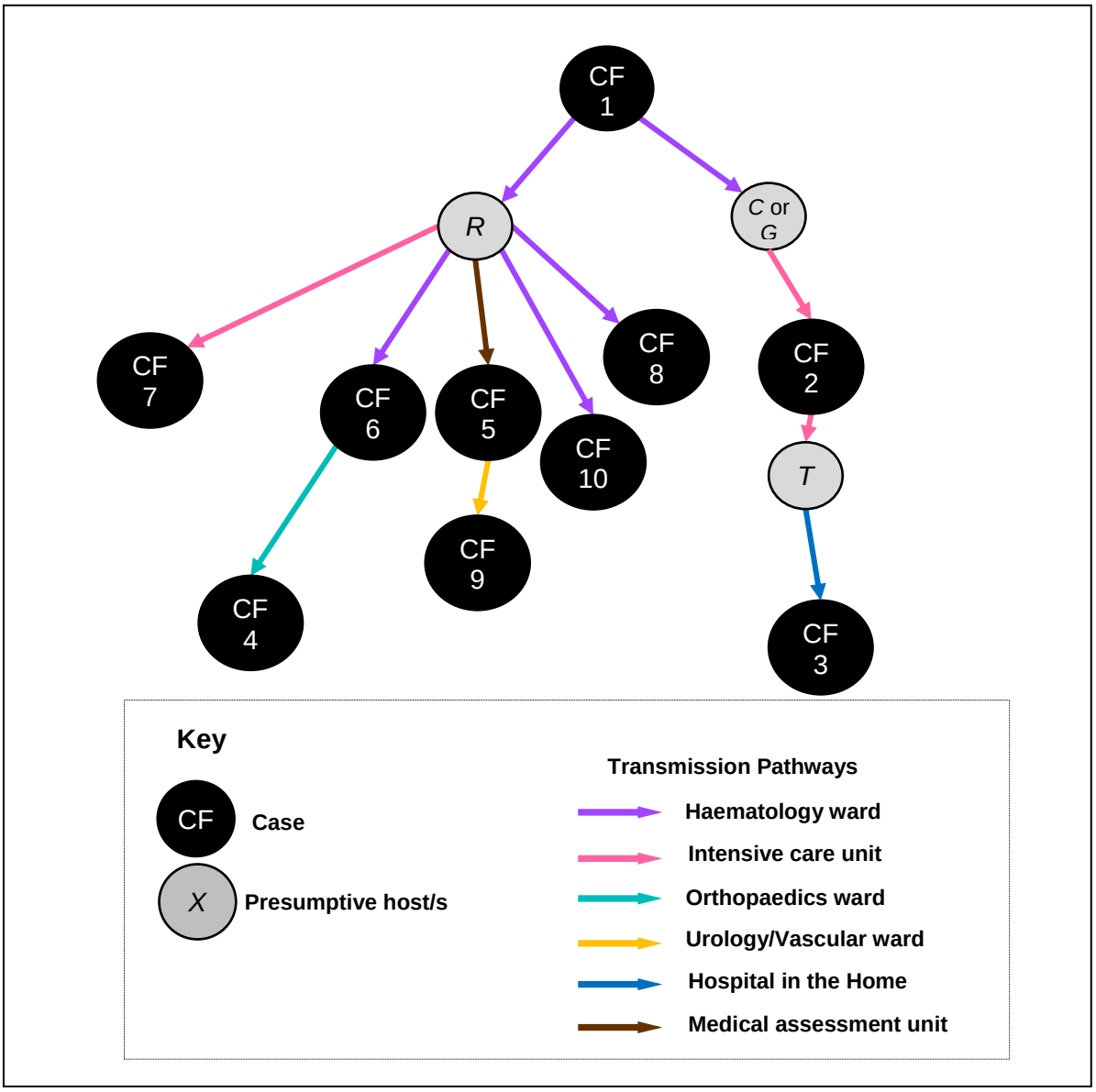

Figure 5 Putative transmission map for the *C. freundii* ST8 or similar (bla_{IMP-4}) outbreak, the Canberra Hospital, 2012-2016.

DISCUSSION

Here we describe the epidemiology of CPE at a tertiary hospital in Canberra, Australia, over a four year period. Based on WGS, local transmission can be inferred in almost one quarter of cases, clustered in two outbreaks each spanning over three years. Epidemiological and environmental data suggest that transmission occurred via persistence of CPE in sinks in the ICU, possibly environmental sources in the haematology ward, and undetected carriers or hosts without clinically significant disease.

The pairwise genetic distances between isolates in the two outbreaks were relatively large. This suggests that genomic variation occurred either in intermediate environmental reservoirs or in patients during the often extended period between CPE acquisition and detection, possibly driven by antimicrobial exposure. Sinks have been implicated as reservoirs in nosocomial outbreaks in Australia (3, 4) and elsewhere (13, 17-19). These reservoirs often persisted despite rigorous cleaning (4, 17-19). In one ICU in the Netherlands, a significant reduction in colonisation with multi-drug resistant organisms was observed after the removal of sinks from patient rooms (20). Recently, Kotay et al (21) demonstrated that when nutrients were added to a model sink system, *E. coli* could grow from the water in a sink's P-trap both up to the sink's strainer, but also to the P-traps of neighbouring sinks. Once the organism has reached the sink strainer, tap water flow can disperse it up to 75cm. The nutrients used in this experiment represent fluids sometimes disposed into hospital hand hygiene sinks, including intravenous fluids, enteral feeds, and beverages. At TCH, the detection of *P. monteilli* containing bla_{IMP} gene in a sink in the haematology ward suggests that *Pseudomonas* spp. in the environment could be reservoirs of CPE genes (22).

Our findings are pertinent to questions of who and how to screen for CPE. Prolonged and undetected carriage was an important feature, consistent with conclusions of other CPE outbreak investigations (15, 23). Zimmerman et al (12) found that most patients with a positive CPE bla_{KPC} culture during hospitalisation still carry CPE at least nine months after discharge. Our epidemiological data indicate that concurrent admission of cases to the same ward was rare, so routine screening only of patients who shared a room or bathroom with a case would be unlikely to assist in outbreak containment. Although universal screening of all inpatients may not be economically justified at low CPE prevalence as is the case for TCH (24), screening of all ICU patients may be highly cost effective (25). Faeces specimens, or rectal plus inguinal swabs also have a higher sensitivity than the specimens (mainly perianal swabs) collected for screening of contacts and ICU surveillance at TCH (26).

As the occurrence of genes other than bla_{IMP} in the 72 cases reported here can largely be explained by international travel, the local picture is one of a range of *Enterobacteriaceae* species containing the $bla_{\text{IMP-4}}$ gene. This is consistent with the epidemiology of human cases within Australia in the eastern jurisdictions of NSW, Queensland, and the ACT (6). A recent study also found that $bla_{\text{IMP-4}}$

Enterobacteriaceae were common in silver gulls (*Chroicocephalus novaehollandiae*) who fed on urban waste dumps in NSW, indicating transmission of CPE outside hospitals (27). A high proportion of our outbreak cases had been admitted to interstate hospitals during the outbreaks, and two were discharged to RACFs, one interstate. Although only 7% of all cases resided in RACFs at the time of CPE specimen collection, it is unknown if further cases were to be discharged to RACFs after isolation. These data indicate that CPE transmission is not a problem solely for tertiary hospitals, but also the community, and a cross-jurisdictional approach to prevention and control is required.

We did not characterise plasmids or integrons, and therefore could not infer the horizontal transfer of carbapenemase-encoding plasmids between species or genera, or between different multilocus sequence types in the same species. Similarly, we have not considered transfer beyond the *Enterobacteriaceae* (eg to *Pseudomonas* spp). Plasmid diffusion is a common mechanism for the spread of carbapenemases (28) and the dissemination of $bla_{\text{IMP-4}}$ among multiple gram-negative genera in Australian hospitals has been demonstrated (29, 30). If such transfers have occurred at TCH then we have underestimated the degree of local transmission of resistance, and may have missed other units of TCH on which transmission has been occurring. Because active surveillance occurred over a few months in 2014 in ICU only, it is likely that asymptomatic carriers in other areas of the hospital, and possibly additional outbreaks, have been missed. We were unable to account for cases' admissions to other hospitals unless they were included in their TCH records.

In this study, WGS data were a valuable addition to epidemiological correlation for identifying outbreaks of CPE cases. If we had clustered cases using resistance gene data collected via other molecular methods (for example, by assuming all *E. cloacae* harbouring $bla_{\text{IMP-4}}$ were related), our investigation would have been unproductive. Multilocus sequence types clarified the picture greatly. The SNP distances between cases were relatively large compared with other CPE outbreaks (10, 31). However, had we given them no weight we would still have reached the same conclusions on mode of transmission and hospital reservoirs.

Epidemiological investigation and WGS have identified two prolonged CPE outbreaks, potentially involving environmental reservoirs and carriers undetected by routine

infection prevention and control investigations. These features imply a risk of escalation of incidence of CPE and clinically significant disease, and increasing demand upon hospital infection control resources. Efforts at TCH will need to focus on identifying CPE hosts to allow effective infection control practices, and on eliminating environmental contamination. Achieving this aim will require the development of cost-effective strategies for highly sensitive screening, and rapid outbreak responses using WGS methods that account for CPE gene transfer between *Enterobacteriaceae* species.

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Transmission of Carbapenemase-producing *Enterobacteriaceae* (CPE) in a tertiary Australian hospital: Assessment of the utility of the Victorian CPE Guideline

ABSTRACT

OBJECTIVES

Infection with carbapenemase-producing *Enterobacteriaceae* (CPE) is relatively uncommon in Australia currently, presenting a critical opportunity to prevent the levels of endemicity of this important antimicrobial resistance experienced elsewhere. Guidance documents have been developed for healthcare-associated CPE prevention and control. We aimed to review the likely impact of guideline implementation on control of two retrospectively-identified CPE outbreaks at the Canberra Hospital, Australia.

METHODS

For two CPE outbreaks that we investigated, we retrospectively determined the effect of applying the *Victorian guideline on carbapenemase-producing Enterobacteriaceae* (2015). The number of cases potentially prevented was estimated from epidemiological data. We assumed 100% sensitivity of screening methods and of control measures.

RESULTS

Application of controls specified for facilities with local transmission at first CPE detection may have prevented all further transmission. The controls specified for facilities with sporadic cases are inadequate because contact tracing is primarily limited to patients who shared a room or bathroom with a case in the month prior to detection.

CONCLUSIONS

Retrospective analysis using outbreak data permits evaluation and revision of CPE control guidelines. Prevention and control measures should address prolonged CPE carriage, and transmission via environmental reservoirs between patients who were admitted to the same room or ward several months apart. A national surveillance and response system to facilitate cross-jurisdictional outbreak detection and contact tracing would enhance outbreak detection and control.

INTRODUCTION

Infection with carbapenemase-producing *Enterobacteriaceae* (CPE) is relatively uncommon in Australia, presenting a critical opportunity to prevent the levels of endemicity experienced elsewhere (1). To prevent increase in incidence, guidance documents have been developed for healthcare-associated CPE prevention and control. We conducted a retrospective case series investigation of CPE detected in the Australian Capital Territory (ACT), using whole-genome sequencing (WGS) and epidemiological data [outbreak paper reference]. We found evidence of limited local transmission of *Enterobacteriaceae* carrying the metallo-β-lactamase gene bla_{IMP} at a tertiary facility, the Canberra Hospital (TCH). The two outbreaks were similar to nosocomial CPE outbreaks described elsewhere, with persistence of the pathogen in the hospital environment (2-5) and prolonged asymptomatic carriage (6, 7).

There is no endorsed guideline for the prevention and control of CPE at TCH. In late 2015, the Victorian Government released a CPE guideline for health services, which recommends different screening and control measures for settings with no cases in the previous 12 months, with sporadic cases, or with local transmission (see Supplementary material) (8). Our objectives were to evaluate whether this guideline is relevant to the TCH context and, if necessary, make recommendations for prevention and control of CPE at TCH.

SETTING

The Canberra Hospital is a 600-bed tertiary referral hospital for the ACT and surrounding region of south-east New South Wales (NSW), comprising a population of approximately 500,000. Most subspecialty services are provided at TCH, including adult and neonatal intensive care, with the exception of solid organ and allogeneic stem transplantation, and paediatric cancer and intensive care services.

METHODS

While recognising that the guideline was not extant at the time of the two outbreaks, we analysed its utility for TCH in CPE case prevention by applying the requirements for Tier 1 (settings with sporadic cases—see the Supplementary material) and Tier 2a (settings with local transmission on one ward) to the transmission maps of two retrospectively identified outbreaks. The epidemiological investigation and methods

used to create these maps have been described previously [reference to Outbreak paper]. We assumed that both screening sensitivity and effectiveness of control measures were 100%.

Seven cases of *Enterobacter cloacae* complex ST24 containing $bla_{\text{IMP-4}}$ were detected between March 2012 and May 2015. We inferred that the *E. cloacae* complex ST24 originated in the haematology ward, and was most likely transmitted to other patients in the outbreak via environmental reservoirs or undetected carriers in the intensive care unit (ICU) and the haematology and renal medicine wards (
Figure 6). This is supported by four positive samples of *E. cloacae* complex ST24 containing $bla_{\text{IMP-4}}$ collected from hand basins in ICU, including basins in the room to which Patients EC3, EC4 and EC7 were admitted. Patients 13 and M were transferred from TCH to residential aged care facilities. Ten cases of *Citrobacter freundii* ST8 or ST8-like containing $bla_{\text{IMP-4}}$ were detected between January 2013 and March 2016. We inferred that transmission occurred primarily through undetected intermediate hosts (for example, Patients G, C, and R) and environmental reservoirs in the haematology ward and ICU (
Figure 7). No environmental samples collected yielded *C. freundii* ST8. Six of the patients in this cluster were admitted to interstate hospitals during the period of the outbreak.

The ethical aspects of this research were approved by the ACT Health Human Research Ethics Committee Low Risk Sub-committee (Protocol No. ETHLR.17.042) and by the Australian National University Human Research Ethics Committee (Protocol No. 2017/108).

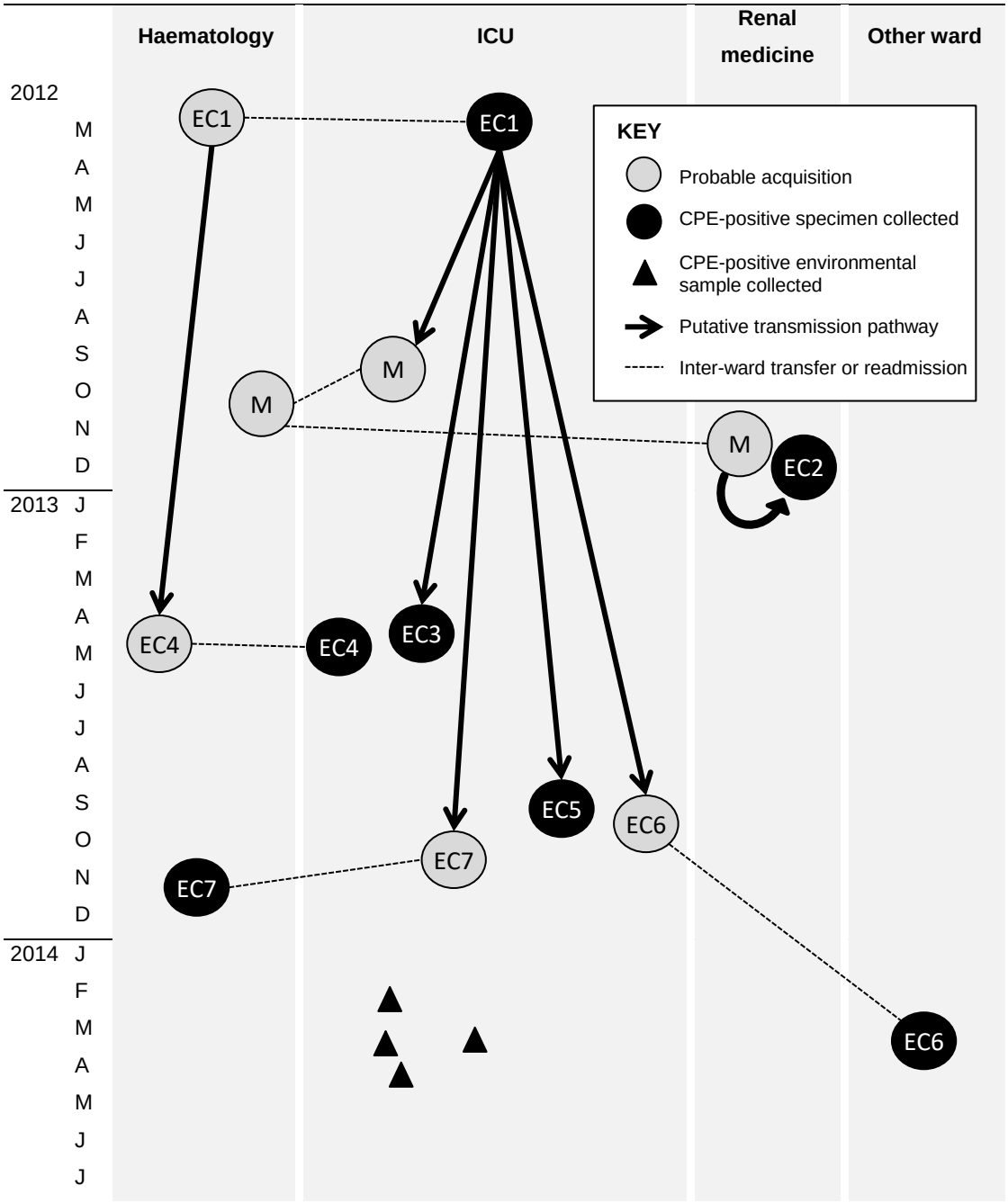

Figure 6 Locations and putative transmission pathways for the *E. cloacae* ST24 (bla_{IMP-4}) outbreak, the Canberra Hospital, 2012-2015. Patient M is a suspected host, his CPE status is unknown. Patients EC5, EC6 and EC7 were detected via surveillance.

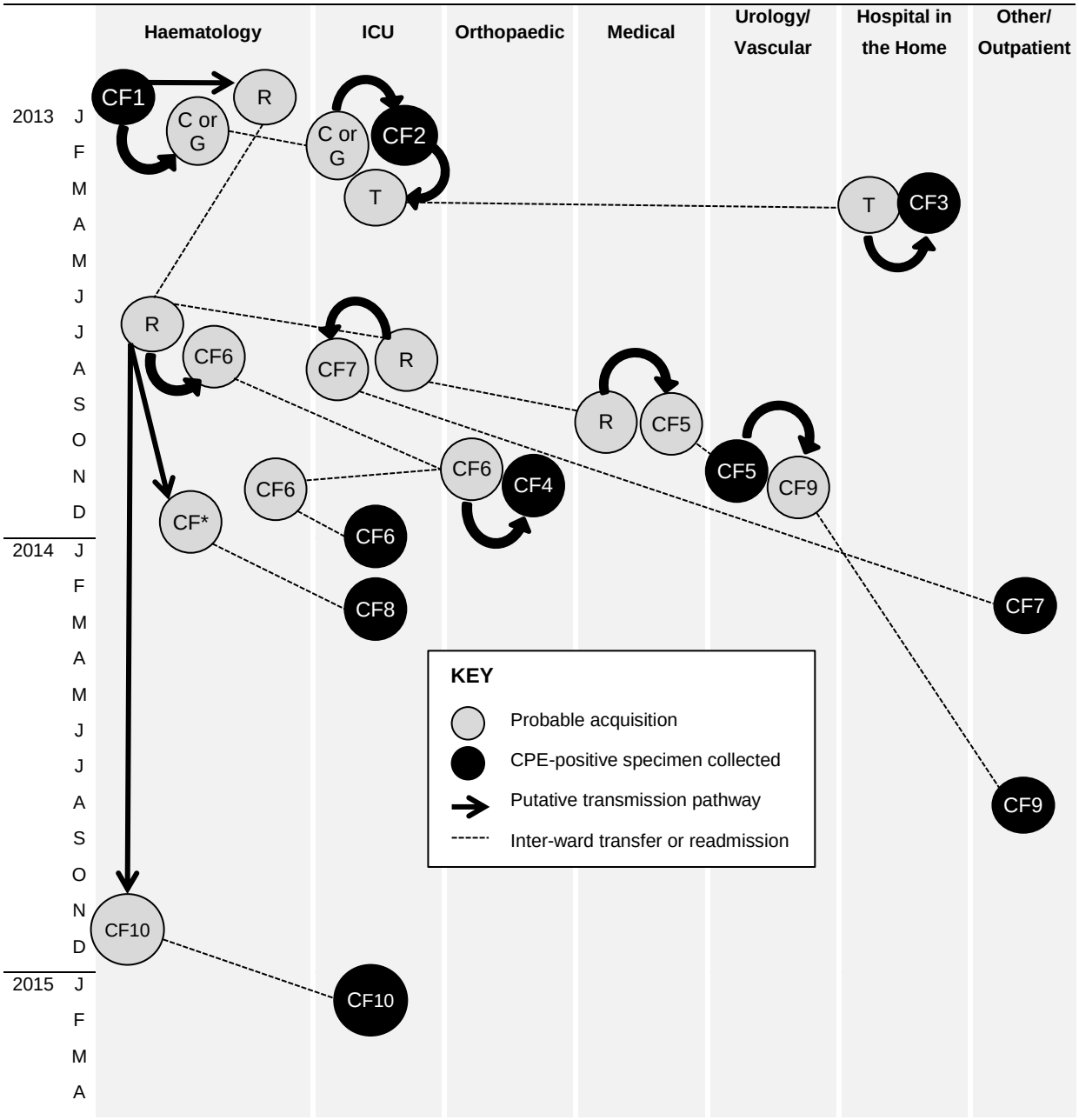

Figure 7 Locations and putative transmission pathways for the *C. freundii* ST8 or similar (bla_{IMP-4}) outbreak, the Canberra Hospital, 2013-2016. Patients G, C, R and T are suspected hosts, their CPE status is unknown. Patients CF6, CF8 and CF10 were detected via surveillance.

RESULTS

The guidelines provide recommendations on data collection for suspected and confirmed cases of CPE. The quality of our outbreak investigation would have been improved if standardised data had been collected from cases or their families at detection rather than retrospectively.

The number of cases in each outbreak that could have been prevented by application of Tier 1 or 2a guidelines is presented in Table 6. If the Tier 1 guidelines (see Supplementary material) were implemented when Patient EC1 was detected in March 2012, environmental reservoirs in the haematology ward and ICU would not have been identified, and no other cases in the *E. cloacae* outbreak would have been detected through screening of room contacts. However, asymptomatic carriers may have been identified by the latter, by the one-off screen of ICU patients who were in the unit on the night that Patient EC1's positive specimen was collected, or by six-monthly screening of ICU and haematology inpatients. It is doubtful that Patient M would have been identified by the last of these measures. The Tier 1 guideline would therefore have been unlikely to prevent the subsequent six cases. The identification of Patient EC2 (405 days after the detection of Patient EC1) would have triggered escalation to Tier 2a (or possibly 2b, see Supplementary material) only if an intermediate carrier other than Patient M was identified by screening room contacts on the renal ward. Although Patients EC2 and M were admitted to the ward concurrently for 34 days, they did not share a room or bathroom. Identification of a carrier or carriers in addition to Patient M would have led to environmental sampling and weekly screening of patients in ICU and haematology, which may have prevented transmission to all subsequent cases in the outbreak. Otherwise, Tier 2a would not have been triggered until the detection of case EC3 (624 days after the after the detection of Patient EC1). Applying Tier 2a measures at this stage may have prevented transmission to Patients EC5, EC6 and EC7.

If the Tier 2a guideline had been implemented upon detection of Patient EC1, intermediate hosts in ICU may have been detected by weekly inpatient screening and contact tracing, but environmental sources would only be identified after the detection of a related case. At most, default application of the Tier 2a guideline could have prevented five of the subsequent six cases in the outbreak (all but Patient EC4), plus transmission to Patient M.

In the context of the *C. freundii* outbreak, implementing the Tier 1 screening of all haematology ward patients admitted on the night of the collection of Patient CF1's CPE-positive specimen may have detected the potential case, Patient R. However, this was unlikely, as Patient R had only recently been admitted to hospital at that time, and he may not yet have been detectably colonised. Patients G and C would not have been detected. The hospital would have escalated to a Tier 2a facility in April 2013, when screening of Patient EC2's ICU contacts would have detected Patients R, C, G and T, and prevented the subsequent eight cases. If the Tier 2a guideline were implemented when Patient CF1 was first detected, weekly screens of haematology inpatients would have detected Patients R, G, and C, and prevented transmission to Patient T and the other nine cases in the outbreak.

Table 6 Maximum number of cases in two outbreaks of CPE detected at TCH that could possibly have been prevented by application of the Victorian guideline on CPE for Tier 1 and Tier 2a facilities (8).

Outbreak	Status of TCH	Number of cases prevented under Tier 1 meausres	Number of cases prevented under Tier 2a measures
E. cloacae ST24 (7 cases)	Tier 1 March 2012	0 + no escalation to Tier 2a for further 405 days	5 + Patient M
	Tier 2a June 2013 (if carrier/s in renal ward identified)	Not recommended	5
	Tier 2a December 2013 (if no carrier/s in renal ward identified)	Not recommended	3
C. freundii ST8 (10 cases)	Tier 1 January 2013	0 + no escalation to Tier 2a for a further 87 days	9 + Patient T
	Tier 2a April 2013	Not recommended	8

DISCUSSION

For both outbreaks, application of controls from the Victorian CPE guideline specified for facilities with local transmission at first CPE detection may have prevented all subsequent cases. It may be prudent to treat an apparently sporadic case of CPE with $bla_{\text{IMP-4}}$ as a marker of ongoing transmission and environmental contamination on any

of the units the case has been admitted to over the previous 12 months. The controls for sporadic cases are inadequate because contact tracing is primarily limited to co-resident room contacts over a maximum period of one month. This does not address transmission between patients admitted to the same room or ward several weeks or months apart via prolonged carriage or environmental reservoirs. We have made a number of recommendations for prevention of transmission of CPE at TCH (Table 7). These have been adapted from the Victorian guideline and the Australian *Recommendations for the control of carbapenemase-producing* Enterobacteriaceae (1).

By assuming 100% screening sensitivity and effectiveness of control measures, we have overestimated the effectiveness of the guideline. To date, screening at TCH has mainly been conducted through perianal swabs, which have a relatively low sensitivity (1). Using faeces specimens for screening and surveillance is a key recommendation arising from this analysis (Table 7). As reported previously, our outbreak investigations were limited by the WGS method used, which did not characterise the plasmids or integrons in the isolated bacteria. This means we were unable to allow for transfer of carbapenemase genes between species, genera, or different multilocus sequence types in the same species. As plasmid diffusion is a common mechanism for the spread of carbapenemases (9), and the dissemination of $bla_{\text{IMP-4}}$ among multiple gram-negative genera has been demonstrated in Australian hospitals (10, 11), it is also important that a useful definition of 'genetically-linked cases' is developed for use in the TCH context.

The movement of CPE cases between interstate hospitals and RACFs underscores the need for a national surveillance and response network for CPE in Australia. Since March 2016, cases have been reportable through the National Alert System for Critical Antimicrobial Resistances (CARAlert), which aims to "enable a timely, responsive approach to preventing the spread" of CPE and other critical resistances (12). However, reporting is not mandatory, and de-identification of data before state, territory and Australian health departments are alerted of a case limits the system's utility for cross-institutional or cross-jurisdictional outbreak detection and contact tracing. In 2016, CPE was made a notifiable condition in Tasmania (13). Mandatory reporting of cases through the National Notifiable Diseases Surveillance System, supported by WGS data, would facilitate the identification of outbreaks, screening of contacts and prevention of transmission.

Using outbreak data to retrospectively analyse CPE control guidelines was a successful method for evaluating their utility and informing their adaptation to a local context. International experience has demonstrated that in countries such as Australia, where carbapenemase resistance is rare, we need “to be alert and prepared for its emergence and preemptively to form centralised plans for detection and control” with “coordinated responses…from policy makers and public health authorities” (14).

Table 7 Recommended bundles for prevention and control of CPE at TCH, 2017.

Bundle		Screening	Prevention and Control measures
1	Once-off actions to define the status of CPE at TCH	• Undertake a point prevalence survey of all TCH inpatients via faeces specimens. Rectal plus inguinal swabs may be taken if faeces specimens cannot be collected. In addition: o if a wound or drain is present, a single wound or drain specimen is required o if an indwelling or supra-pubic catheter is present or the patient is having intermittent urinary catheterisations, a urine specimen is required o if an endotracheal tube (ETT) is present, an ETT aspirate is required.	• Develop a definition of 'genetically-linked cases' • Establish a procedure for epidemiological and genetic review of cases
2	On-going screening and prevention measures	• On admission, screen (as for Bundle 1) and isolate all patients at significantly higher risk of CPE colonisation or infection, including those who o were transferred directly from an overseas hospital o had an overnight stay in an overseas hospital in the previous 12 months o were room contacts of CPE cases who have not achieved criteria for being cleared. Room contacts are patients who resided overnight in a shared room (or in a separate room but shared a bathroom) with the case during the case's period of potential infectiousness o were ward contacts of CPE cases from a ward with ≥2 genetically linked cases who have not achieved criteria for being cleared • Screen all patients in the haematology ward and intensive care unit (ICU) every six months • Screen patients on re-admission who have ever had CPE isolated at any point in the past, unless screening within the four weeks of the last admission	• Conduct regular education and reminders to clinical staff on all units to only dispose of water and soap down hand-hygiene sinks

Bundle		Screening	Prevention and Control measures

3	For all CPE cases	• Screen all ward contacts back to the date of likely acquisition, or six months prior to the date of identification of CPE in the case, whichever is more recent. This includes patients who have been discharged.
		• Screen all patients who subsequently resided in the room/s occupied by the case in the period between the date of likely acquisition and detection
			• Collect standardised data on the case's history of travel, hospitalisation, medical/surgical procedures and antimicrobial use
			• Place in a single room with ensuite bathroom
			• Place under contact precautions
			• Place an alert on the case's file
			• Limit bed transfers within TCH
			• Cleaning and disinfection (with an agent registered with the Therapeutic Goods Administration)
			  ○ daily for the case's room, medical devices and equipment
			  ○ twice daily for the case's bathroom/sink, frequently touched surfaces and equipment
			• If the case is transferred out of TCH, advise the receiving health service to place the case under contact precautions
			• Notify the receiving health service/CARAlert* representative to ensure alerts are placed within that health service's system
			• Upon discharge, clean case's room using no-touch methods (e.g. ultraviolet (UV-C) or hydrogen peroxide vapour)

*National Alert System for Critical Antimicrobial Resistances

Bundle		Screening	Prevention and Control measures

4	Upon detection of ≥2 genetically linked cases (see Bundle 1)	• Implement Bundle 3 actions (cohorting may be appropriate)
		• Conduct weekly screens of all patients on wards that each case was admitted to for longer than one week in the previous 12 months
		• Conduct environmental screening on the wards that the case was admitted to in the previous 12 months:
		  ○ all sinks in ICU
		  ○ all bathrooms used by the case on other wards.
		• Continue with this bundle until there are at least four consecutive weeks of negative screens
			• Conduct weekly audits of infection control processes on wards that the cases were admitted to for longer than one week in the previous 12 months

5	Upon detection of a positive environmental sample	• Screen all patients on the ward weekly • Screen the contaminated element weekly, after cleaning • Continue with this bundle until there are at least four consecutive weeks of negative screens	• Clean the contaminated element daily using no-touch methods (e.g. ultraviolet (UV-C) or hydrogen peroxide vapour) • Conduct weekly audits of infection control processes on the ward

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SUPPLEMENTARY MATERIAL

Summary of screening and infection control measures from the *Victorian guideline on carbapenemase-producing* Enterobacteriaceae, 2015 (8).

Facility Status	Screening	Control measures
Tier 0 Settings with no cases	Screen all patients in all haematology wards, intensive care units and transplant wards every six months as a part of a point prevalence study Screen patients on re-admission who have ever had CPE isolated at any point in the past, unless screening within the four weeks prior to admission On admission, screen and isolate all **patients at significantly higher risk of CPE colonisation or infection**, including • direct transfer from an overseas hospital • overnight stay in an overseas hospital in the previous 12 months • room contacts* of CPE cases who have not achieved criteria for being cleared. • ward contacts[†] of CPE cases from a unit with local transmission[‡] who have not achieved criteria for being cleared No environmental screening is recommended	All patients at significantly higher risk of CPE colonisation or infection should be placed in contact precautions until cleared
Tier 1 Settings with sporadic cases	As for Tier 0 above Screen room contacts* of sporadic cases back to the date of likely acquisition, or one month prior to the date of identification of CPE in the case, whichever is more recent. For cases with an elevated risk of onwards transmission (see definition in Tier 0), screen all room contacts back to the date of likely acquisition, or six months prior to the date of identification of CPE in the case, whichever is more recent. Undertake a single one-off screen of all patients who resided overnight on the ward at the same time of a sporadic case being identified who has an elevated risk of onwards transmission (including patients admitted to ICU, malignant haematology patients; patients with a urinary catheter, copious/uncontained wound drainage, respiratory secretions or urine; or patients with diarrhoea, intestinal stoma or colorectal procedure/surgery) Environmental screening is not generally required	As for Tier 0 Apply contact precautions to all suspected cases until cleared Apply contact precautions to all room contacts[1] until cleared Daily cleaning and disinfection of case's room and bathroom; twice daily disinfection of frequently touched surfaces and equipment Terminal room cleaning on discharge of the case Hand hygiene and personal protective equipment audits Use objective methods for auditing cleaning eg fluorescent gel markers

*** Room contact:** a person who resided overnight in a shared room (or in a separate room but shared a bathroom) with the case during the case's period of potential infectiousness.

[†] **Ward contact:** a person who resided overnight in a ward with local transmission before that ward has returned four consecutive negative point prevalence screens spaced at least a week apart.

[‡] **Criteria for local transmission**: two or more confirmed cases of genetically-related CPE; **and** at least one case is locally acquired; **and** there is a plausible epidemiological connection between the two cases, either through geographic proximity or shared staff, equipment or other exposures.

Facility Status	Screening	Control measures
Tier 2a Settings with local transmission‡ in a single ward or unit in the previous 12 months	As for Tier 0 and Tier 1 above Screen all patients in the unit each week until there are at least four consecutive weeks of negative screens Ensure that all ward contacts† are screened within the seven days prior to transfer to another health service and are negative, otherwise the health service receiving the patient must ensure the patient is placed in contact precautions until cleared Ensure that all discharged ward contacts have alerts placed on their medical record so they are placed into contact precautions and screened if readmitted within the next 12 months Environmental screening should be undertaken to identify an environmental reservoir of CPE when there is local transmission on a ward/setting where cases were not always cared for in a shared room or with a shared bathroom Endoscopes should be screened / microbiologically tested if more than one patient with confirmed CPE is found to have had a common exposure to an endoscope	As for Tier 1 Cohorting of same genotype CPE infected or colonised patients can be considered Cohorting is appropriate while room contacts are being screened Daily cleaning and disinfection of the ward; twice daily disinfection of frequently touched surfaces and equipment Consider the use of no-touch methods for terminal disinfection (eg hydrogen peroxide vapour) Monthly audits of infection control measures
Tier 2b Settings with local transmission‡ in two or more wards or units in the previous 12 months	Follow Tier 2a guideline above	Additional control measures should be considered, for example • daily or weekly audits of infection control processes • wider or more frequent screening measures • the establishment of a dedicated ward or wing for suspected and confirmed cases

*** Room contact:** a person who resided overnight in a shared room (or in a separate room but shared a bathroom) with the case during the case's period of potential infectiousness.

† **Ward contact:** a person who resided overnight in a ward with local transmission before that ward has returned four consecutive negative point prevalence screens spaced at least a week apart.

‡ **Criteria for local transmission**: two or more confirmed cases of genetically-related CPE; **and** at least one case is locally acquired; **and** there is a plausible epidemiological connection between the two cases, either through geographic proximity or shared staff, equipment or other exposures.

CHAPTER 3 – DETERMINANTS OF SOCIAL AND EMOTIONAL WELLBEING IN ABORIGINAL AND TORRES STRAIT ISLANDER CHILDREN: RESULTS FROM THE FOOTPRINTS IN TIME STUDY

We all need to recognise that children's sense of themselves as Aboriginal people—who they are and where they come from—is of both practical and spiritual value. In bestowing identity we also bestow dignity. It is a good deal more than symbolic—it has profound practical effects.

Professor Mick Dodson

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ABBREVIATIONS

BITSEA	Brief Infant-Toddler Social Emotional Assessment
BSTL	Better Start to Life
CI	Confidence interval
DSS	Department of Social Services
IQR	Interquartile range
IRISEO	Index of Relative Indigenous Socio-Economic Outcomes
KMO	Kaiser-Meyer-Olkin measure of sampling adequacy
LORI	Level of Relative Isolation
LSIC	Longitudinal Study of Indigenous Children
NAPLAN	National Assessment Program–Literacy and Numeracy
NCEPH	National Centre for Epidemiology and Population Health
NSW	New South Wales
PCA	Principal component analysis
PMC	Department of Prime Minister and Cabinet
RAO	Research Administration Officer
SD	Standard deviation
SDQ	Strengths and Difficulties Questionnaire
SEARCH	Study of Environment of Aboriginal Resilience and Child Health
SEWB	Social and emotional wellbeing
VET	Vocational education and training
WAACHS	Western Australian Aboriginal Child Health Survey

Prologue

This project was proposed by my first placement supervisor, Dr Annie Dullow, who wanted to answer a policy question about determinants of social and emotional wellbeing (SEWB) in early childhood. She wanted to take a social determinants perspective and include protective factors, and knew that the Longitudinal Study of Indigenous Children (LSIC) was a rich and under-utilised source of data. We participated in two teleconferences with officers from the Department of Social Services (DSS, who are the custodians of the LSIC data), the Australian Institute of Health and Welfare, and the Department of Prime Minister and Cabinet (PMC) to discuss planned departmental projects using the LSIC data and ensure they would be complementary.

MY ROLE

For this project, I

- developed the proposal and the data analysis plan
- applied for access to the LSIC data
- developed the ethics application
- cleaned, recoded and analysed the data
- presented the preliminary results to the Indigenous Health Divisional Forum (Department of Health, see Appendix 3.1) and at the Australian *Longitudinal Data Conference 2016* (Appendix 3.2).
- drafted the thesis chapter
- drafted the article for submission to the *Family Matters* journal (Appendix 3.3)[1].

My academic supervisor, David Harley, provided excellent feedback and guidance, particularly during the planning and writing stages.

LESSONS LEARNT

There is a massive amount of data collected by the LSIC: it would be easy to drown in it. I'm grateful to Martyn Kirk, who recommended a book at the MAE courseblock called

[1] This article has been accepted for publication in *Family Matters*, Issue 100, 2018.

The workflow of data analysis using Stata[2]. It recommends techniques for planning, documenting and organising work that increased my efficiency, and surely saved me many hours of pain. I used these techniques in all my Stata projects.

For this project I used Principal Component Analysis (PCA). As I spent so long working out how to do it, it became the topic for my Lesson from the Field. I rushed to submit a conference abstract not long after completing my first analysis of the data, in which the PCA had been unsuccessful. It was not until after presenting the results to my Division and at the conference that I checked my analysis and found an error in the Stata code. Once this was fixed, I could successfully perform PCA on the outcome variables. I learnt a valuable lesson about checking and rechecking my analyses.

PUBLIC HEALTH IMPACT

The equivocal results of the analysis limited the potential impact of this project. However, I have emphasised the main conclusion of the study: that those in policy development and program planning and management need to be mindful that using flawed measures can adversely affect decision making. Following my conference presentation, my slides were requested by an LSIC officer, who forwarded them to the Steering Committee members and policy areas for use in discussions about content development.

ACKNOWLEDGEMENTS

I am grateful to the families who participated in the Longitudinal Study of Indigenous Children, and the Indigenous Research Administration Officers who work so hard to maintain relationships with the families and collect the data. I would also like thank

- Dr Annie Dullow, who posed the policy question that led to this research, and gave guidance and encouragement early in the project
- Kirrily Harrison (PMC), who suggested developing an index of cultural connection
- Professor Tom Calma and Menessia Nagie (Department of Health) with whom I discussed the SEWB conceptual model

[2] Long, J.S., College Station, Texas: Stata Press; 2009.

- Dr Katherine Thurber (National Centre for Epidemiology and Population Health, NCEPH), who gave advice about using LSIC data
- Dr Alice Richardson (NCEPH), who gave statistical advice
- Dr Liana Leach (NCEPH), who gave advice about the study design
- Fiona Skelton, Laura Bennetts-Kneebone and Debora Kikkawa (DSS), who gave helpful feedback on the data analysis plan
- my colleagues at my field placement, Sam Siripol and Amy Burroughs (MAE scholars), who gave feedback on my conference presentation.

DISCLAIMER

This chapter uses unit record data from the LSIC. The Longitudinal Study of Indigenous Children was initiated and is funded and managed by the Australian Government Department of Social Services. The findings and views reported in this paper, however, are those of the author and should not be attributed to DSS or the Indigenous people and their communities involved in the study.

Abstract

BACKGROUND

Social and emotional development is an important factor in a child's readiness to participate in school-based learning. Understanding the determinants of social and emotional wellbeing (SEWB) in Aboriginal and Torres Strait Islander children will help to direct policy and investment in child and maternal health. Social and emotional wellbeing is a positive, holistic and culturally-specific concept that is not captured by Western mental health instruments. I aimed to identify factors antenatally and in the first two years of life associated with SEWB in children at the time of starting school. A secondary purpose was to develop a more useful indicator of SEWB.

METHODS

I selected a sample of children from the Longitudinal Study of Indigenous Children (LSIC) who were aged two years or under at Wave 1, or who entered in Wave 2 aged three years or under. I developed a conceptual framework to represent SEWB in Aboriginal and Torres Strait Islander children and guide the selection of outcome measures from Waves 5 and 6, around the time of starting school. Children's prosocial behaviour and mental health were measured using the two Strengths and Difficulties Questionnaire (SDQ) subscale scores. I used Principal Component Analysis (PCA) to reduce a number of outcome measures (SDQ Prosocial Behaviours score, a measure of the primary carer's SEW; and questions about connection of the child and family to community, culture, ancestry, spirituality and country) to a new index of SEWB. I selected early life exposure variables from Waves 1 or 2 based upon factors found by previous studies to be associated with SDQ scores, factors that have a biologically or socially plausible link to SDQ scores, and factors that reflect the activities or intended outcomes of maternal and child health services. I used PCA to reduce the number of exposure variables. I incorporated exposures with a p value of 0.25 or less from the univariable analyses into linear and ordinal regression models, as appropriate.

RESULTS

There were 726 children included in the analysis. Children of eligible age who were excluded because they did not have a SDQ Prosocial Score at Wave 5 or 6 were more likely to be low birthweight, have a young, unemployed primary carer, to have a mother

who smoked while pregnant, and to live in a remote or very remote area. Exposure variable data were not suitable for reduction by PCA. Three principal components ("Child's connection", "Child's helping, sharing and mental health", and "Primary carer's SEWB factors") were generated from the outcome measures. Higher household occupancy and exposure to fewer major life events were associated with a poorer "Child's helping, sharing and mental health" score (adjusted effect size coefficients -0.33, 95% CI -0.63–-0.03, p= 0.03; -0.29, -0.54–-0.04, 0.02, respectively), and a poorer score for "Primary carer's SEWB factors" (-0.26, -0.47– -0.53, 0.02; -0.28, -0.47–-0.10, 0.003, respectively). However, more people in the household and exposure to more events were weakly associated with greater "Child's connection" to community, culture and country (0.09, 0.01–0.16, 0.03; 0.06, 0.001–0.12, 0.05, respectively). None of the early life exposures was associated with prosocial behaviours. Greater social, emotional and behavioural competence as an infant or toddler predicted better outcomes at school commencement.

CONCLUSIONS

The prominence of life events and household occupancy in this analysis lends weight to social determinants theory and holistic, trans-portfolio approaches for promoting SEWB in Aboriginal and Torres Strait Islander children. I could not create a single index for SEWB using variables from the LSIC. Those seeking evidence to support SEWB policy development, program planning and evaluation must be cautious in applying Western biomedical health and wellbeing measures to Indigenous concepts and states. Communities should be supported to develop their own measures of wellbeing that privilege Indigenous ways of knowing and being.

Background

SOCIAL AND EMOTIONAL DEVELOPMENT AND SCHOOL READINESS

Optimising the mental health and wellbeing of all Aboriginal and Torres Strait Islander people is a key priority in the National Aboriginal and Torres Strait Islander Health Plan 2013-2023 (1). In this plan, social and emotional wellbeing (SEWB) is seen as a "central platform for prevention and clinical care". Furthermore, social and emotional development—together with cognition and general knowledge, language development, and physical wellbeing—is an important factor in children's readiness to participate in school-based learning experiences (2). Parents' most commonly reported hope for their children in the Longitudinal Study of Indigenous Children (LSIC—also known as Footprints in Time) is a good education (3), meaning at least school completion to Year 12, the final year of high school (4). Although the Year 12 retention rate for Aboriginal and Torres Strait Islander students has nearly doubled since the late 1990s, it was still only at 60% in 2014 (5). As a smooth transition to school predicts school completion (6), optimising SEWB in early childhood could contribute to improving the rate of school completion and its attendant benefits.

Through the Indigenous Australians' Health Programme, the Australian Government invests in the Better Start to Life (BSTL) approach. This approach involves the expansion of maternal, child and family health programs that support Aboriginal and Torres Strait Islander families and early childhood development to ensure children are ready to learn when they start school. Currently, there are two programs under the BSTL approach: the New Directions Mothers and Babies Services, and the Australian Nurse-Family Partnership program (Figure 1). To guide programs such as these, it is important to understand the nature and determinants of social and emotional wellbeing (SEWB) of Aboriginal and Torres Strait Islander children.

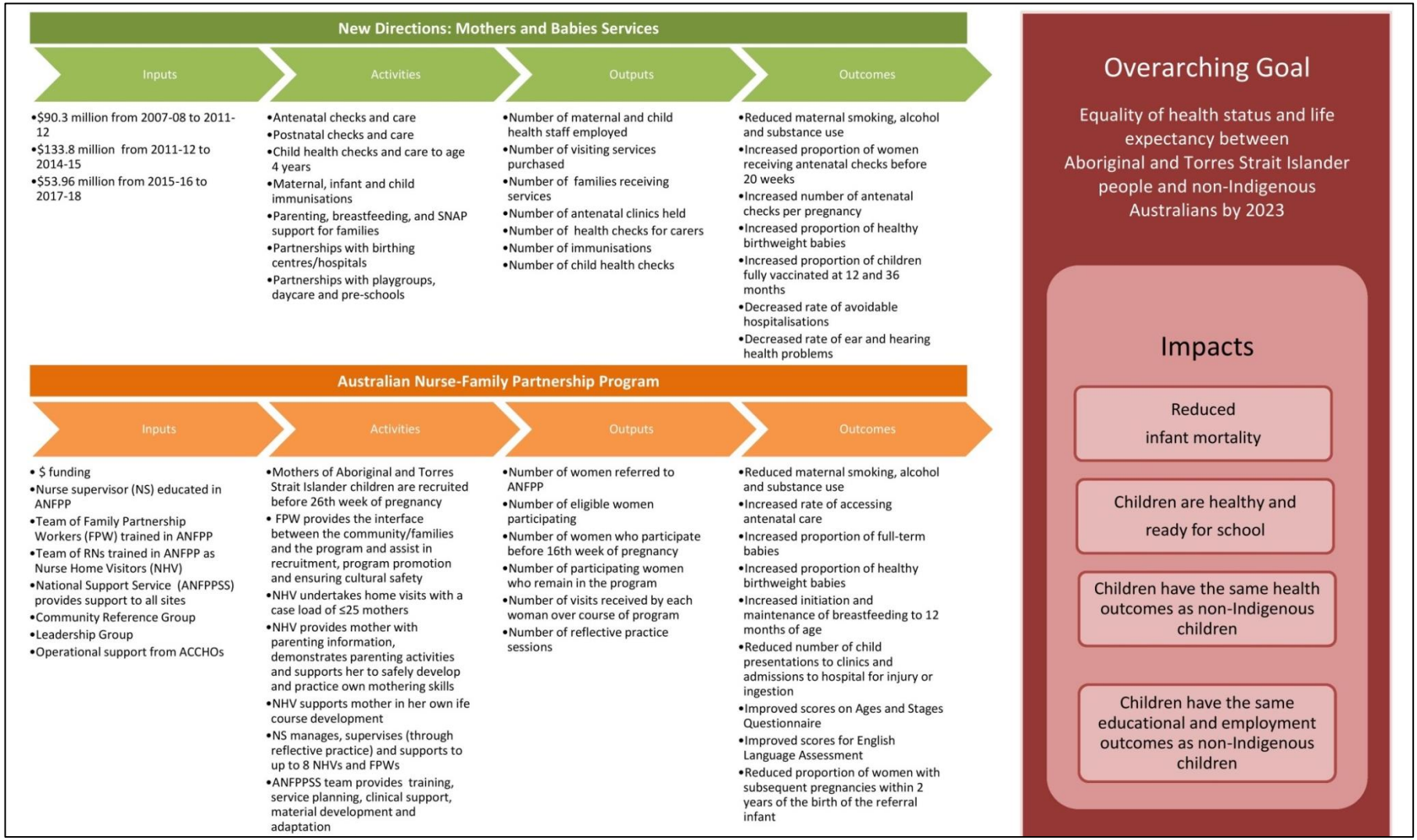

Figure 8 Program logic for the Better Start to Life approach**.**

SOCIAL AND EMOTIONAL WELLBEING IN ABORIGINAL AND TORRES STRAIT ISLANDER CHILDREN

Social and emotional wellbeing is central to the holistic view of health held by Aboriginal and Torres Strait Islander people (7). Social and emotional wellbeing is a much broader concept than Western understandings of mental health and resilience. Rather, the wellbeing of the individual is

> *…intimately associated with collective wellbeing, It involves harmony in social relationships, in spiritual relationships and in the fundamental relationship with the land and other aspects of the physical environment* (8).

Social and emotional wellbeing is a positive concept which recognises these relationships as strengths, and goes beyond the absence of mental ill-health (9). The individual wellbeing of a child is nested within family and community wellbeing; with deep connections to ancestry, culture, spirituality and country; and with mental health part of, but not central to, the individual SEWB of the child (Figure 9).

Limited quantitative studies indicate that Aboriginal and Torres Strait Islander children have significantly higher rates of social and emotional difficulties, mental health problems and psychological distress than non-Indigenous children (10-12). This disparity is apparent by three years of age (13). However, as discussed below, the measurement of these health states is not straightforward,

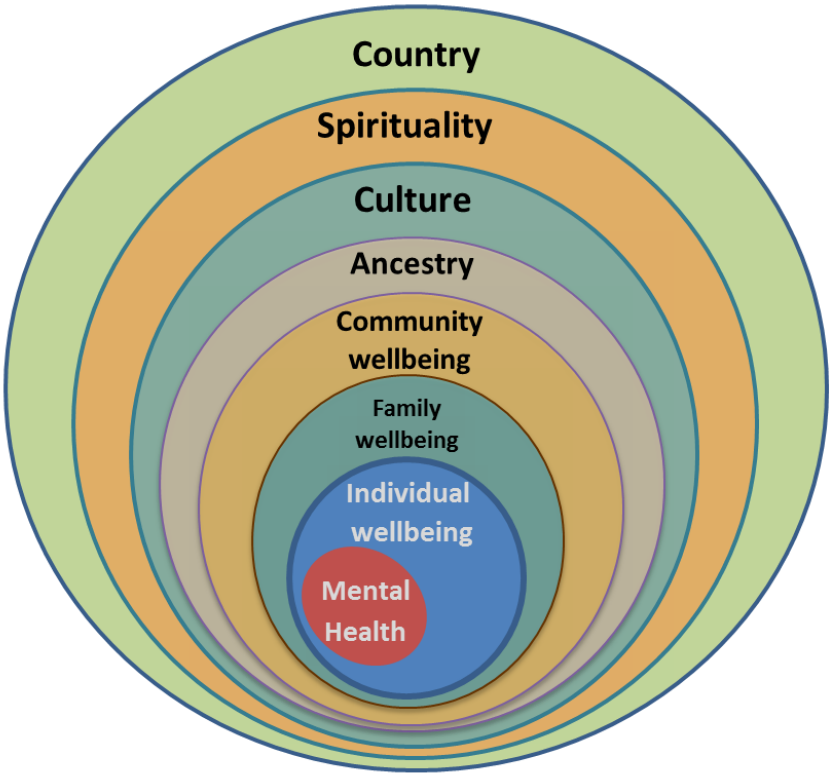

Figure 9 Conceptual framework for social and emotional wellbeing (SEWB) of Aboriginal and Torres Strait Islander children.

MEASURING CHILDREN'S SOCIAL AND EMOTIONAL WELLBEING

Mental health assessment tools used in non-Indigenous Australians do not reflect the broader concept of social and emotional wellbeing (9). Normal behaviour is culturally constructed, and tools may not account for Aboriginal and Torres Strait Islander societal norms or language (14). In recognition of this, a SEWB module was developed to collect national data for adults in the 2004–05 National Aboriginal and Torres Strait Islander Health Survey (15). The module consists of eight domains reflecting a holistic view of social and emotional wellbeing, but it is not designed for use in children. Strong Souls is a 25-item tool developed for a longitudinal study of Aboriginal and Torres Strait Islander adolescents "with the help of these young people themselves" (16). It assesses four aspects of SEWB, anxiety, depression, suicide risk, and resilience. The tool was found to be valid, reliable and culturally-appropriate for SEWB screening in people aged 16 to 19 years in over 70 urban, rural, and remote communities across the Northern Territory (16). However, its usefulness in other Aboriginal and Torres Strait Islander communities and age groups has not been assessed.

All children in the Footprints in Time study are assessed using the standard version of the Strengths and Difficulties Questionnaire (SDQ). This 25-item questionnaire was designed to assess the "psychological adjustment" of children aged three to 16 years, and can be completed by parents, carers, teachers, or the child or adolescent (17). The SDQ consists of five scales which score emotional symptoms, conduct problems, hyperactivity-inattention, peer problems, and prosocial behaviour (Table 8). The first four scales are summed to generate a Total Difficulties Score, with a higher score indicating more difficulty. The fifth scale is summed to generate a Prosocial Behaviours score, with a higher score indicating better behaviours. The items and their groupings were selected based on their relationship to categories of mental disorders (17). Risk groupings for emotional or behavioural problems based on Total Difficulties scores are defined as "close to average" (0-13), "slightly raised" (14-16), "high" (17-19) and "very high"(above 19) (18). Hawes and Dadds (19) confirmed that the SDQ, when administered using the parent-report form, has sound psychometric properties for Australian children aged four to nine years.

Table 8 The Strengths and Difficulties Questionnaire (SDQ) items, with scoring, for completion by the child's parent, carer or teacher (20).

	Score		
	Not True	**Somewhat True**	**Certainly True**
Emotional Symptoms Scale			
• Often complains of headaches, stomach aches or sickness	0	1	2
• Many worries or often seems worried	0	1	2
• Often unhappy, depressed or tearful	0	1	2
• Nervous or clingy in new situations, easily loses confidence	0	1	2
• Many fears, easily scared	0	1	2
Conduct problems Scale			
• Often loses temper	0	1	2
• Generally well behaved, usually does what adults request	2	1	0
• Often fights with other children or bullies them	0	1	2
• Often lies or cheats	0	1	2
• Steals from home, school or elsewhere	0	1	2
Hyperactivity scale			
• Restless, overactive, cannot stay still for long	0	1	2
• Constantly fidgeting or squirming	0	1	2
• Easily distracted, concentration wanders	0	1	2
• Thinks things out before acting	2	1	0
• Good attention span, sees chores or homework through to the end	2	1	0
Peer Problems Scale			
• Rather solitary, prefers to play alone	0	1	2
• Has at least one good friend	2	1	0
• Generally liked by other children	2	1	0
• Picked on or bullied by other children	0	1	2
• Gets on better with adults than with other children	0	1	2
Summed to generate the Total Difficulties Score*:		**___ / 40**	
Prosocial Scale			
• Considerate of other people's feelings	0	1	2
• Shares readily with other children, for example, toys, treats, pencils	0	1	2
• Helpful if someone is hurt, upset or feeling ill	0	1	2
• Kind to younger children	0	1	2
• Often volunteers to help others (parents, teachers, other children)	0	1	2
Summed to generate the Prosocial Behaviours Score†:		**___ / 10**	

*A higher score indicates greater difficulties

† A higher score indicates greater prosocial behaviours

Zubrick and others (21) tested the reliability of a modified SDQ for Aboriginal children across Western Australia and concluded that, with some changes to the wording of response categories, it was "a reasonable measure of mental health and well-being" in this population. However, the SDQ does not reflect the importance of relationships inherent in the concept of SEWB. Parents, researchers, youth workers and health workers in a study based in Aboriginal communities in Sydney indicated that the standard SDQ was acceptable as a measure of mental health, but it does not assess "connection to or relationship with extended family, Aboriginal identity, feeling that you are accepted by and belong to an Aboriginal community, and the impact and experience of racism" (20). The Total Difficulties score of the SDQ has been used as a measure of SEWB in several studies of Aboriginal and Torres Strait Islander children, including studies using LSIC data (10, 12, 22-24), but includes only deficit-focused subscales. However, work by Williamson et al. (20) indicates that the Prosocial Behaviours scale of the SDQ, which has not been explored by these previous studies, provides information about an Aboriginal child's relationship with their family that is central to SEWB.

Using data from the Australian Early Development Census, Goldfield et al. (25) developed a measure of "mental health competence" that has a strong positive association with the SDQ Prosocial Behaviours scale, and an inverse relationship with the Peer Problems scale. Although it has been used to investigate the epidemiology of positive mental health for all Australian children at school entry, the extent to which this competence measure reflects values and norms of child mental health held by Indigenous communities is uncertain (26). The Brief Infant Toddler Social Emotional Assessment (BITSEA) tool is designed for use in screening children aged 12 to 36 months for social-emotional and behavioural problems and delays in competence (27). Whilst it has been used to assess social and emotional wellbeing in Aboriginal and Torres Strait Islander children (13), including the younger cohort of LSIC children (28), it has not been validated for this population and does not *prima facie* encompass the full breadth of the concept of SEWB.

PURPOSE OF THIS STUDY AND RESEARCH QUESTIONS

My principal purpose was to provide guidance to policy makers and program managers—particularly those working in the area of maternal and child health—

regarding interventions and approaches that will promote SEWB and thus school readiness for Aboriginal and Torres Strait Islander children. A secondary purpose was to attempt to develop a new indicator of SEWB for Aboriginal and Torres Strait Islander children.

My research question was, which factors, antenatal to age two years, are associated with SEWB and prosocial behaviours and protect against social and emotional difficulties in Aboriginal and Torres Strait Islander children at the time of starting school? Families generally have the most contact with maternal and child health services antenatally and in the first two years of life when the majority of childhood immunisations and health and development checks are delivered. To answer this question, I undertook an exploratory analysis of data from the LSIC. Previous analyses of the LSIC dataset have aimed to identify the risk factors for poor mental health from cross-sectional analyses. Instead, I analysed these data longitudinally to identify factors potentially protective for SEWB.

ACKNOWLEDGING MY RESEARCH STANDPOINT

Licensed users of the LSIC data are required to openly acknowledge their research standpoint in reports or publications (29). I am a non-Indigenous Australian with a privileged, middle-class background. I was educated at a private school and studied environmental science and nursing. It was while nursing in rural and remote emergency and primary care that I became interested in Aboriginal and Torres Strait Islander health. I felt that many of the illnesses and injuries I assessed and managed were preventable and I worried about sending people home to the same conditions that made them unwell. I felt ashamed that there was such inequity in my own country. Undertaking a Master in Public Health opened my eyes to the social determinants of health and the structural inequities creating and sustaining poor health. Following Pyett, Waples-Crowe and van der Sterren (30), in this study I have attempted to interpret the data through a strengths-based lens and challenge the deficit model of Aboriginal and Torres Strait Islander health. Also, by recognising and favouring Indigenous understandings of SEWB, I have used a decolonising approach.

Methods

STUDY DESIGN

The Longitudinal Study of Indigenous Children is a prospective cohort study.

DATA SOURCE

I obtained a Deed of Licence to access LSIC data. The Department of Families, Housing, Community Services and Indigenous Affairs (now the Department of Social Services) initiated the LSIC in 2003, with the aim of improving "the understanding of, and policy response to, the diverse circumstances faced by Aboriginal and Torres Strait Islander children, their families and communities" (1). The LSIC team has collected data yearly since 2008 (Wave 1). Important features of the LSIC include extensive and ongoing community engagement and consultation, and leadership from a steering committee with a majority of Aboriginal and Torres Strait Islander members (31).

SAMPLE

The study employed a non-random purposive sampling technique, in which Centrelink and Medicare records were used to identify Aboriginal and Torres Strait Islander children and their families living in areas clustered around 11 sampling sites (Figure 10) (31). These sites were chosen to broadly represent the range of urban, regional and remote settings in which Aboriginal and Torres Strait Islander children live. Families were approached to participate by Indigenous Research Administration Officers (RAOs), who also identified eligible children through word-of-mouth and local knowledge. Children targeted for selection were in two age groups at baseline in 2008: between six months and two and a half years of age; and between three and a half and five years of age. In Wave 2 in 2009, additional children were enrolled in order to "maintain the viability of the sample in remote regions and meet the requests of a small number of families who expressed a strong wish to be part of the study" (32).

For this analysis eligibility criteria were (Figure 10):

- children who were aged two years or under at Wave 1;
- children who entered in Wave 2 aged three years or under; and
- children for whom a SDQ Prosocial Behaviours score could be calculated at Wave 6 (or at Wave 5 if there was no score available for Wave 6).

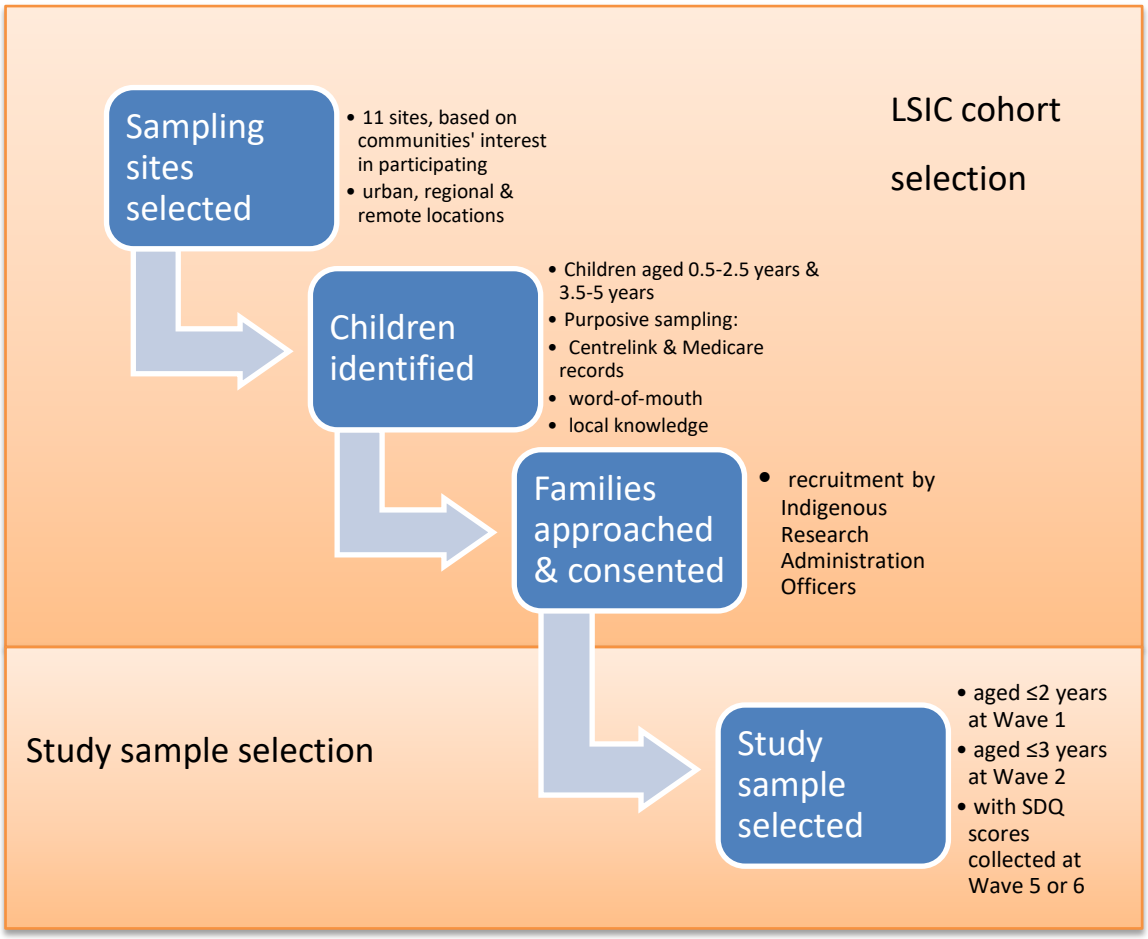

Figure 10 Procedure for selecting the LSIC cohort (31) and the sample for this study.

MEASURES

OUTCOMES

Children's prosocial behaviour and emotional and behavioural difficulties were measured using SDQ subscale scores, as assessed by the primary carer at Wave 6. If these scores were missing, scores obtained from the child's teacher assessment in Wave 5 were used. I analysed the Prosocial Behaviours score and the Total Difficulties score as categorical and continuous variables, respectively.

To answer the secondary research question, I selected variables from the LSIC dataset that most closely reflected other facets of SEWB, as identified in the conceptual framework. As a surrogate measure of family wellbeing, I summed the raw values for seven questions which were used to assess the primary carer's SEWB in interviews with

RAOs in Wave 6, as described by Kikkawa (33). These were adapted by the LSIC team from questions developed for the Strong Souls tool (16), and for this analysis, a higher total primary carer's SEWB score indicates better SEWB. I chose five additional variables to indicate the connection of child and family to community, culture, ancestry, spirituality and country. These variables were primary carers' answers to questions ('connection questions') asked in interviews with RAOs in Waves 4, 5 and 6 (Table 9). These questions have not been assessed for validity or reliability. Therefore, aspects of SEWB beyond individual wellbeing are not well captured. There was no available variable that assessed spirituality, for example, and although primary carers were asked about the child's connection to country no assessment was made of the child's access to or health of that country. The relationship between the outcome measures and the SEWB conceptual framework is shown in Figure 11.

Table 9 List of Primary carer SEWB and Connection Questions, with response options and data collection wave included in this analysis.

Group	Question wording	Values	Wave
SEWB of primary carer ('Strong Souls questions')	*In the last three months, have you stopped liking things that used to be fun? (Don't want to go fishing; don't want to hang out with your mates?)*	Lots ; Fair bit; Little bit; Never	6
	In the last three months, have you felt like everything is hard work (even little jobs are too much)? Felt too lazy to do anything?		
	In the last three months, have you felt so worried your stomach (tummy) has got upset? Big worries make you sick.		
	In the last three months, have you felt so worried that you had trouble breathing?		
	In the last three months, do you get angry or wild real quick?	Lots of times; Fair bit; Sometimes; Not much (or never)	
	In the last three months, have you felt so sad that nothing could cheer you up? Not even your friends make you feel better.		
	In the last three months, do you do silly things without thinking that you feel shame about the next day?		
'Connection questions' asked of primary carer	*How many days per week does [child's name] spend time with Aboriginal/Torres Strait Islander/Aboriginal and Torres Strait Islander leaders or elders in your community?*	Every day; 5 to 6 days per week; 2 to 4 days per week; Once per week; Less than once per week; Never	5
	What sort of activities does [child's name] do with you or other family members to learn about Aboriginal/Torres Strait Islander/ Aboriginal and Torres Strait Islander culture?	Please specify; None	5
	I want you to pick a number between zero and ten that indicates your level of satisfaction with…feeling part of your local community?	0-10 Higher number indicates greater satisfaction	5
	Do you identify [child's name] with a tribal group, a language group or a clan?	Yes; No	4
	Does [child's name] have a connection to country or place?	Yes; No	4

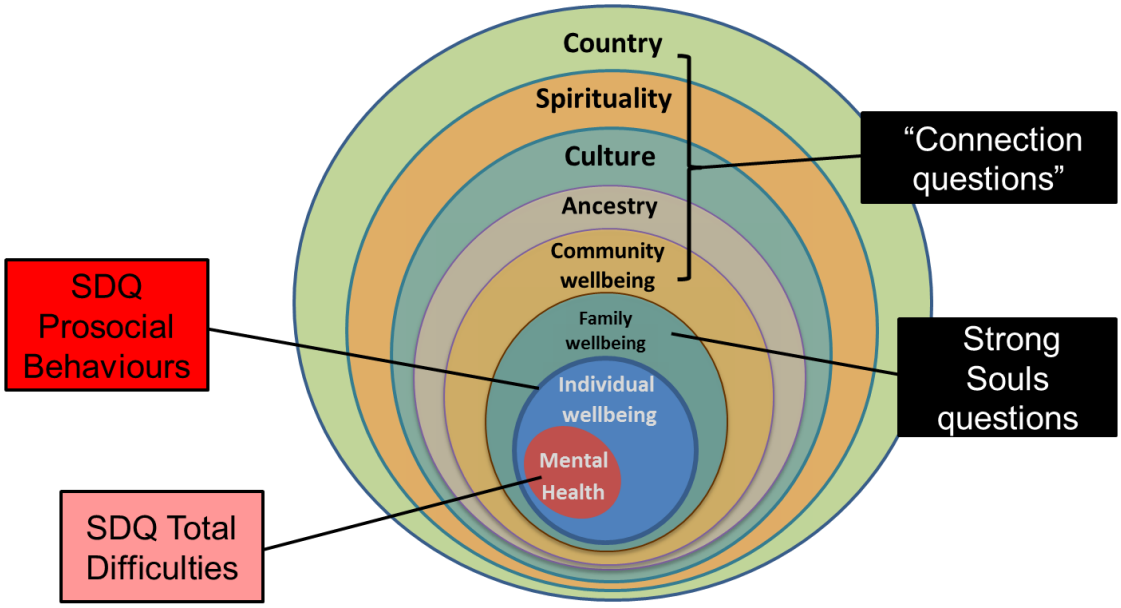

Figure 11 The relationship between the outcome measures and the SEWB conceptual framework.

EXPOSURES

I selected exposure variables based upon factors found by previous studies to be associated with SDQ scores, factors that have a biologically or socially plausible link to SDQ scores, and factors that reflect the activities or intended outcomes of maternal and child health services. These are broadly categorised as:

- child characteristics (including intrauterine risk factors)
- characteristics of the primary carer
- parenting and care
- home life and events
- intergenerational trauma and racism
- macro-level socio-economic indicators.

Most of these exposure data were obtained by the LSIC team through interviews with primary carers at Wave 1. Other than checking the family-held birth record for birthweight, the LSIC does not directly collect any clinical measures or conduct clinical record review.

The two macro-level socio-economic indicators I included in the analysis were derived from the child's home address by the LSIC team. The Index of Relative Indigenous Socio-Economic Outcomes (IRISEO) is a relative ranking of Indigenous Areas based on

nine measures of employment, education and housing, calculated from 2001 and 2006 Census data (34). The Level of Relative Isolation (LORI) measure was developed for the Western Australian Aboriginal Child Health Survey (WAACHS) to represent geographic isolation from basic services (35), and in the LSIC has been grouped into four categories (none; low; moderate; and high or extreme isolation) (28).

I used data from Wave 2 for children who entered at Wave 2, and for children who entered in Wave 1 but were missing data. Data regarding family experience of racism was only collected in Wave 3. I recoded variables to emphasise the positive behaviour or favourable circumstance, in line with the strengths-based approach of this study. Details of the exposure variables are presented in Table 10. Figure 12 shows an overview of the temporal relationship between the exposure and outcome variables for the children in the sample.

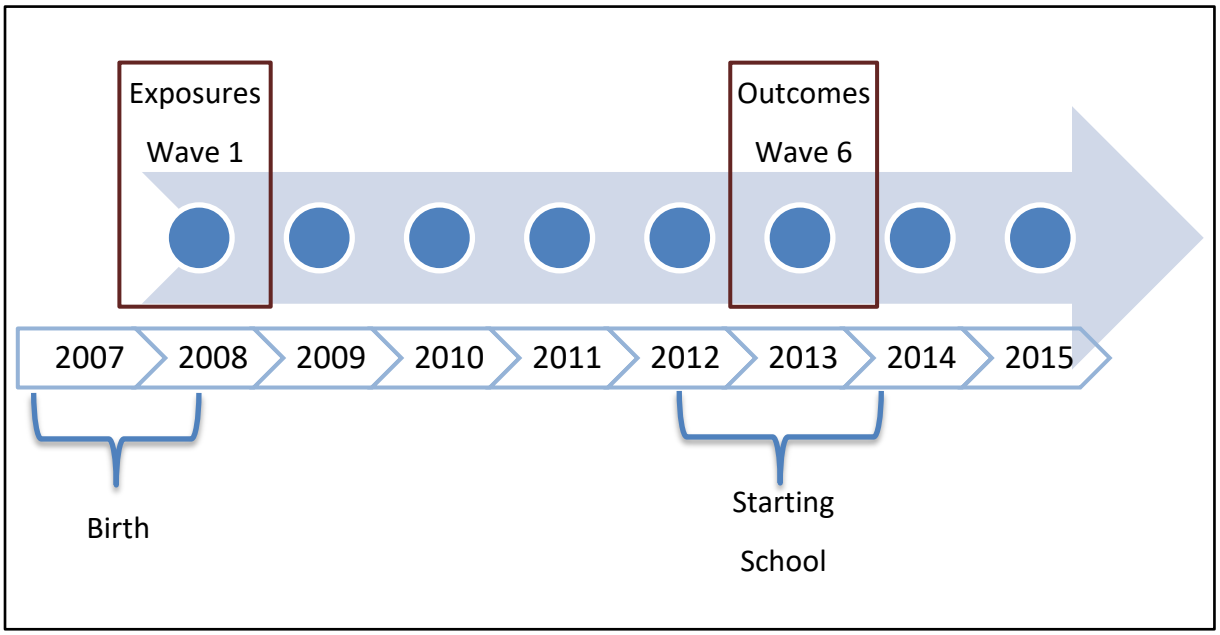

Figure 12 Temporal relationship between the exposure and outcome variables for the children in the sample.

Table 10 Description and coding details for LSIC variables included as exposures in the Principal Component Analysis (PCA) and univariable analysis.

Variable	Description/ LSIC Interview question wording (28)	Values and recoding details	Wave/s[‡]	PCA?	Univariable analysis?
Mother received first antenatal visit < 20 weeks gestation	*How far along [in weeks] [were you/was she] in [your/her] pregnancy when [you/she] had [your/her] first check-up?*	Yes= <20 weeks No=≥ 20 weeks	1 or 2	✓	✓
Mother did not drink alcohol during pregnancy	*After finding out you were pregnant with [child's name] did you drink any alcohol during the pregnancy?*	Yes/No [coding reversed to positive]	1 or 2	✓	✓
Mother did not smoke during pregnancy	*After finding out you were pregnant with [child's name] did you smoke any cigarettes during the pregnancy?*	Yes/No [coding reversed to positive]	1 or 2	✓	✓
Mother did not use any substances during pregnancy	*We aren't after any details here, but after finding out you were pregnant with [child's name] did you use any other substances like smoking marijuana, drinking kava, sniffing petrol, or taking any illicit drugs during the pregnancy?*	Yes/No [coding reversed to positive]	1 and 2	✓	✓
Child born at full term gestation	*How many weeks pregnant [were you/was the birth mother] when [child's name] was born?* *IF RESPONDENT CAN'T REMEMBER, ASK: Do you remember how many weeks early or late you were when [child's name] was born?*	Yes = 37-42 weeks No=<37 or >42 weeks	1 or 2	✓	×
Low birth weight	*Can you read out the birth weight from the record book? How much did [child's name] weigh at birth?* If the baby health book is available they are asked to read the weight, otherwise they are asked to recall the weight.	Yes= <2500g No = ≥ 2500g	1 or 2	✓	×

[‡] Wave 1 data used unless missing or not collected in that wave

Variable	Description/ LSIC Interview question wording (28)	Values and recoding details	Wave/s‡	PCA?	Univariable analysis?
Child was ever breastfed	*Was [child's name] ever breastfed?*	Yes/No	1 and 2	✓	×
Mother probably did not have post-natal depression	*After [child's name]'s birth, did [you/the child's mother] suffer from baby blues or post-natal depression for at least a month?*	Yes/No [recoded from: Yes; Probably; No]	1	✓	×
Global health measure	*In general, would you say [child's name]'s health is excellent, very good, good, fair or poor?*	Poor; Fair; Good; Very good: excellent	1 or 2	✓	✓
Not hospitalised in last 12 months	*In the last 12 months, did [child's name] stay in hospital because (he/she) was sick, injured, or required surgery?*	Yes/No [coding reversed to positive]	1 or 2	✓	✓
Child never had any ear problems	*Has [child's name] ever had runny ears/perforated eardrum/ hearing loss (total/partial/one ear) /other ear problem?*	Yes/No [coding reversed to positive]	1 or 2	✓	✓
Attends childcare, daycare or family daycare	*Does [child's name] go to childcare, day-care or family day care?*	Yes/No	1 and 2	✓	✓
Attends playgroup	*In the past month, has [child's name] gone to playgroup, mother's group, father's group, early learning circles or any other baby group/class?*	Yes/No	1 and 2	✓	×
Primary carer has a partner	Derived from household data	Yes/No	1 and 2	✓	×
Primary carer is employed	*Do you have a job?*	Yes/No	1 or 2	✓	✓
Highest qualification of the primary carer	*What was the highest qualification that you have completed?*	Year 9 or less; Year 10 or 11; Year 12; Vocational Education and Training (VET) qualification; Bachelor degree or higher	2	✓	✓
Parental warmth measure (primary carer)	*When answering, please say whether you Always, Often, Sometimes, Rarely, or Never do each thing I ask about:*	Mean score for the six questions (min=0; max=5) [coding reversed to positive]	2	✓	✓

Variable	Description/ LSIC Interview question wording (28)	Values and recoding details	Wave/s‡	PCA?	Univariable analysis?
	• *How often do you hug or hold [child] for no particular reason?* • *How often do you enjoy listening to [child]?* • *How often do you enjoy doing things together with [child]?* • *How often do you feel close to ([child] when [he/she] is happy?* • *How often do you feel close to ([child] when [he/she] is upset?* • *When [child] does something really well, how often do you go out of your way to say how pleased you are?*	A higher score indicates greater parental warmth Score not calculated if > 2 responses missing			
Stolen generations	*Were you or any of your (or your partner's) relatives removed from your family by welfare or the government or taken away to a mission?*	Yes/No	2	✓	✓
Frequency with which family experiences racism	*How often does your family experience racism, discrimination or prejudice?*	Every day; Every week; Sometimes; Only occasionally; Never or hardly ever	3	✓	✓
Total number of people living in household	Derived from household survey question: *What are the first and last names of all the people who live in this household, starting with you?*	continuous variable	1 or 2	✓	✓
Number of major life events in previous year	*I'd like to ask you about any big things that have happened to you, your family or [child] in the last year: Pregnancy/close family member been badly hurt or sick/close family member or friend passed away/carer got a job or returned to study/carer lost their job/family had serious worries about money/you or your family humbugged (harassed for money)/ felt too*	continuous variable	1 or 2	✓	✓

Variable	Description/ LSIC Interview question wording (28)	Values and recoding details	Wave/s‡	PCA?	Univariable analysis?
	crowded where you live, moved house, or had housing problems/you or a close family member had an alcohol or drug problem/ you or a close family member been mugged, robbed or assaulted/you or a close family member been arrested, been in jail/prison, or had problems with the police/ [child] or any other child of yours been involved in or upset by family arguments/any of [child]'s parents or carers left because of a family split-up/ [child] or any other child of yours had to be cared for by someone else for a while (at least a week)/ any other major events or stressful situations happened to you, your family or [child] in the last year				
Number of homes child has lived in since birth	*How many homes has [child's name] lived in since he/she was born?*	continuous variable	1 or 2	✓	✓
Family financial stress	*Which words best describe your family's money situation?*	We run out of money before payday; We are spending more money than we get; We have just enough money to get us through to the next payday; There's some money left over each week but we just spend it; We can save a bit every now and then; We can save a lot	1 or 3	✓	✓
Index of Relative Indigenous Socio-economic Outcomes (IRISEO)	Based on Indigenous Area of child's residential address	Decile 1=most favourable outcome; 10=least favourable outcome	1 or 2	✓	✓
Level of Relative Isolation (LORI)	Based on geocoding of child's residential address	None; Low; Moderate; High/Extreme	1 or 2	✓	✓

STATISTICAL ANALYSIS

Version 13 of Stata was used (36). To describe the sample I calculated means and standard deviations (continuous variables), or frequencies and percentages (categorical variables). I used Pearson's chi square and t-tests to assess the differences between children who were included and excluded from the sample based on having an SDQ Prosocial Behaviours score at Waves 5 or 6. All tests of significance were two-sided, and I considered *p* values of less than 0.05 to be statistically significant.

PRINCIPAL COMPONENT ANALYSIS

Because of the large number of outcome and exposure variables, I sought to limit the number of tests for association using Principal Component Analysis (PCA). Principal Component Analysis is a data reduction technique that creates new variables (called components) that express the patterns of correlation between variables and the underlying constructs that they measure (37). It is a method often used to build indices or proxy measures (38, 39):

> *The components are ordered so that the first component explains the largest possible amount of variation in the original data…The second component is completely uncorrelated with the first component, and explains additional but less variation than the first component …Subsequent components are uncorrelated with previous components; therefore, each component captures an additional dimension in the data, while explaining smaller and smaller proportions of the variation of the original variables. The higher the degree of correlation among the original variables in the data, the fewer components required to capture common information.*

A successful PCA results in a handful of components to which "common sense meanings" can be assigned (37). Principal components are continuous variables that can be used in analyses in place of the many variables that were used to create them. I used PCA to reduce the number of exposure variables. I performed a second PCA of SDQ Prosocial Behaviours score, the primary carer's SEWB score and the 'connection questions', with the aim of constructing a new index of SEWB for Aboriginal and Torres Strait Islander children.

I began by constructing a correlation matrix of the exposure variables listed in Table 10. As these variables consisted of a mixture of binary, ordinal and continuous data types, I used the user-written Stata command `-polychoric-` to calculate the appropriate coefficients for these relationships (38). The command assumes that binary and ordinal variables were obtained by categorising an underlying normally-distributed continuous variable, and treats ordinal variables with more than 10 categories as continuous.

To determine if it was feasible to perform PCA on the matrix, I used Bartlett's test of sphericity (Stata user-written command `-factortest-`) (40) to check that the matrix was significantly different from a matrix of non-correlated variables. I performed PCA using the matrix with Stata's `–pcamat-` command. I selected principal components with eigenvalues greater than one (39), and rotated the loading matrix of these for ease of interpretation. Orthogonal rotations result in uncorrelated components, while oblique rotations allow for some correlation, which would be expected given the nature of the data (41). I used both orthogonal (varimax) and oblique (promax) rotation methods and compared the output. I calculated scores for each of the principal components, which represent the weighted sums of the variables which load most heavily onto the component. I calculated Kaiser-Meyer-Olkin measures of sampling adequacy to assess the suitability of the data for PCA and hence the usefulness of the resulting components (42). I repeated this procedure for the outcome measures and intended to use the resulting component scores in univariable and multivariable analyses.

UNIVARIABLE ANALYSIS

I performed three sets of univariable analyses. I analysed the associations between a smaller number of exposure variables (as shown in in Table 10 [above]) and outcome principal components, and the two SDQ subscale scores. I estimated the effect of binary exposure variables by calculating Harrell's *C* and 95% confidence intervals. Harrell's *C* estimates the probability that a child in the exposed group has a higher score than a child in the unexposed group (43). This estimate is equivalent to the probability output from the Wilcoxon rank-sum test (44), which I used to calculate *p* values for these estimates. To estimate the effect of ordinal and continuous exposure variables I calculated Spearman's rank correlation coefficients (ρ), together with confidence intervals and *p* values.

MULTIVARIABLE ANALYSIS

For all outcome measures, I incorporated exposures with a *p* value of 0.25 or less from the univariable analysis into regression models. I also included the potentially confounding factors that had a statistically significant association with the outcomes in univariable analyses. I adjusted for the geographic clustering in the LSIC sample using the 'rcluster' variable. This variable is provided with the LSIC data and is derived from the Indigenous Area in which the child lived (28). Hypothesis test statistics from analyses of unadjusted clustered data may be underestimated, increasing the likelihood of Type I error (45).

I used linear regression to identify exposures associated with the Principal Components scores and SDQ Total Difficulties score. I checked for goodness-of-fit by assessing the R-squared value and plotting scores against scores predicted by the models. I tested for normality of the residuals by graphing histograms, standardised normal probability plots, and quantiles of residuals against the quantiles of a normal distribution. I assessed the homoscedasticity[4] of the residuals by plotting them against the predicted scores.

For the Prosocial Behaviours outcome, I incorporated exposures into an ordinal logistic regression model. Ordinal logistic regression is based on the proportional odds assumption, under which the relationship between any one of the 11 Prosocial Behaviours categories and all the other 10 categories is the same (46). I tested whether this assumption had been violated by performing a likelihood ratio test (using the user-written `omodel` command) and the Brant test. As the regression coefficients from the `ologit` output are not interpretable, I predicted the probability of a Prosocial Behaviours score of 10 for categories of variables with a *p* value of less than 0.05 using the `margins` command.

ETHICAL REVIEW

This research was approved by the Australian National University Human Research Ethics Committee (Protocol 2016/583). I discussed the ethical aspects of the research

[4] Homogeneity of variance

questions and the validity of the SEWB conceptual framework with Professor Tom Calma, Co-Chair of Reconciliation Australia and former Aboriginal and Torres Strait Islander Social Justice Commissioner and Race Discrimination Commissioner. He confirmed both to be sound.

Results

CHARACTERISTICS OF CHILDREN IN THE STUDY SAMPLE

Nine hundred and fifty children met the age eligibility criteria, but only 726 of these (76%) had a SDQ Prosocial Behaviours score at endpoint and were included in the sample (Table 11). Children of eligible age who were excluded were more likely to be low birthweight, have a younger and unemployed primary carer, to have a mother who smoked while pregnant, and to live in a remote or very remote area (Table 12).

Table 11 Selected baseline characteristics of children in the study sample.

Variable	Class or statistic	n	%*
Sex	Female	360	50%
Age at Wave 1 (Wave 1 entrants, months)	Mean (SD)	14.9	(4.5)
Age at Wave 2 (Wave 2 entrants, months)	Mean (SD)	26.8	(4.6)
Age of primary carer (years)	Mean (SD)	28.4	(7.0)
Relationship of primary carer to child	Mother	692	95.0%
	Grandparent	16	2.3%
	Father	12	2.0%
	Aunty	3	0.4%
	Adoptive/foster mother	3	0.4%
Indigenous status of primary carer	Aboriginal and/or Torres Strait Islander	606	83%
Primary carer had a partner	Yes	416	57%
Child spoke an Indigenous language	Yes	155	22%†
Low birthweight	Yes	46	8%‡
BITSEA Problem Score, Wave 2	Mean (SD)	11.7	(6.1)
BITSEA Competency Score, Wave 2	Mean (SD)	16.8	(2.5)
Number of children reporting major life events in previous 12 months	Pregnancy/new baby in family	469	65%
	Someone close to them passed away	350	48%
	Household crowding, moved house, or had housing problems	282	39%
	Carer got a job or returned to study	236	33%
	Family member badly hurt or sick	232	32%
Location	Major cities	207	29%
	Inner regional	177	24%
	Outer regional	99	14%
	Remote	92	13%
	Very remote	150	21%
IRISEO	Deciles 1 & 2	88	20%
	Deciles 3 & 4	123	17%
	Deciles 5 & 6	288	40%
	Deciles 7 & 8	105	15%
	Deciles 9 & 10	122	17%

*Due to rounding, percentages may not sum to 100; †4 missing observations; ‡149 missing observations; SD - Standard deviation

Table 12 Comparison of selected baseline characteristics of children included in and excluded from the study sample. Characteristics with a statistically significant difference (p<0.05) between groups are shown in **bold**.

Characteristic at baseline	Included in sample %	Excluded from sample* %	*p* value for difference
Female	49.6	49.1	0.90
Low birthweight	**8.0**	**15.1**	**0.01**
Mother did not smoke after discovering she was pregnant	**50.9**	**41.1**	**0.02**
Mother did not drink alcohol after discovering she was pregnant	78.7	74.1	0.17
BITSEA Problems score (mean, 95% CI)	11.7 (11.1 – 12.1)	11.4 (10.4 – 12.4)	0.66
BITSEA Competency score (mean, 95% CI)	16.8 (16.6 – 17.0)	16.5 (16.1 – 16.9)	0.24
Very good or excellent general health	79.5	76.2	0.30
Primary carer aged <20 years	**7.1**	**13.1**	**<0.01**
Primary carer completed Year 12	41.1	33.1	0.74
Primary carer employed	**30.2**	**17.9**	**0.00**
Primary carer parental warmth score (mean, 95% CI)	4.8	4.7	0.18
Lived in remote or very remote area	**33.4**	**49.1**	**0.00**

* Children of eligible age at baseline were excluded if SDQ Prosocial Behaviours score was missing for Waves 5 and 6.

Table 13 shows key statistics for the sample children's SDQ subscale scores at around the time of starting school, which are also illustrated in Figure 13 and Figure 14. The mean age of SDQ assessment was 6.0 years (standard deviation 0.5 years). Only 15 (2.2%) children had not commenced school by Wave 6. Primary carer's SEWB scores ranged from seven to 28, with most carers scoring 26 or higher (Table 13).

Table 13 Key statistics for children's Strengths and Difficulties subscale scores and primary carer's SEWB scores, at around the time of starting school, for the study sample.

	Mean	95% CI	Median	IQR
Prosocial Behaviours score n=726	8.5	8.4 – 8.6	9	8 - 10
Total Difficulties Score n=725	11.5	11.0 – 12.0	11	7 – 16
Primary carer SEWB score * n=695	24.4	24.1 – 24.7	26	23 - 27

CI – confidence interval; IQR – interquartile range; * A higher score indicates better SEWB, possible range 0-28

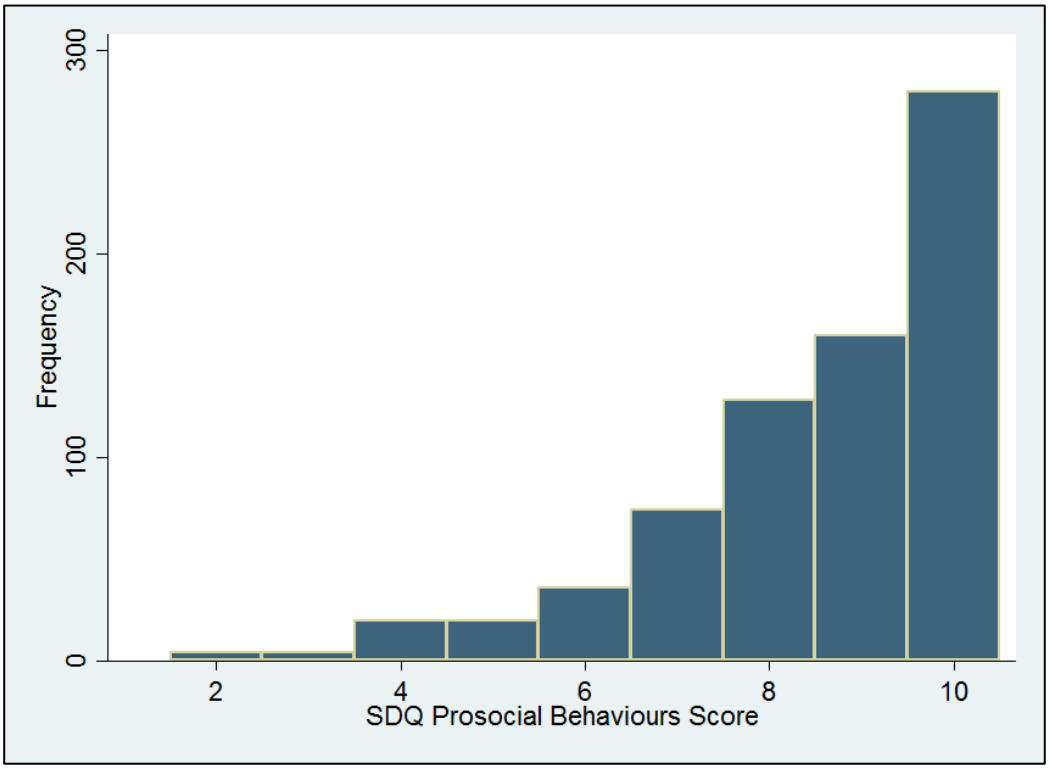

Figure 13 Distribution of SDQ Prosocial Behaviours scores at the time of starting school for children in the sample. A higher score indicates better prosocial behaviours.

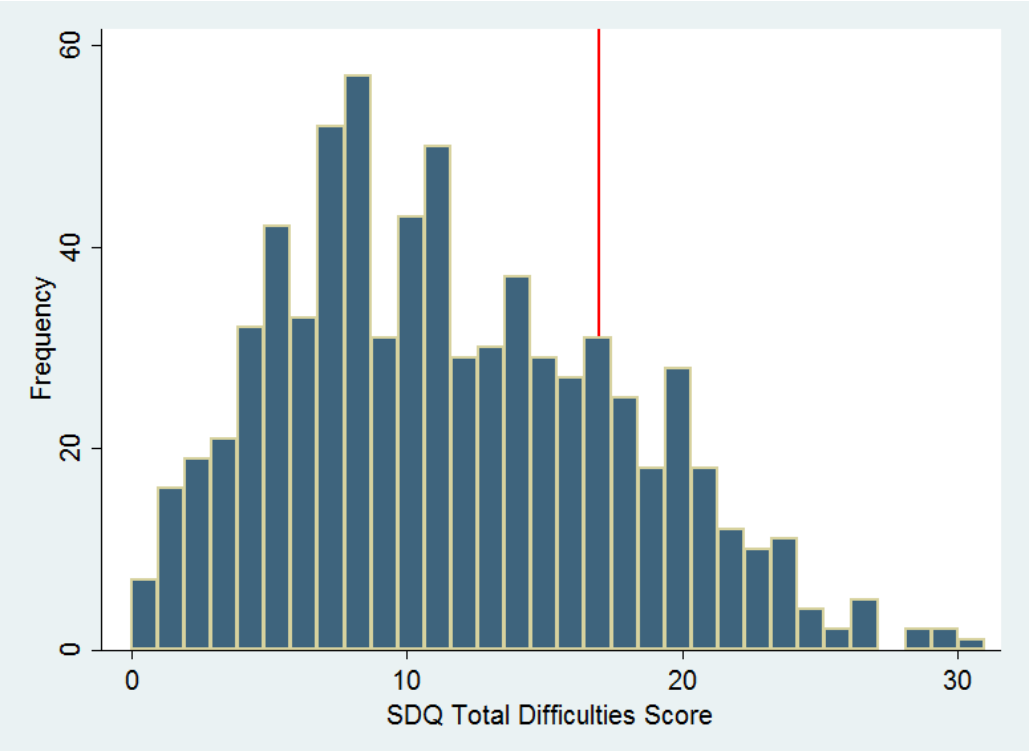

Figure 14 Distribution of SDQ Total Difficulties scores at the time of starting school for children in the sample. A higher score indicates greater difficulties. The red line (at 17) indicates the threshold above which children are considered at high or very high risk of emotional or behavioural problems.

PRINCIPAL COMPONENT ANALYSIS RESULTS

The Bartlett's test for sphericity of the exposure variables indicated that these data could be reduced using PCA (chi-squared=894, *p*=0.00). The principal component analysis of the exposure variables would only run using data for 269 children, or 37% of the sample. When I excluded the 'stolen generations' variable, which was missing data for 42% of children, the analysis ran with data for 402 children. Nine principal components had eigenvalues greater than one, explaining 68% of data variance. Variable loadings for both varimax and promax rotations did not lend themselves to easy interpretation. The Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy was unacceptably low (0.24), indicating the data were not suitable for reduction by PCA (42). The results of the PCA of the exposure variables were not used in further analyses and are therefore not presented here.

The Bartlett's test for sphericity of the outcome variables indicated that these data could be reduced using PCA (chi-squared=468, *p*=0.00). The PCA of the outcome variables included data for 444 children (Table 14, Figure 15). Three principal components had

eigenvalues greater than one and explained 66% of data variance. The loadings for varimax or promax rotations of these components were very similar. Around one third of the data variance was explained by the first principal component (which I have named "Child's connection") comprising variables measuring the child's connection to community and country. The second component ("Child's helping, sharing and mental health") comprised the child's two SDQ scores; while the third ("Primary carer's SEWB factors") comprised mainly the primary carer's SEWB score and connection to community. A higher component score indicates, respectively: a stronger connection; greater helping, sharing and mental health; and greater connection and SEWB of the carer. The KMO measure for this analysis was 0.64, indicating adequate–but not optimal–sampling adequacy (42).

Table 14 Rotated components and loadings from Principal Component Analysis of outcome measures, using oblique promax rotation (n=444). Only loadings greater than 0.2, or less than -0.2, are shown.

	Component 1	**Component 2**	**Component 3**
Assigned Component Name	"Child's connection"	"Child's helping, sharing and mental health"	"Primary carer's SEWB factors"
Eigenvalue	2.62	1.64	1.04
Proportion of variance explained	32%	18%	16%
Variable Loadings			
SDQ Prosocial behaviours score		0.73	
SDQ Total Difficulties Score		-0.64	
Child has a connection to country or place	0.55		
Child identifies with a tribal group, a language group or a clan	0.53		
Child does activities with family members to learn about culture	0.46		
Number of days per week child spends time with leaders or elders in community	0.39		
Degree to which primary carer feels part of his/her local community			0.70
SEWB of primary carer			0.65
Component Scores			
Minimum – maximum	-4.0 – 2.2	-13.7 – 11.6	0.6 – 17.9
Mean (Standard deviation)	-1.5 (1.1)	2.7 (5.0)	13.3 (3.3)

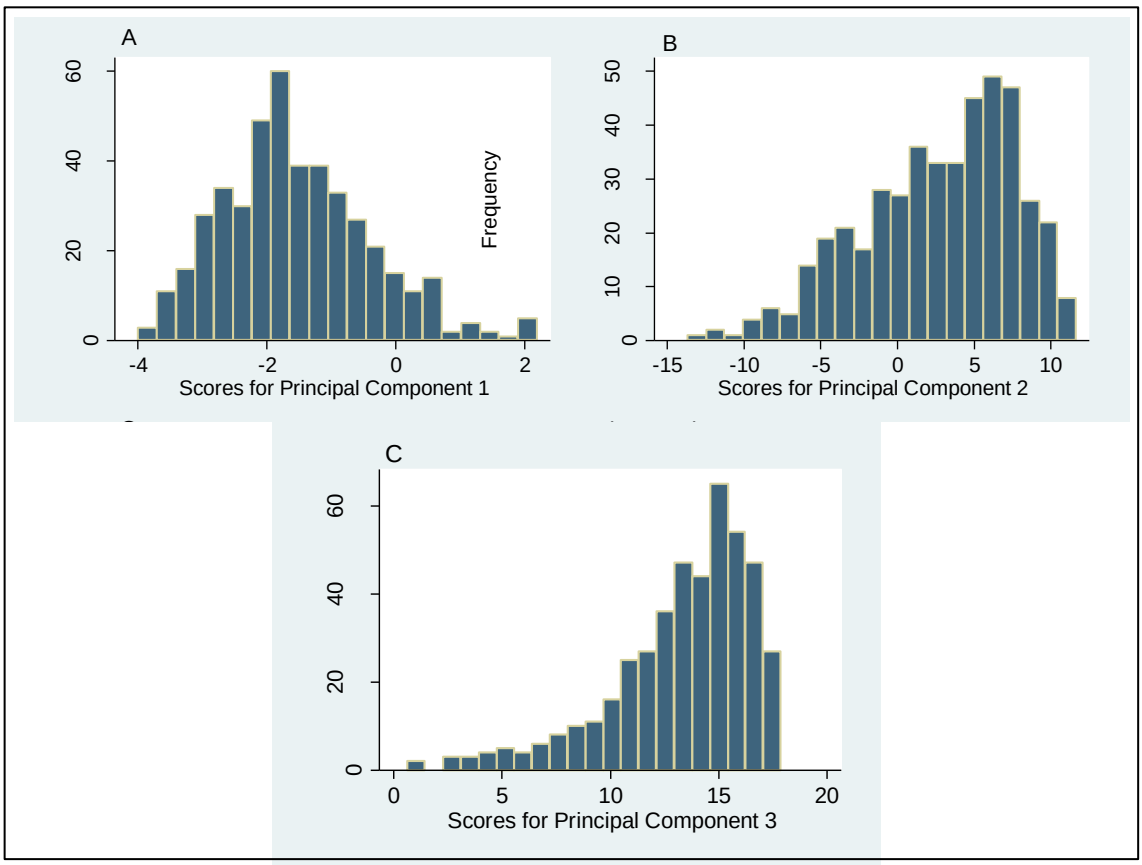

Figure 15 Distributions of the three principal components from analysis of the outcome variables: (A) "Child's connection" component; (B) "Child's helping, sharing and mental health"; and (C) "Primary carer's SEWB factors". For each of these components, a higher score indicates a more favourable outcome.

ASSOCIATIONS BETWEEN PRINCIPAL COMPONENTS AND EXPOSURE VARIABLES

PRINCIPAL COMPONENT 1 – "CHILD'S CONNECTION"

In univariable analyses, there were negligible but statistically significant positive associations between the "Child's connection" component score and several early life exposures, including: the primary carer or any of his/her (or his/her partner's) relatives being removed from their family or taken away to a mission; and experiencing more major life events (Table 15). Abstaining from alcohol during pregnancy and living in an area of greater relative socio-economic disadvantage were associated with a poorer score.

Table 15 Results of univariable analyses of factors (antenatal to two years) associated with a higher "Child's connection" component score at the time of starting school, Footprints in Time cohort 2008-2013. Results with $p<0.05$ are shown in **bold**.

Exposure	n in analysis	effect size		*p* value
		Harrell's *C**	95% CI	
Mother had antenatal visit <20 weeks	379	0.49	0.38 – 0.61	0.90
Mother did not drink alcohol during pregnancy	**405**	**0.39**	**0.33 – 0.46**	**<0.01**
Mother did not smoke during pregnancy	407	0.45	0.40 – 0.51	0.10
Mother did not use other substances during pregnancy	407	0.45	0.33 – 0.57	0.42
Low birthweight	362	0.49	0.39 – 0.59	0.90
Child not hospitalised in the past 12 months	444	0.47	0.41 – 0.53	0.36
Child never had any ear problems	444	0.46	0.39 – 0.52	0.25
Attends childcare, daycare or family daycare	444	0.46	0.40 – 0.52	0.19
Excellent, very good or good global health	444	0.49	0.35 – 0.64	0.92
Primary carer is employed	444	0.46	0.40 – 0.51	0.16
Stolen generations	**278**	**0.58**	**0.50 – 0.64**	**0.03**
Excellent, very good or good global health at time of SDQ assessment †	444	0.39	0.24 – 0.54	0.20
Female†	444	0.48	0.42 – 0.54	0.56
		ρ	95% CI	*p* value
Highest qualification of the primary carer	**444**	**-0.10**	**-0.19 – -0.01**	**0.03**
Parental warmth measure (primary carer)	414	-0.06	-0.15 – 0.04	0.23
Frequency with which family experiences racism	**404**	**-0.21**	**-0.31 – -0.12**	**<0.01**
Number of people living in household	**444**	**0.17**	**0.08 – 0.26**	**<0.01**
Number of life events in previous year	**444**	**0.20**	**0.11 – 0.29**	**<0.01**
Number of homes child lived in since birth	436	0.07	-0.01 – 0.18	0.07
Family financial stress	**441**	**-0.10**	**-0.19 – -0.00**	**<0.05**
IRISEO	**444**	**-0.23**	**-0.32 – -0.14**	**<0.01**
Level of Relative Isolation	**443**	**0.21**	**0.11 – 0.29**	**<0.01**
BITSEA Competency score†	**414**	**-0.16**	**-0.19 – -0.00**	**0.04**
BITSEA Problem score†	**413**	**0.26**	**0.17 – 0.35**	**<0.01**
Age at time of SDQ assessment†	444	0.05	-0.05 – 0.14	0.35

CI - Confidence Interval; * Harrell's *C* - Probability that an exposed child has a higher score than an unexposed child; *ρ* - Spearman's rank correlation coefficient; †Potential confounding factor

However, most of these factors were no longer significant in the linear regression model (Table 16). The model predicted a "Child's connection" component score of -1.83 (95% CI -2.08 to -1.58) for children in two person households, and a slightly better score of -1.06 (95% CI -1.55 to -0.59) for those with 11 people (Figure 16A). The highest qualification of the primary carer had a non-linear relationship with this component, with only Year 12 completion being a statistically significant predictor (Figure 16B). For children of families with different levels of exposure to racism, predicted scores differed only between those whose experience was daily and those who never or hardly ever experienced racism (Figure 16C). Although the association with the number of major life events was statistically significant, the effect was mild. The child's BITSEA Problem score at Wave 2, which was included in the model as a confounder, also had a modest, positive, dose-response correlation with the score for this component (Figure 16D).

Table 16 Results of linear regression of factors (antenatal to two years) associated with "Child's connection" component score at the time of starting school, Footprints in Time cohort 2008-2013. Variables with $p \leq 0.25$ from univariable analysis were included in the regression model. Results with $p < 0.05$ are shown in **bold**.

Exposure		Adjusted effect size (n=230)*		*p* value
		coefficient	95% CI	
Mother did not drink alcohol during pregnancy		-0.22	-0.55 – 0.11	0.19
Mother did not smoke during pregnancy		-0.06	-0.39 – 0.27	0.71
Mother did not use other substances during pregnancy		0.19	-0.35 – 0.72	0.49
Child never had any ear problems		-0.14	-0.44 – 0.15	0.33
Attends childcare, daycare or family daycare		0.08	-0.26 – 0.42	0.66
Primary carer is employed		0.18	-0.19 – 0.55	0.34
Stolen generations		0.09	-0.18 – 0.35	0.51
Highest qualification of the primary carer	Less than Year 10	ref	-	-
	Year 10/11	-0.27	-0.61 – 0.07	0.12
	Year 12	**-0.56**	**-1.02 – -0.10**	**0.02**
	VET qualification	0.16	-0.30 – 0.60	0.50
	Bachelor degree or higher	0.06	-0.53 – 0.66	0.83
Parental warmth measure (primary carer)		-0.05	-0.61 – 0.52	0.87
Number of people in the household		**0.09**	**0.01 – 0.16**	**0.03**
Number of major life events in previous year		**0.06**	**0.00 – 0.12**	**0.05**
Number of homes child has lived in since birth		0.03	-0.11 – 0.16	0.71

CI - Confidence Interval; ref – reference group; *Adjusted for 95 clusters

Exposure		Adjusted effect size (n=230)*		*p* value
		coefficient	95% CI	
Frequency with which family experiences racism	Every day	ref	-	-
	Every week	-0.03	-0.96 – 0.90	0.95
	Sometimes	-0.62	-1.25 – 0.00	0.05
	Only occasionally	-0.55	-1.29 – 0.20	0.15
	Never or hardly ever	**-0.86**	**-1.53 – -0.18**	**0.01**
Family financial stress	Run out of money before payday	ref	-	-
	Spending more money than we get	0.25	-0.29 – 1.19	0.59
	Have just enough money to get us through to next pay day	0.27	-0.18 – 0.73	0.24
	Some money left over each week but we just spend it	0.10	-0.64 – 0.84	0.79
	Can save a bit every now and then	0.02	-0.55 – 0.57	0.96
	Can save a lot	0.22	-0.60 – 1.03	0.60
IRISEO		-0.04	-0.11 – 0.02	0.19
Level of Relative Isolation	None	ref	-	-
	Low	0.12	-0.18 – 0.43	0.43
	Moderate	0.51	-0.05 – 1.07	0.07
	High/Extreme	0.70	-0.67 – 2.07	0.31
BITSEA Competency score†		-0.03	-0.11 – 0.05	0.50
BITSEA Problem score†		**0.04**	**0.02 – 0.06**	**<0.01**
Global health measure at time of SDQ assessment†	Poor/Fair	ref	-	-
	Good/ Very good/ Excellent	-0.25	-0.96 – 0.46	0.49

CI - Confidence Interval; ref – reference group; *Adjusted for 95 clusters; †Potential confounding factor

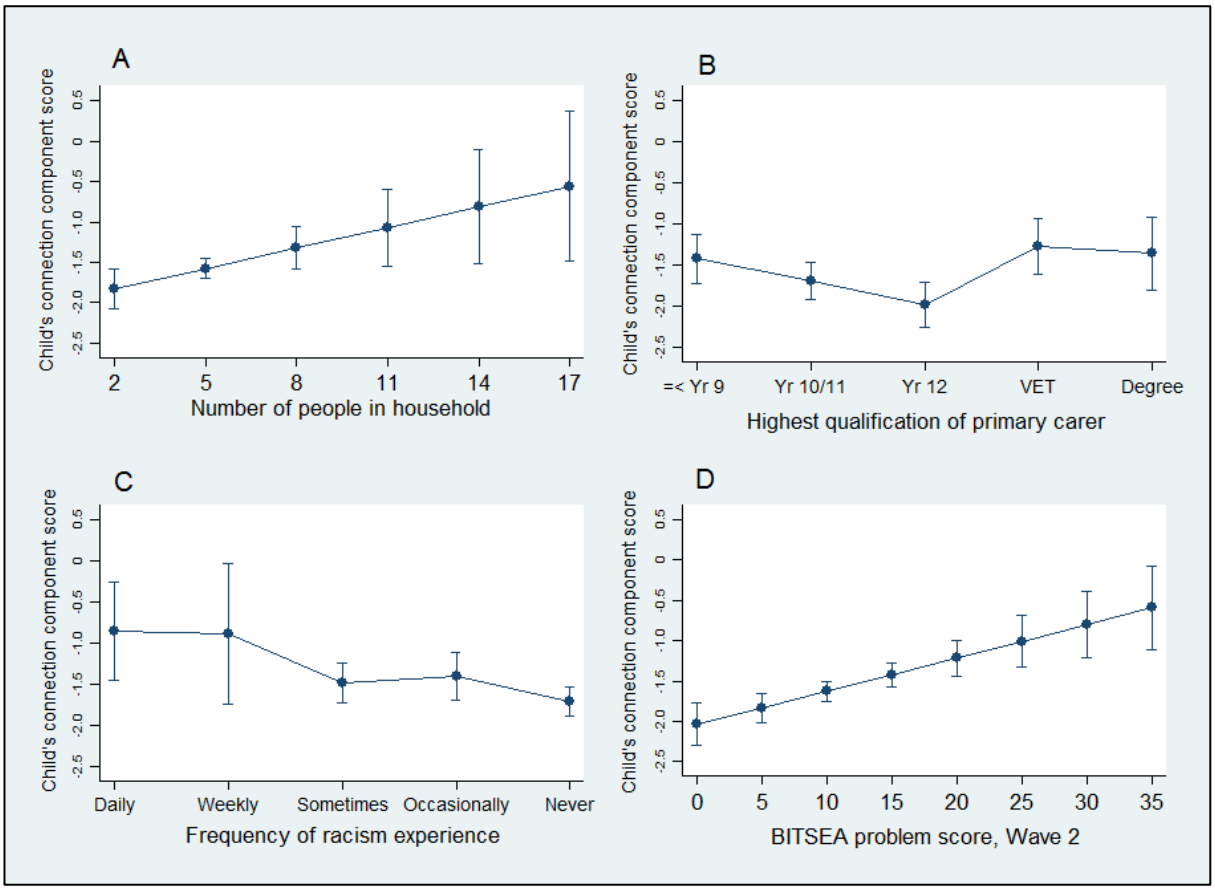

Figure 16 Predicted "Child's connection" component scores (with 95% CIs) from linear regression for (A) number of people in the household; (B) highest qualification of the primary carer; (C) frequency with which the family experiences racism; and (D) BITSEA problem score at Wave 2. A higher component score indicates a greater degree of connection.

Overall, this linear model was statistically significant (F-statistic=7.5, p=0.00), and explained 20% of the variability in the "Child's connection" component scores (Appendix 3.4, Figure A). The histogram of the residuals, standardised normal probability plot, and residual quantile plot indicated that the residuals have a close to normal distribution (Appendix 3.4, Figure B*i-iii*). The trend towards smaller residuals at extreme predicted values suggests mild heteroscedasticity of the residuals (Appendix 3.4, Figure B*iv*).

PRINCIPAL COMPONENT 2 – "CHILD'S HELPING, SHARING AND MENTAL HEALTH"

In univariable analyses, there were small but statistically significant associations between a better score for the "Child's helping, sharing and mental health" component and the child's mother not smoking during pregnancy, the primary carer having a higher

level of qualification, and living in a more socio-economically disadvantaged area (Table 17). Experiencing a greater number of major life events and living in a more isolated area were associated with poorer scores for this component.

Table 17 Results of univariable analyses of factors (antenatal to two years) associated with a higher "Child's helping, sharing and mental health" component score at the time of starting school, Footprints in Time cohort 2008-2013. Results with $p<0.05$ are shown in **bold**.

Exposure	n in analysis*	effect size		*p* value
		Harrell's *C*†	95% CI	
Mother received first antenatal visit < 20 weeks gestation	379	0.44	0.34 – 0.55	0.34
Mother did not drink alcohol during pregnancy	405	0.56	0.49 – 0.63	0.09
Mother did not smoke during pregnancy	**407**	**0.59**	**0.54 – 0.65**	**<0.01**
Mother did not use other substances during pregnancy	407	0.58	0.46 – 0.70	0.20
Low birthweight	362	0.43	0.34 – 0.53	0.21
Child not hospitalised in the past 12 months	444	0.55	0.49 – 0.62	0.11
Child never had any ear problems	444	0.53	0.46 – 0.60	0.40
Attends childcare, daycare or family daycare	444	0.54	0.48 – 0.60	0.24
Excellent, very good or good global health	444	0.60	0.45 – 0.77	0.20
Primary carer is employed	444	0.55	0.50 – 0.61	0.07
Stolen generations	278	0.44	0.37 – 0.51	0.07
Excellent, very good or good global health at time of SDQ assessment ‡	444	0.65	0.48 – 0.83	0.07
Female‡	444	0.54	0.48 – 0.59	0.18

CI - Confidence Interval; * n differs between variables due to missing data; † Harrell's *C* - Probability that an exposed child has a higher score than an unexposed child

Exposure	n in analysis*	effect size		*p* value
		ρ	95% CI	
Highest qualification of the primary carer	**444**	**0.17**	**0.08 – 0.26**	**0.003**
Parental warmth measure (primary carer)	414	0.09	-0.003 – 0.19	0.06
Frequency with which family experiences racism	404	0.82	-0.11 – 0.09	0.82
Number of people living in household	444	-0.09	-0.18 – 0.01	0.06
Number of major life events in previous year	**444**	**-0.20**	**-0.29 – -0.11**	**0.00**
Number of homes child has lived in since birth	436	-0.08	-0.18 – 0.01	0.09
Family financial stress	441	0.33	-0.05 – 0.14	0.33
IRISEO	**444**	**0.16**	**0.07 – 0.25**	**<0.01**
Level of Relative Isolation	**443**	**-0.11**	**-0.2 – -0.02**	**0.02**
BITSEA Competency score‡	**414**	**0.11**	**0.01 – 0.20**	**0.03**
BITSEA Problem score‡	**413**	**-0.32**	**-0.41 – -0.26**	**0.00**
Age at time of SDQ assessment‡	444	-0.06	-0.15 – 0.03	0.19

CI - Confidence Interval; * n differs between variables due to missing data; *ρ* - Spearman's rank correlation coefficient; ‡Potential confounding factor

In the linear regression model, only the number of people in the household and the number of major life events retained statistical significance (Table 18). The model predicted a "Child's helping, sharing and mental health" component score of 4.39 (95% CI 3.30 to 5.46) for children with two people in the household, and a poorer score of 1.40 (95% CI -0.57 to 3.37) for those with 11 people (Figure 17A). Children who experienced no major life events had a predicted component score of 4.70 (95% CI 3.41 to 5.99), compared with 1.79 (95% CI 0.26 to 3.32) for those with 10 events (Figure 17B). The child's BITSEA Problem score at Wave 2, which was included in the model as a confounder, also had a modest negative correlation with the score for this component (Figure 17C).

Table 18 Results of linear regression of factors (antenatal to two years) associated with "Child's helping, sharing and mental health" component score at the time of starting school, Footprints in Time cohort 2008-2013. Variables with $p \leq 0.25$ from univariable analysis were included in the regression model. Results with $p<0.05$ are shown in **bold**.

Exposure		Adjusted effect size (n=230)*		*p* value
		coefficient	95% CI	
Mother did not drink alcohol during pregnancy		0.03	-1.66 – 1.71	0.98
Mother did not smoke during pregnancy		1.20	-0.46 – 2.86	0.15
Mother did not use other substances during pregnancy		-0.59	-0.43 – 1.24	0.52
Low birthweight		-0.90	-3.08 – 1.28	0.41
Child not hospitalised in the past 12 months		-0.20	-1.77 – 1.37	0.80
Attends childcare, daycare or family daycare		-0.15	-1.65 – 1.36	0.85
Excellent, very good or good global health		-1.00	-6.93 – 4.92	0.74
Primary carer is employed		-0.27	-1.87 – 1.33	0.74
Stolen generations		-0.11	-1.56 – 1.34	0.88
Highest qualification of the primary carer	Less than Year 10	ref	-	-
	Year 10/11	1.00	-1.45 – 3.45	0.42
	Year 12	1.81	-0.55 – 4.18	0.13
	VET qualification	0.72	-1.77 – 0.28	0.57
	Bachelor degree or higher	1.02	-2.72 – 4.75	0.59
Parental warmth measure (primary carer)		-0.40	-2.37 – 1.58	0.69
Number of people in household		**-0.33**	**-0.63 – -0.03**	**0.03**
Number of major life events in previous year		**-0.29**	**-0.54 – -0.04**	**0.02**
Number of homes child has lived in since birth		-0.24	-0.87 – 0.35	0.45
IRISEO		-0.16	-0.45 – 0.14	0.29
Level of Relative Isolation	None	ref	-	-
	Low	0.04	-1.48 – 0.56	0.96
	Moderate	-0.53	-2.02 – 1.84	0.66
	High/Extreme	-2.27	-4.71 – 0.17	0.07
BITSEA Competency score†		0.12	-0.20 – 0.44	0.47
BITSEA Problem score†		**-0.22**	**-0.34 – -0.10**	**<0.01**
Female†		0.44	-0.94 – 1.81	0.53
Age at time of SDQ assessment†		0.03	-0.11 – 0.16	0.81
Global health measure at time of SDQ assessment†	Poor/Fair	ref	-	-
	Good/ Very good/ Excellent	6.7	-0.71 – 13.25	0.08

CI - Confidence Interval; ref – reference group; *Adjusted for 95 clusters; †Potential confounding factor

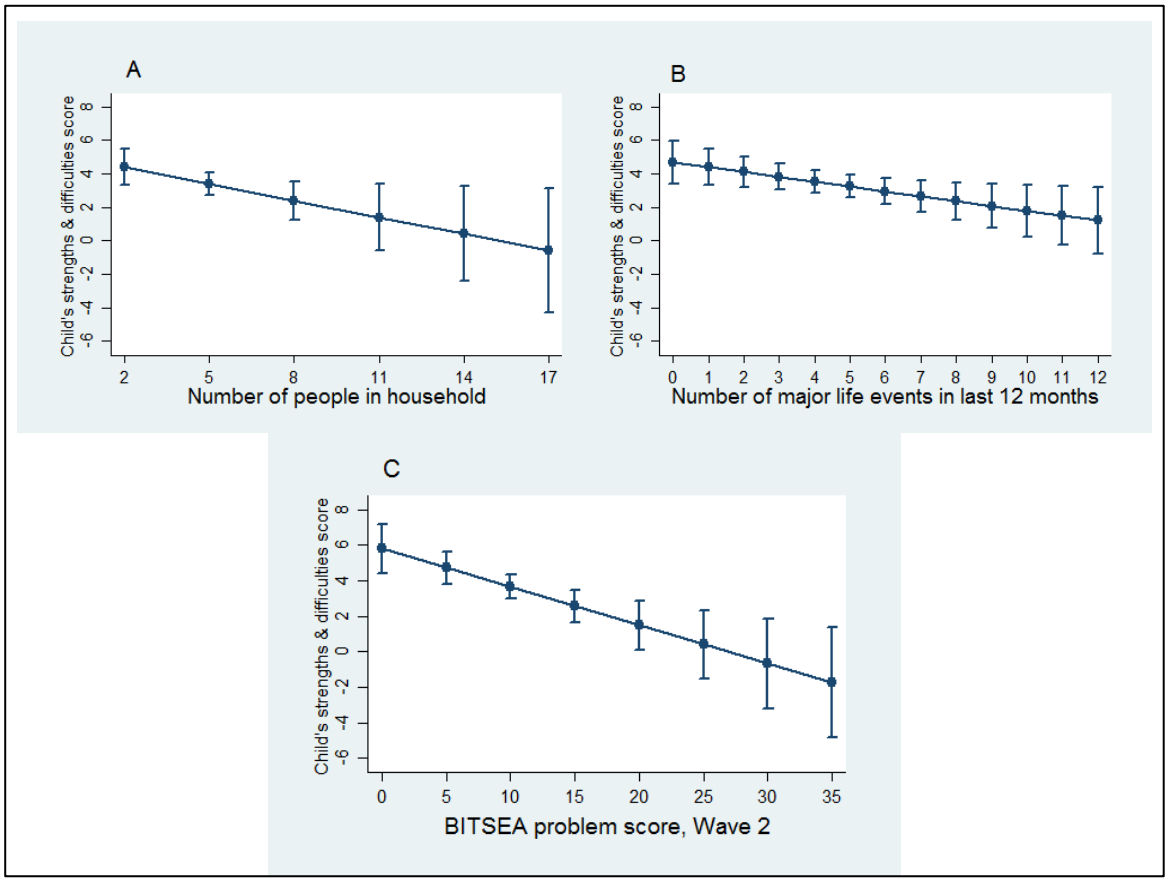

Figure 17 Predicted "Child's helping, sharing and mental health" component scores from linear regression for (**A)** number of people in the household; (**B**) number of major life events in previous year; and (**C**) BITSEA problem score at Wave 2.

Overall, this linear model was statistically significant (F-statistic=6.0, p=0.00), and explained 12% of the variability in the component scores (Appendix 3.4, Figure C). The histogram of the residuals, standardised normal probability plot, and residual quantile plot indicated that the residuals deviate from a normal distribution slightly (Appendix 3.4, Figure D*i-iii*). The funnel-shaped graph of residuals plotted against predicted values suggests mild heteroscedasticity of the residuals (Appendix 3.4, Figure D*iv*).

PRINCIPAL COMPONENT 3 – "PRIMARY CARER'S SEWB FACTORS"

In univariable analyses, there were modest associations between a better "Primary carer's SEWB factors" component score and the child's mother not drinking alcohol during pregnancy, and the child experiencing fewer major life events. Negligible positive effects were also detected for: the mother not smoking during pregnancy; the primary carer being employed; having a higher level of qualification and greater

parental warmth; the family not being affected by the stolen generations; suffering less financial stress; and the child living in fewer homes in the first two years of life (Table 19).

Table 19 Results of univariable analyses of factors the first years of life associated with a higher "Primary carer's SEWB factors" component score at the time of starting school, Footprints in Time cohort 2008-2013. Results with $p<0.05$ are shown in **bold**.

Exposure	n in analysis	effect size		*p* value
		Harrell's *C**	95% CI	
Mother received first antenatal visit < 20 weeks gestation	379	0.48	0.36 – 0.59	0.68
Mother did not drink alcohol while pregnant	**405**	**0.62**	**0.56 – 0.69**	**<0.01**
Mother did not smoke during pregnancy	**407**	**0.59**	**0.54 – 0.65**	**<0.01**
Mother did not use other substances during pregnancy	407	0.56	0.43 – 0.69	0.32
Low birthweight	362	0.44	0.35 – 0.52	0.26
Child not hospitalised in the past 12 months	444	0.55	0.49 – 0.62	0.11
Child never had any ear problems	444	0.52	0.46 – 0.59	0.53
Attends childcare, daycare or family daycare	444	0.53	0.47 – 0.60	0.32
Excellent, very good or good global health	444	0.56	0.41 – 0.70	0.43
Primary carer is employed	**444**	**0.58**	**0.52 – 0.63**	**0.01**
Stolen generations	**278**	**0.42**	**0.35 – 0.49**	**0.03**
Excellent, very good or good global health at time of SDQ assessment †	**444**	**0.67**	**0.53 – 0.82**	**0.04**
Female†	444	0.51	0.45 – 0.56	0.85
		ρ	95% CI	*p* value
Highest qualification of the primary carer	**444**	**0.17**	**0.08 – 0.26**	**<0.01**
Parental warmth measure (primary carer)	**414**	**0.10**	**0.00 – 0.19**	**0.04**
Frequency of family's experience of racism	404	0.07	-0.03 – 0.17	0.17
Number of people living in household	444	-0.08	-0.17 – 0.02	0.10
Number of life events in previous year	**444**	**-0.25**	**-0.34 – -0.16**	**<0.01**
Number of homes child lived in since birth	**436**	**-0.10**	**-0.19 – 0.00**	**0.04**
Family financial stress	**441**	**0.11**	**0.01 – 0.20**	**0.03**
IRISEO	444	0.09	-0.01 – 0.08	0.07
Level of Relative Isolation	443	-0.03	-0.21 – 0.07	0.56
BITSEA Competency score†	**414**	**0.04**	**0.08 – 0.26**	**<0.01**
BITSEA Problem score†	**413**	**-0.30**	**-0.38 – -0.21**	**<0.01**
Age at time of SDQ assessment†	444	-0.08	-0.17 – 0.01	0.09

CI - Confidence Interval; * Harrell's *C* - Probability that an exposed child has a higher score than an unexposed child; *ρ* - Spearman's rank correlation coefficient; †Potential confounding factor

In the linear regression model, only the number of people in the household and the number of major life events had statistically significant coefficients (Table 20). The model predicted a "Primary carer's SEWB factors" component score of 14.13 (95% CI 13.40 to 14.86) for children with two people in the household, and a poorer score of 11.79 (95% CI 10.40 to 13.19) for those with 11 people (Figure 18A). Children who experienced no major life events had a predicted component score of 14.60 (95% CI 13.74 to 15.47), compared with 13.18 (95% CI 12.72 to 13.64) for those with five events (Figure 18B). The highest qualification of the primary carer had a non-linear relationship with this component, with only Year 12 qualification being a statistically significant predictor (Figure 18C). The child's BITSEA Problem score at Wave 2, which was included in the model as a confounder, also had a negligible negative correlation with the score (Figure 18D).

Table 20 Results of linear regression of factors (antenatal to two years) associated with "Primary carer's SEWB factors" component score at the time of starting school, Footprints in Time cohort 2008-2013. Variables with $p \leq 0.25$ from univariable analysis were included in the regression model. Results with $p < 0.05$ are shown in **bold**.

Exposure		Adjusted effect size (n=230)*		*p* value
		coefficient	95% CI	
Mother did not drink alcohol during pregnancy		0.71	-0.41 – 1.81	0.21
Mother did not smoke during pregnancy		0.68	-0.34 – 1.70	0.19
Child not hospitalised in the past 12 months		0.31	-0.77 – 1.39	0.57
Primary carer is employed		-0.50	-1.60 – 0.59	0.36
Stolen generations		-0.29	-1.07 – 0.49	0.46
Highest qualification of the primary carer	Less than Year 10	ref	-	-
	Year 10/11	0.48	-0.53 – 1.49	0.35
	Year 12	**1.68**	**0.39 – 2.97**	**0.01**
	VET qualification	-0.31	-1.59 – 0.98	0.64
	Bachelor degree or higher	1.04	-0.67 – 2.75	0.23
Parental warmth measure (primary carer)		0.31	-1.11 – 1.74	0.66
Frequency with which family experiences racism	Every day	ref	-	-
	Every week	-1.77	-3.71 – 3.35	0.92
	Sometimes	1.40	-1.22 – 4.02	0.29
	Only occasionally	0.41	-2.34 – 3.16	0.77
	Never or hardly ever	0.70	-1.96 – 3.35	0.60
Number of people in household		**-0.26**	**-0.47 – -0.05**	**0.02**
Number of major life events in previous year		**-0.28**	**-0.47 – -0.10**	**<0.01**
Number of homes child has lived in since birth		0.00	-0.40 – 0.40	0.99
Family financial stress	Run out of money before payday	ref	-	-
	Spending more money than we get	-1.20	-3.71 – 1.31	0.35
	Have just enough money to get us through to next pay day	-0.50	-1.73 – 0.73	0.42
	Some money left over each week but we just spend it	-0.41	-2.38 – 1.55	0.68
	Can save a bit every now and then	-0.23	-1.70 – 1.25	0.76
	Can save a lot	-1.16	-3.58 – 1.25	0.34
IRISEO		0.04	-0.13 – 0.21	0.64
BITSEA Competency score†		0.01	-0.23 – 0.25	0.93
BITSEA Problem score†		**-0.09**	**-0.17 – -0.02**	**0.01**
Age at time of SDQ assessment†		-0.05	-0.14 – 0.04	0.24
Global health measure at time of SDQ assessment†	Poor/Fair	ref	-	-
	Good/ Very good/ Excellent	2.09	0.03 – 4.15	0.05

CI - Confidence Interval; ref – reference group; *Adjusted for 95 clusters; †Potential confounding factor

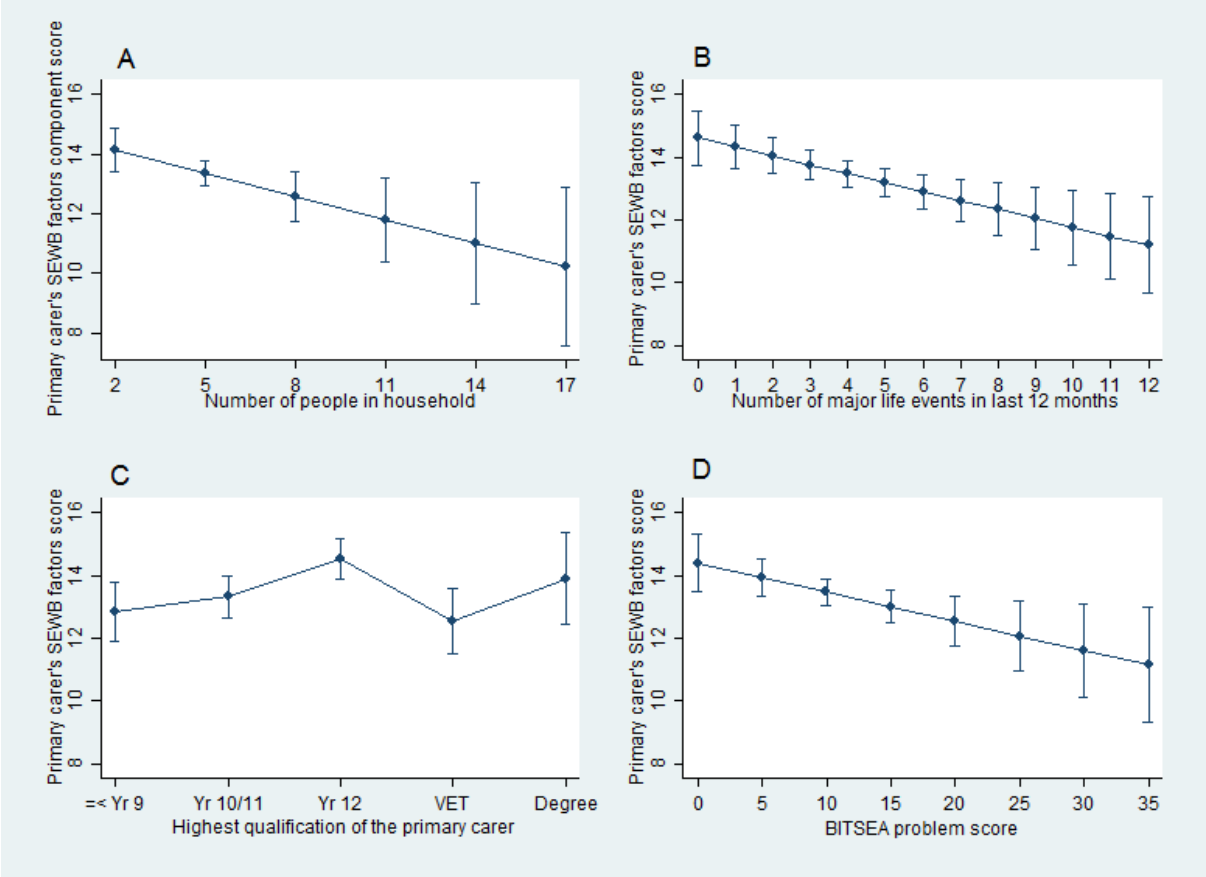

Figure 18 Predicted "Primary carer's SEWB factors" component scores from linear regression for (**A**) number of people in the household; (**B**) number of major life events in previous 12 months; (**C**) highest qualification of the primary carer; and (**D**) BITSEA problem score at Wave 2.

Overall, this linear model was statistically significant (F-statistic=5.3, p=0.00), and explained 18% of the variability in the component scores (Appendix 3.4, Figure E). The histogram of the residuals, standardised normal probability plot, and residual quantile plot indicated that the residuals have a skewed distribution (Appendix 3.4, Figure F*i-iii*). The funnel-shaped graph of residuals plotted against predicted values, and greater spread of the negative residuals suggests moderate heteroscedasticity (Appendix 3.4, Figure F*iv*).

ASSOCIATIONS BETWEEN SDQ SCORES AND EXPOSURE VARIABLES

Factors with a statistically significant association with higher SDQ Prosocial Behaviours scores in univariable analyses (Table 21) were the child's mother not smoking during pregnancy, the family experiencing racism and discrimination less

frequently, the child experiencing fewer major life events in the previous 12 months, and living in a less isolated area.

In the ordinal logistic regression model, none of these negligible effects remained statistically significant (Table 22). Although the occasional experience of racism and discrimination had a statistically significant association in the model, contrasting the marginal linear predicted probabilities of this variable's categories revealed that it had no overall effect (chi-square=6.3, p=0.18). The only factors that were statistically significant in this model were the global health of the child at the time of starting school, and the child's BITSEA competency score at Wave 2, both of which were included in the model as potential confounding factors. Children with good, very good or excellent global health at the time of starting school had a five-fold probability of a perfect prosocial score, compared with children with fair or poor health (Figure 19). The predicted probability of a SDQ Prosocial Behaviours score for children with a BITSEA Competency score of two at Wave 2 was 0.14 (95% CI -0.03 to 0.31) (Figure 20). In contrast, children with a BITSEA Competency score of 20 at Wave 2 had a predicted probability of 0.47 (95% CI 0.39 to 0.55) of a perfect Prosocial Behaviours score.

The log likelihood-ratio test of proportionality of odds across the response categories was not significant (p=0.15), indicating that the model did not violate the proportional odds assumption. The Brant test could not be performed because there were too many empty cells in the cross-tabulation of exposures and Prosocial Behaviours scores.

Table 21 Results of univariable analysis of factors in first years of life associated with higher SDQ Prosocial Behaviours Score at the time of starting school, Footprints in Time cohort 2008-2013. Results with $p<0.05$ are shown in **bold**.

Exposure	n in analysis	effect size		*p* value
		Harrell's *C**	95% CI	
Mother received first antenatal visit <20 weeks gestation	604	0.50	0.43 – 0.58	0.94
Mother did not drink alcohol during pregnancy	658	0.55	0.49 – 0.60	0.09
Mother did not smoke during pregnancy	**660**	**0.56**	**0.52 – 0.60**	**0.01**
Mother did not use other substances during pregnancy	660	0.52	0.43 – 0.62	0.58
Low birthweight	577	0.47	0.39 – 0.55	0.46
Child not hospitalised in the past 12 months	725	0.50	0.45 – 0.55	0.99
Child never had any ear problems	726	0.52	0.47 – 0.57	0.49
Attends childcare, daycare or family daycare	725	0.50	0.46 – 0.55	0.95
Excellent, very good or good global health	726	0.49	0.36 – 0.61	0.83
Primary carer is employed	725	0.49	0.45 – 0.53	0.62
Stolen generations	419	0.53	0.49 – 0.59	0.22
Excellent, very good or good global health at time of SDQ assessment†	**726**	**0.12**	**0.04 – 0.19**	**<0.01**
Female†	**726**	**0.58**	**0.54 – 0.62**	**<0.01**
		ρ	**95% CI**	***p* value**
Highest qualification of the primary carer	726	0.04	-0.03 – 0.13	0.28
Parental warmth measure (primary carer)	657	0.03	-0.05 – 0.11	0.42
Frequency with which family experiences racism	**639**	**-0.08**	**-0.16 – -0.01**	**0.04**
Number of people living in household	726	-0.05	-0.13 – 0.02	0.15
Number of major life events in previous year	**726**	**-0.08**	**-0.16 – -0.01**	**0.03**
Number of homes child has lived in since birth	711	-0.01	-0.09 – 0.06	0.75
Family financial stress	720	-0.004	-0.08 – 0.07	0.91
IRISEO	726	0.05	-0.02 – 0.12	0.17
Level of Relative Isolation	**725**	**-0.10**	**-0.17 – -0.02**	**0.01**
BITSEA Competency score†	**657**	**0.13**	**0.05 – 0.20**	**<0.01**

CI - Confidence Interval; * Harrell's *C* - Probability that an exposed child has a higher score than an unexposed child; *ρ* - Spearman's rank correlation coefficient; †Potential confounding factor

Table 22 Results of ordinal logistic regression of factors in first years of life associated with higher SDQ Prosocial Behaviours Score at the time of starting school, Footprints in Time cohort 2008-2013. Variables with $p \leq 0.25$ from univariable analysis were included in the regression model. Results with $p < 0.05$ are shown in **bold**.

Exposure		Adjusted effect size (n=341)*		*p* value
		coefficient	95% CI	
Mother did not drink alcohol during pregnancy		-0.83	-0.65 – 0.48	0.08
Mother did not smoke during pregnancy		0.42	-0.03 – 0.86	0.07
Stolen generations		0.23	-0.19 – 0.66	0.28
Frequency with which family experiences racism	Every day	ref	-	-
	Every week	0.62	-1.01 – 2.26	0.46
	Sometimes	0.99	-0.24 – 2.22	0.11
	Occasionally	**1.13**	**0.09 – 2.54**	**0.04**
	Never/hardly ever	0.68	-0.37 – 1.73	0.20
Number of people living in household		-0.06	-0.15 – 0.04	0.23
Number of major life events in previous year		-0.05	-0.14 – 0.04	0.25
IRISEO		-0.07	-0.17 - 0.04	0.21
Level of Relative Isolation	None	ref	-	-
	Low	-0.27	-0.72 – 0.19	0.26
	Moderate	-0.29	-1.10 – 0.50	0.47
	High/Extreme	-0.84	-1.76 – 0.08	0.07
Female†		0.39	-0.02 – 0.79	0.06
BITSEA Competency score†		**0.10**	**0.00 – 0.19**	**0.04**
Global health measure at time of SDQ assessment†	**Poor /Fair**	**ref**	**-**	**-**
	Good/ Very good/ Excellent	**2.16**	**0.80 – 3.52**	**<0.01**

CI - Confidence Interval; ref – reference group; * Adjusted for 120 clusters; †Potential confounding factor

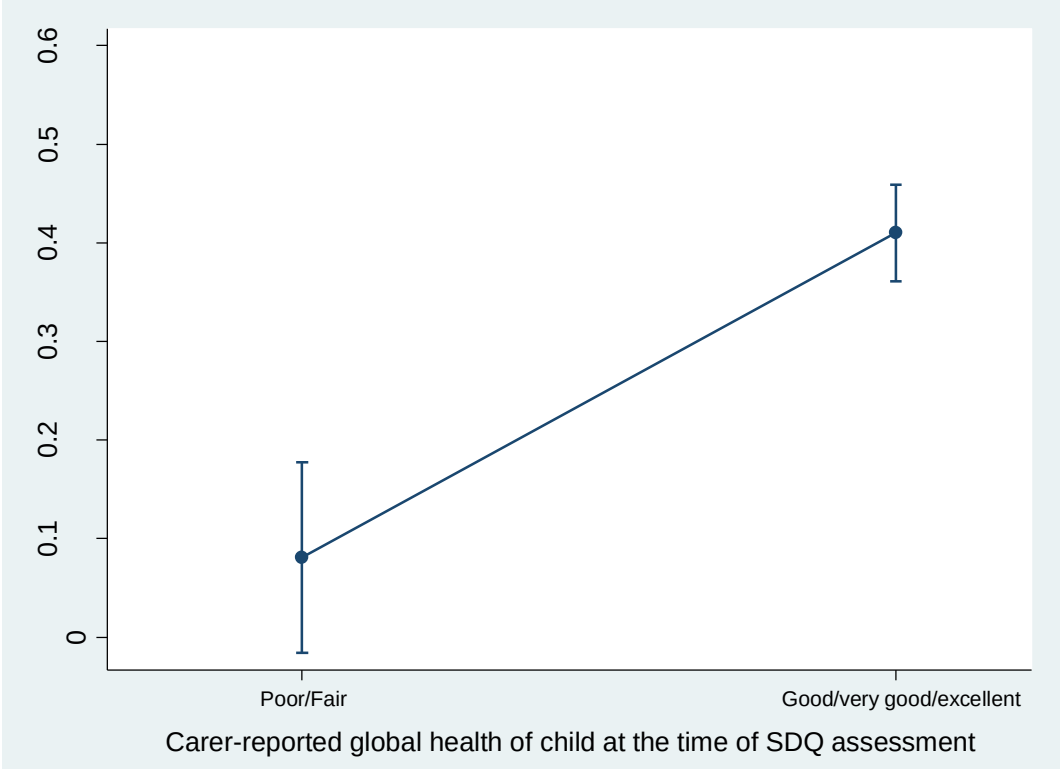

Figure 19 Probability of a SDQ Prosocial Behaviours Score of 10, by health of the child at the time of SDQ assessment, with 95% confidence intervals.

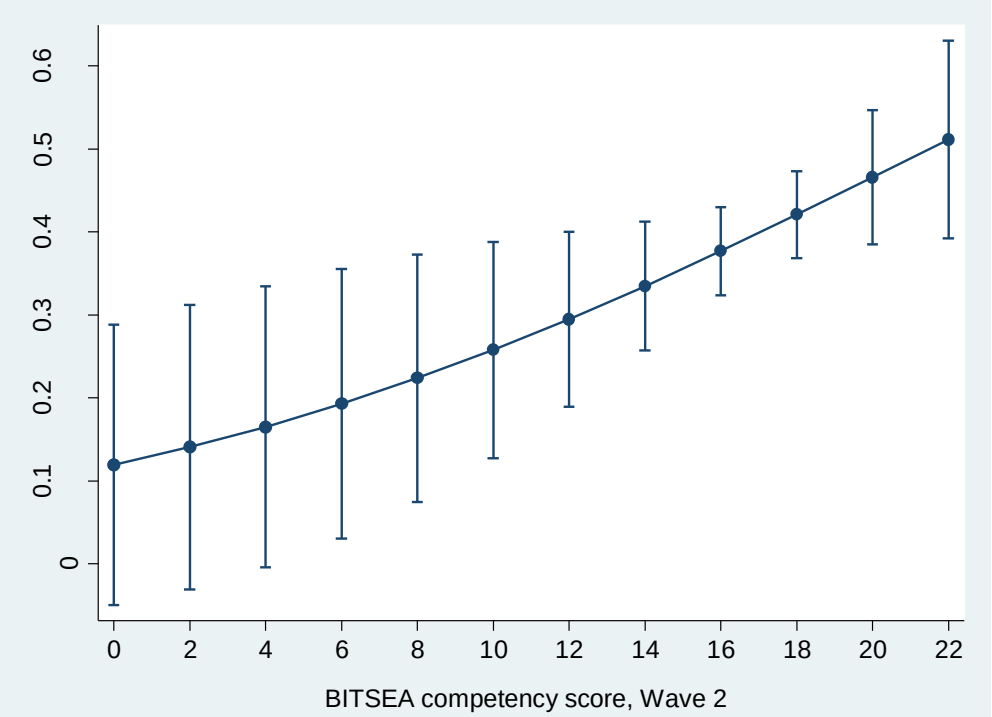

Figure 20 Probability of a SDQ Prosocial Behaviours Score of 10, by BITSEA Competency score at Wave 2, with 95% confidence intervals.

Six early life exposures had statistically significant association with higher SDQ Total Difficulties scores in univariable analyses (Table 23), including the child's mother smoking during pregnancy, and the child experiencing fewer major life events in the previous 12 months. However, after linear regression, only the number of major life events remained significant (Table 24), as well as the child's BITSEA problem score at Wave 2, which was included in the model as a potential confounding factor. Higher values for both of these exposures were associated with poorer scores on this outcome. Predicted SDQ total difficulties score for children with one event was 9.53 (95% CI 8.54 to 10.52) while predicted score for children with 8 events was a poorer 11.70 (95% CI 10.62 to 12.78) (Figure 21). Predicted scores for children with BITSEA problem score of five was 8.81 (95% CI 8.00 to 9.63), while a BITSEA score of 25 predicted a poorer SDQ Total Difficulties score of 14.67 (95% CI 13.14 to 16.19) (Figure 22). As these two factors were shared with the "Child's connection" component, I conducted a *post hoc* analysis to check the relationship between this component and SDQ Total Difficulties score. There was a moderate positive correlation between these two variables (ρ=0.55, 95% CI 0.48 to 0.61, p=0.00).

Overall, the linear model was statistically significant (F-statistic=7.5, p=0.00), but explained only 12% of the variability of SDQ Total Difficulties Scores (Appendix 3.4, Figure G). The histogram of the residuals, standardised normal probability plot, and residual quantile plot indicated that the residuals have a near normal distribution (Appendix 3.4, Figure H*i-iii*). The slight funnel shapes of the graphs of residuals against predicted values, for both the overall model and the two statistically significant exposure variables, suggest mild heteroscedasticity of the residuals (Appendix 3.4, Figure H*iv*).

Table 23 Results of univariable analysis of factors in first years of life associated with higher SDQ Total Difficulties score at the time of starting school, Footprints in Time cohort 2008-2013. Results with $p<0.05$ are shown in **bold**.

Exposure	n in analysis	effect size		*p* value
		Harrell's *C**	95% CI	
Mother received first antenatal visit < 20 weeks gestation	602	0.50	0.43 – 0.58	0.91
Mother did not drink alcohol during pregnancy	656	0.45	0.39 – 0.51	0.07
Mother did not smoke during pregnancy	**658**	**0.43**	**0.38 – 0.47**	**<0.01**
Mother did not use other substances during pregnancy	658	0.42	0.33 – 0.52	0.09
Low birthweight	576	0.56	0.48 – 0.65	0.15
Child not hospitalised in the past 12 months	723	0.46	0.40 – 0.51	0.08
Child never had any ear problems	724	0.48	0.43 – 0.54	0.57
Attends childcare, daycare or family daycare	723	0.47	0.42 – 0.52	0.28
Excellent, very good or good global health	724	0.42	0.28 – 0.56	0.26
Primary carer is employed	**723**	**0.44**	**0.40 – 0.49**	**0.01**
Stolen generations	**419**	**0.56**	**0.51 – 0.62**	**0.03**
Excellent, very good or good global health at time of SDQ assessment †	724	0.37	0.26 – 0.49	0.05
Female†	**724**	**0.45**	**0.41 – 0.49**	**0.03**
		ρ	95% CI	*p* value
Highest qualification of the primary carer	**724**	**-0.14**	**-0.21 – -0.06**	**<0.01**
Parental warmth measure (primary carer)	**656**	**-0.13**	**-0.20 – -0.05**	**<0.01**
Frequency of family's racism experience	638	0.02	-0.06 – 0.10	0.56
Number of people living in household	724	0.04	-0.03 – 0.11	0.30
Number of major life events in previous year	**724**	**0.15**	**0.07 – 0.22**	**<0.01**
Number of homes child lived in since birth	709	0.07	0.00 – 0.14	0.06
Family financial stress	718	-0.05	-0.12 – 0.02	0.18
IRISEO	724	**-0.10**	**-0.24 – -0.10**	**0.00**
Level of Relative Isolation	723	**0.10**	**0.03 – 0.18**	**0.01**
BITSEA Problem score†	654	**0.32**	**0.25 – 0.39**	**0.00**
Age at time of SDQ assessment†	724	0.07	-0.01 – 0.14	0.08

CI - Confidence Interval; * Harrell's *C* - Probability that an exposed child has a higher score; *ρ* - Spearman's rank correlation coefficient; †Potential confounding factor

Table 24 Results of linear regression of factors in first years of life associated with lower SDQ Total Difficulties score at the time of starting school, Footprints in Time cohort 2008-2013. Variables with p≤0.25 from univariable analysis were included in the regression model. Results with *p*<0.05 are shown in **bold**.

Exposure		Adjusted effect size (n=321)*		*p* value
		coefficient	95% CI	
Mother did not drink alcohol during pregnancy		-0.30	-0.19 – 1.32	0.71
Mother did not smoke during pregnancy		-0.56	-2.16 – 1.04	0.49
Mother did not use other substances during pregnancy		0.29	-1.95 – 2.53	0.80
Low birthweight		1.43	-0.74 – 3.60	0.19
Child not hospitalised in the past 12 months		0.13	-1.40 – 1.67	0.86
Primary carer is employed		-0.51	-2.06 – 1.05	0.52
Stolen generations		0.39	-0.85 – 1.63	0.53
Highest qualification of the primary carer	Less than Year 10	ref	-	-
	Year 10/11	-1.72	-4.12 – 0.68	0.16
	Year 12	-1.44	-4.01 – 1.14	0.27
	VET qualification	-1.29	-3.69 – 1.12	0.29
	Bachelor degree or higher	-0.53	-3.78 – 2.73	0.75
Parental warmth measure (primary carer)		-0.04	-2.25 – 2.18	0.98
Number of major life events in previous year		**0.31**	**0.08 – 0.54**	**0.01**
Number of homes child has lived in since birth		0.45	-0.22 – 1.12	0.19
Family financial stress	Run out of money before payday	ref	-	-
	Spending more money than we get	1.25	-2.41 – 4.90	0.50
	Have just enough money to get us through to next pay day	2.21	-0.09 – 4.52	0.06
	Some money left over each week but we just spend it	2.36	-0.55 – 5.27	0.11
	Can save a bit every now and then	1.67	-0.67 – 4.02	0.16
	Can save a lot	2.80	-0.82 – 6.42	0.13
IRISEO		-0.14	-0.49 – 0.20	0.42
Level of Relative Isolation	None	ref	-	-
	Low	-0.23	-2.11 – 1.17	0.57
	Moderate	-0.23	-2.71 – 2.25	0.86
	High/Extreme	1.51	-1.22 – 4.25	0.28
BITSEA Problem score†		**0.29**	**0.20 – 0.39**	**0.00**
Female†		-1.17	-2.59 – 0.21	0.10
Age at time of SDQ assessment†		0.01	-0.12 – 0.14	0.92
Global health measure at time of SDQ assessment†	Poor/Fair	ref	-	-
	Good/ Very good/ Excellent	-5.34	-10.78 – 0.10	0.05

CI - Confidence Interval; ref – reference group; VET – vocational education and training; * Adjusted for 120 clusters; †Potential confounding factor

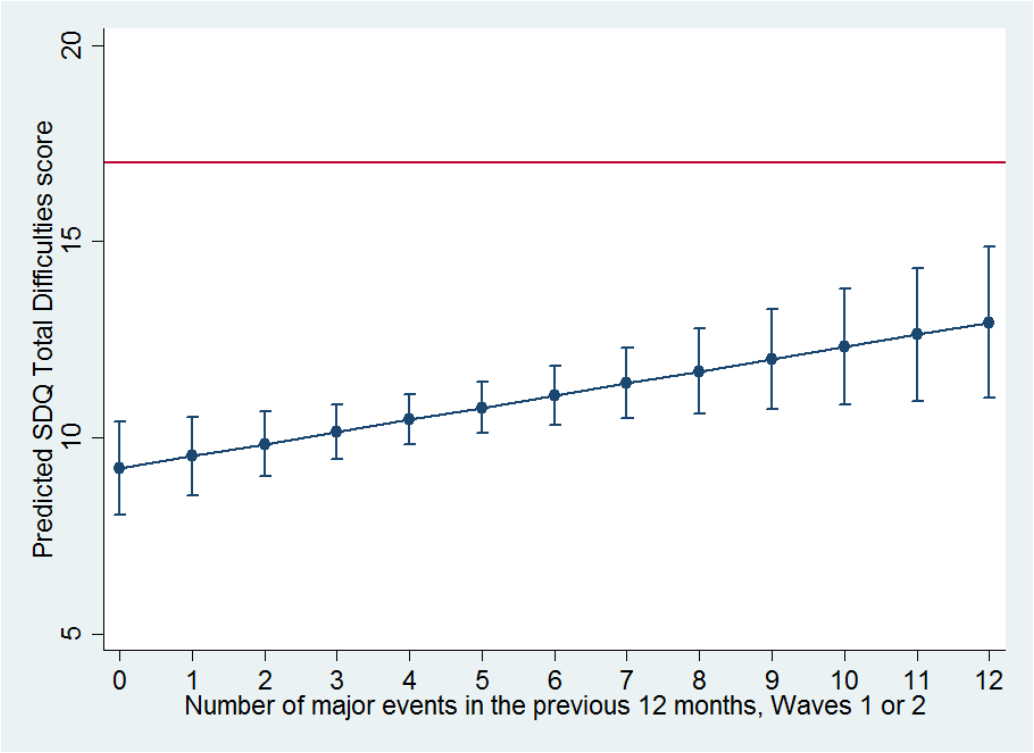

Figure 21 SDQ Total Difficulties scores at the time of starting school, predicted by linear regression of number of major life events in the previous 12 months reported at Waves 1 or 2, with 95% confidence intervals. A higher score indicates greater social and emotional difficulties. The red line (at 17) indicates the threshold above which children are considered at high or very high risk of emotional or behavioural problems.

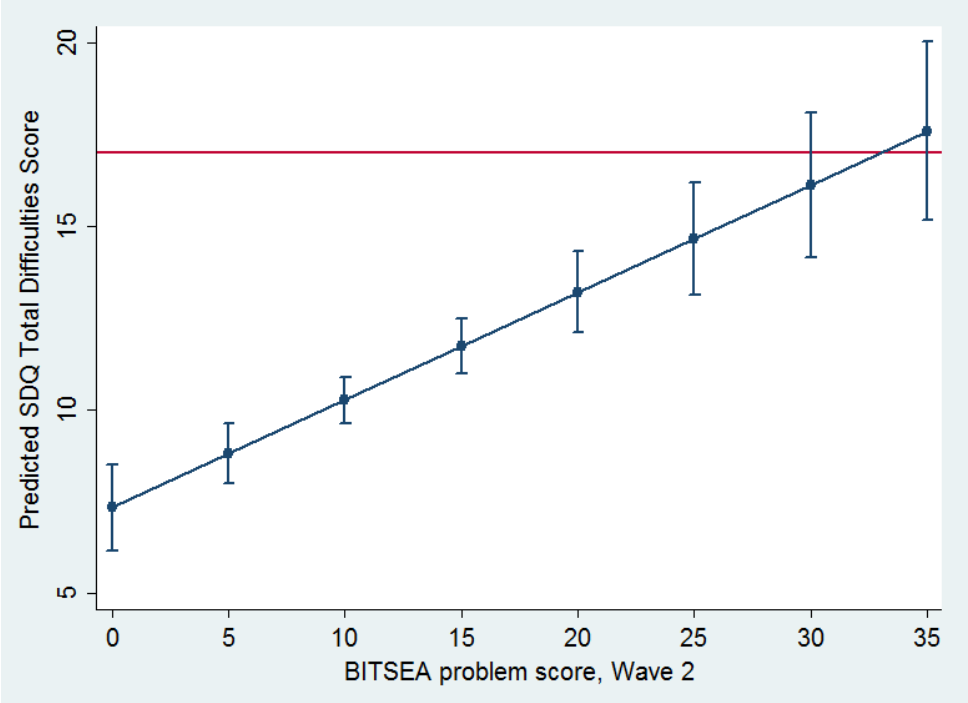

Figure 22 SDQ Total Difficulties scores at the time of starting school, predicted by linear regression of BITSEA score at Wave 2, with 95% confidence intervals. A higher score indicates greater social and emotional difficulties. The red line (at 17) indicates the threshold above which children are considered at high or very high risk of emotional or behavioural problems.

Discussion

MAIN FINDINGS

The early life exposures associated with surrogate measures of SEWB at the time of starting school were the number of people living in the household and major life events experienced by the child. While larger households and more events were associated with reduced sharing, helping and mental health in the child and poorer wellbeing in the primary carer; more people in the household and exposure to more events was weakly associated with greater connection of the child to community, culture and country. As a stand-alone measure, prosocial behaviours at school commencement was not associated with any of the early life exposures analysed in this study (including intrauterine risk factors; characteristics of the primary carer; parenting and care arrangements; home life and events; exposure to intergenerational trauma and racism; and macro-level socio-economic indicators).

Consistent with previous research (47), better social, emotional and behavioural competence as an infant or toddler weakly predicted better scores for most outcomes at the time of starting school. However, greater difficulties as an infant or toddler predicted greater connection of the child to community, culture and country, although this effect was negligible. Children with good, very good or excellent global health at the time of starting school had markedly increased probability of a perfect prosocial score, compared with children with fair or poor health.

The most salient finding is that the SDQ screening tool does not capture the culturally-specific, multi-faceted and positive concept of SEWB. I was unable to create an index of SEWB using PCA and, surprisingly, *post hoc* analysis revealed that measures of connectedness and relationship were positively correlated with SDQ Total Difficulties scores. Those seeking evidence to support SEWB policy development, program planning and evaluation must be cautious in applying Western biomedical health and wellbeing measures to Indigenous concepts and states.

I could not use PCA to reduce the exposure data. This may have been due to missing data and use of categorical variables, which have smaller correlations than the (unobserved) continuous variables from which they derive (48). An alternative, but less

likely, explanation is that the variables were unrelated, and there were no patterns in the population to detect with respect to these factors.

COMPARISON WITH OTHER STUDIES – WHAT DOES THIS STUDY ADD?

MENTAL HEALTH OF ABORIGINAL AND TORRES STRAIT ISLANDER CHILDREN

The distributions of SDQ scores for the sample were comparable with other studies of Aboriginal children of this age. Scores were similar to those for the LSIC older cohort at around age six years at Wave 3 (49), for six year olds in the WAACHS study (12), and for children aged four to 17 years in the Study of Environment of Aboriginal Resilience and Child Health (SEARCH) study in urban New South Wales (NSW) (which examined Total Difficulties scores only) (50). While the WAACHS study found no difference in SDQ Prosocial Behaviours scores for Aboriginal and non-Aboriginal children, both these and the scores from the present study were higher than scores for children participating in a validation study of the SDQ involving a sample of mostly non-Indigenous children in Brisbane (19). Mean Total Difficulties scores were higher in the present study than for six-year-old non-Aboriginal children in a survey conducted to provide comparison data for the WAACHS (12). These results suggest that Aboriginal and Torres Strait Islander children exhibit better prosocial behaviours but have poorer mental health, compared with non-Indigenous children. Using data from the Australian Early Development Census, Goldfield (26) also found that Aboriginal and Torres Strait Islander children had markedly poorer mental health competence than non-Indigenous children at school entry.

DETERMINANTS OF SEWB AND MENTAL HEALTH

Exposure to a greater number of major life events in the early years appeared to be mildly detrimental to SDQ scores. In a study of the older LSIC cohort at Wave 4, when the children were aged around seven years, Skelton and Kikkawa (51) found a similar strength of association between SDQ Total Difficulties score and exposure to major life events in the previous 12 months. In a cross-sectional analysis of WAACHS data for children aged four to 17 years, Zubrick et al. (12) found that exposure to more than seven major life events in the preceding year increased by over fivefold the likelihood

of a child being at high risk of clinically significant difficulties (SDQ Total Difficulties >17), compared with children who experienced two or fewer events.

In the present study, however, experiencing a greater number of events was also associated with greater connectedness to elders, culture and country. It is important to note that, unlike in the WAACHS, not all of the events reported in LSIC are inherently negative. Two of the four most commonly reported events in this sample were pregnancy or a new baby in the household, and one of the child's carers returning to work or study (Table 11). Exposure to more life events, including death of someone close, is to some extent a result of larger and stronger family and community networks. However, the likelihood for these deaths to be traumatic must be considered. In reporting findings from the National Aboriginal and Torres Strait Islander Health Survey 2004–05, Zubrick et al. (52) state

> *...grief and loss was the largest single factor to impact on the wellbeing of Aboriginal and Torres Strait Islander people. Many deaths involving infants, children, young adults, and men and women in their prime were sudden, unexpected and preventable and therefore very traumatic.*

In this study, having more people living in the household had a negligible positive association with better "Child's connection" component scores. However, an opposite and stronger effect of this exposure was observed for the "Primary carer's SEWB factors" component scores. Interestingly, children in the WAACHS living with high household occupancy levels were half as likely to have a high risk SDQ Total Difficulties score, compared with those living with low occupancy. Zubrick et al. (12) suggest this "may relate to more help being available within the household, greater flexibility in managing stresses, and greater buffering of risk exposures".

It is not possible to infer household crowding (and related stress) from reported household size. The LSIC survey question simply asks for the names of "all the people who live in the household" (53), with no clarification about temporary or regular visitors, or people who may sleep elsewhere but use the kitchen and bathroom facilities of the home. In contrast to the WAACHS analysis (12), I did not calculate household occupancy from the number of bedrooms or number of people who lived in the home. The international standard measure for household utilisation also takes into account the age, sex and relationship status (couples or singles) of occupants (54). However, as Memmot et al. (54) note, it is important to distinguish between high density of household occupants and household crowding. They argue that crowding is a

perception of spatial inadequacy, influenced by a range of factors including the physical setting, an individual's experience and expectations, their relationship to other occupants, and the occupants' activities and behaviour. Crowding is an experience that is culturally defined and, for some families and communities, "[high] density may be an expression of proper intimacy with kin and others, which in fact reduces stress" (54). However, in the present study, the effects of the number of people in the household generally mirror those of the number of major life events, possibly reflecting the fact that a problem with housing (including the primary carer feeling too crowded where he or she lived, and moving house) was a commonly reported major event (Table 11).

Previous cross-sectional studies of Aboriginal and Torres Strait Islander children of similar ages have found associations between lower SDQ Total Difficulties scores and better general health (49, 51); ear health (12); higher qualification of the primary carer; living in an area of less socioeconomic disadvantage (49) or greater geographic isolation (12); lower household financial stress (55); having a primary carer who was employed; and living in fewer than four (50) or five homes (12). In the only published examination of the determinants of better SDQ Prosocial Behaviours scores in Aboriginal and Torres Strait Islander children, Armstrong et al.'s (49) study of the older LSIC cohort found negligible positive effects at Wave 3 for the children who lived in a relatively socioeconomically advantaged area at Wave 2. However, none of these factors, occurring in early life, were significant at school entry in this longitudinal study. Zubrick et al. (12) note that the lack of association in the WAACHS between carer education and SDQ Total Difficulties scores is also inconsistent with findings from a large study of the general Australian population. The authors suggest that, for Aboriginal and Torres Strait Islander families, the benefits of improved education are attenuated by the effects of "life stress, poor family functioning and carer health".

CHALLENGES IN MEASURING SOCIAL AND EMOTIONAL WELLBEING

In developing a conceptual framework for SEWB, I quickly discovered that I could not operationalise this outcome using only the SDQ Total Difficulties subscale, the most commonly used measure of Aboriginal and Torres Strait Islander child mental health in large studies. By including the strengths-based SDQ Prosocial Behaviours subscale as an outcome measure I, as did Goldfield et al. (26), have challenged the common assumption that child mental health is the same as the absence of mental illness. These

authors argue for a dual continuum model in which mental health is seen as correlated to, but distinct from, mental disorder. However, measuring only these two states fails to capture the Indigenous concept of SEWB. For operationalising SEWB, perhaps what is needed is a 'triple continuum model', which includes a domain of relational health of community, culture, spirituality and country. I could not achieve this using the 'connection variables' available for this sample of LSIC children, which *prima facie* cannot quantify a concept that encompasses a rich web of relationships between flourishing individuals, families, language, culture, spirituality and country.

Taylor (56) names the intersection between Indigenous culture and government reporting frameworks the 'recognition space' (Figure 23). This space is

> *…where policy makers and Indigenous people can seek to build meaningful engagement and measurement. This is the area that allows for a necessarily reductionist translation of Indigenous people's own perceptions of their well-being into measurable indices sought by government. What is captured in this space is obviously far from the totality of Indigenous understandings of well-being.*

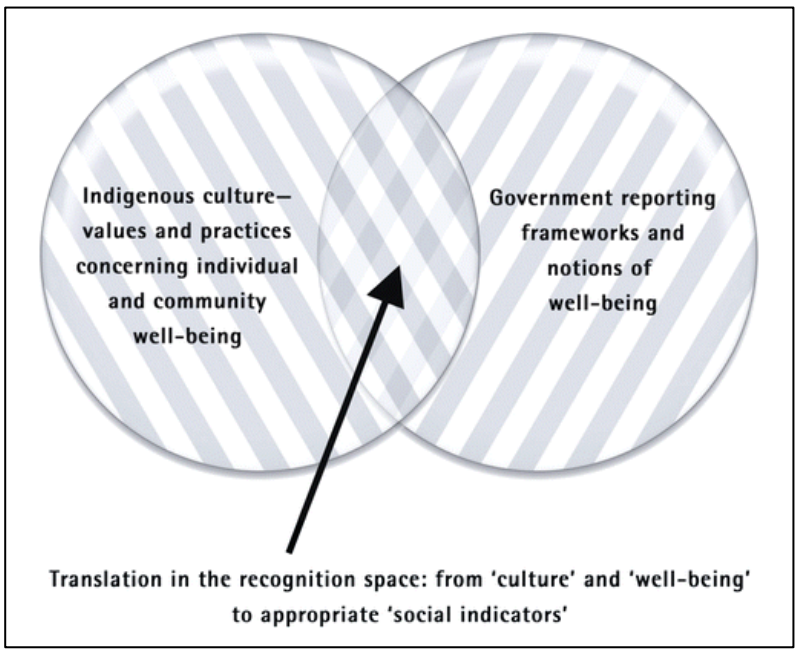

Figure 23 The 'recognition space' for indicators of Indigenous wellbeing (56).

We may feel that by choosing standard measures we are ensuring objectivity. However, Prout (57) warns that reducing Indigenous notions to narrow conventional indicators is a political exercise. In so doing, this "invisibilises many of the positive, enduring and

protective factors, associated with Indigenous ways of life which are not amenable to this kind of analysis and reporting" (57). Our own values and worldviews also influence our interpretation of these indicators, and may be in conflict with Indigenous perceptions of wellbeing. Furthermore, Prout argues, by using non-Indigenous populations as the reference group we are assuming that equity based on these flawed indicators is the ambition for Indigenous populations.

Walter and Andersen (58) suggest that power should be returned to communities by framing research through lenses of Indigenous values, ways of being and of knowing. A recent project auspiced by the Kimberley Institute aimed to develop culturally relevant measures of wellbeing for the Yawuru people, who live in and around Broome (59). In this qualitative project, Yawuru men and women described their concept of wellbeing and selected relevant indicators to develop gender-specific and collective wellbeing frameworks. The community specific indicators for collective wellbeing derived from the study (Table 25) highlight the complexity of the wellbeing concept and contrast with the much narrower constructs measured by the SDQ scales (Table 25).

Table 25 Examples of activities and states for Yawuru men and women that contribute to Yawuru's experience of wellbeing (59).

Wellbeing themes	Potential indicators
Family, identity and relatedness	• Sharing your fish or kill with family and friends • Seeing and spending time with family
Community	• Participating in community cultural events • Being able to have a say or have control over what happens in my community
Connection to country	• Looking after country • Eating bush tucker, eating fish that was caught in season and meat that was hunted in season
Connection to culture	• Speaking and understanding the Yawuru language • Participation in law and ceremonies
Safety and respect	• Feel respected and show respect to Indigenous groups in my community • Feel respected and show respect to family and friends
Standard of living	• Adequate housing conditions • Having a secure income stream including a diversity of sources of income
Rights and recognition	• Environment free from pollutants and hazards • Feel recognised and proud to be Native Title holders
Health	• Healthy body to enjoy life • Minimise ill health from too much alcohol or drugs

STRENGTHS OF THIS STUDY

As far as possible, and recognising the constraints of my own worldview and social position, I have attempted to use an Indigenous quantitative methodology for this study. Walter (58) defines this methodology as one in which "the practices and processes of research are conceived and framed through an Indigenous standpoint". I was fortunate to have access to the LSIC data—data which was collected using protocols that exemplify this methodology (58). I have also taken advantage of the power of the longitudinal design of the LSIC, and explored the determinants of the SDQ Prosocial Behaviours score which has been largely neglected thus far.

LIMITATIONS OF THIS STUDY

The non-random purposive sampling technique used for the LSIC means generalisation to all Aboriginal and Torres Strait Islander children requires caution. Because of exclusions for absence of SDQ scores at Waves 5 or 6, I may have underestimated the effects of low birthweight, primary carer employment, remote living and maternal smoking. For the same reason, and based on the findings of previous studies, the SDQ scores for the sample may have been more favourable than for the whole cohort. Similarly, missing exposure data reduced sample size for the regression models, possibly lessening the effect of factors significant in univariable analyses.

Little of the variation in outcomes is explained by the regression models presented here. This means either there is a great deal of random variation in the outcome measures chosen, or there are other factors that I did not include or consider that determine these outcomes. I was constrained in my selection of both outcome and exposure variables by the Waves in which certain questions were asked by the LSIC team. Because no clinical measurements or record reviews are conducted for LSIC, there may be measurement error for questions about the child's health and birthweight.

The results may have been influenced by decisions about categorising variables. For example, I placed the categories of the primary carer's highest qualification on an ordinal scale, with a VET qualification placed higher than completing Year 12 education only. The non-linear relationship of this variable with outcome measures suggest this was an inappropriate order—probably reflecting the fact that school

attainment is not usually a prerequisite for enrolment in VET courses. Other studies have dichotomised the Total Difficulties score, using screening cut-offs for risk of clinically-significant emotional and behavioural problems (12, 50), but I aimed to explore factors associated with better SDQ scores so the approach used was appropriate. Dichotomising continuous variables also reduces their precision, and the effect sizes estimated will be smaller than for the continuous variables from which they are derived (60).

The construct validity of the SDQ has been established for Aboriginal children in urban NSW (61), but not for Aboriginal children elsewhere in Australia, nor for Torres Strait Islander children. It is unknown whether better SDQ scores lead to better school performance or completion rates for Aboriginal and Torres Strait Islander children. However, in a large British study of seven year old children, Hartas (62) found a strong association between higher SDQ Total Difficulties score and below average teacher-rated listening, reading and writing skills. A similar effect was found for reading and spelling in another large study in the United Kingdom (63). Linkage of the LSIC data with data from the National Assessment Program–Literacy and Numeracy (NAPLAN) assessments will shed light on this for the current context (28).

IMPLICATIONS

Because of modest effect sizes and poor explanatory power of the regression models, my study provides little guidance to policy makers working in maternal and child health on interventions to promote SEWB in children before school. Generally, the prominence of life events and household occupancy lend weight to the social determinants theory of SEWB (9) and adds justification for holistic, trans-portfolio approaches. The results also provide support for social and emotional screening early in life to prevent mental health problems later, and for the benefit in prosocial behaviours from promotion of physical health.

Measuring SEWB for Aboriginal and Torres Strait Islander children for the purposes of policy development, program planning or evaluation is not straightforward. If mainstream measures of mental health are used to plan and evaluate programs, then their limitations must be acknowledged. Communities should be supported to develop their own measures of wellbeing. This presents a challenge: striking a balance between

the need to privilege Indigenous ontologies and epistemologies, and the governments' requirement to demonstrate investment accountability using indicators that can be applied throughout jurisdictions cost-effectively.

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CHAPTER 4 – EVALUATION OF AUSTRALIA'S ENHANCED INVASIVE PNEUMOCOCCAL DISEASE SURVEILLANCE PROGRAM

Truth is ever to be found in simplicity, and not in the multiplicity and confusion of things.

Isaac Newton

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ABBREVIATIONS

13vPCV	13-valent pneumococcal conjugate vaccine
23vPPV	23-valent pneumococcal polysaccharide vaccine
7vPCV	7-valent pneumococcal conjugate vaccine
ACIR	Australian Childhood Immunisation Register
AIDS	Acquired Immune Deficiency Syndrome
AIR	Australian Immunisation Register
AMR	Antimicrobial resistance
AOM	Acute otitis media
ATAGI	Australian Technical Advisory Group on Immunisation
AURA	Antimicrobial Use and Resistance
CDNA	Communicable Diseases Network Australia
CSF	Cerebrospinal fluid
EIPDSWG	Enhanced Invasive Pneumococcal Disease Surveillance Working Group
GP	General Practitioner
HIV	Human Immunodeficiency Virus
IPD	Invasive Pneumococcal Disease
NCIRS	National Centre for Immunisation Research and Surveillance
NIP	National Immunisation Program
NNDSS	National Notifiable Diseases Surveillance System
NTIR	Northern Territory Immunisation Register
OHP	Office of Health Protection
OM	Otitis media
PCR	Polymerase chain reaction
PHN	Public Health Nurse
PHU	Public Health Unit
QALY	Quality-adjusted life-years
VIVAS	Vaccination Information and Vaccination Administration System
WGS	Whole-genome sequencing

Prologue

My interest in pneumococcal diseases stems from working as a research nurse on middle ear disease projects in the Northern Territory, including a program monitoring pneumococcal carriage in children. When I discovered that the national Invasive Pneumococcal Disease (IPD) surveillance program had never been evaluated, I took the opportunity to contribute to improving a system that has such relevance for the health of Aboriginal and Torres Strait Islander children.

MY ROLE

I approached Rhonda Owen and Cindy Toms at the Office of Health Protection (OHP) for permission to conduct the evaluation. Cindy's support and guidance early in the project proved very valuable, and she facilitated access to the Enhanced IPD Surveillance Working Group (EIPDSWG). With regular review from my academic supervisor, I

- developed the questionnaires for consultation with the Working Group members and OHP data managers (Appendix 4.2), conducted the phone interviews and collated and analysed the data
- prepared the ethics application
- developed the stakeholder survey (Appendix 4.3) and analysed the results
- analysed the surveillance data for completeness, quality and timeliness
- wrote the interim report for comment from the EIPDSWG (Appendix 4.4)
- wrote the final report and the article for submission to *Communicable Diseases Intelligence* (Appendix 4.1).

LESSONS LEARNT

I already knew that response rates to surveys can be very low, but I was disappointed that only 28 people responded to the stakeholder survey. I made a particular effort to ensure appropriate contacts in vaccine companies were sent the link to the survey, and this was rewarded. However, I could have made greater attempts to liaise with professional organisations and networks to ensure a better response from laboratories and medical doctors.

I proposed a capture-recapture analysis using hospitalisation data to assess the sensitivity of the program and applied to data custodians for estimates of data and linkage costs, but OHP did not have the resources to cover this. In hindsight, I think such an analysis would have added little to the evaluation, and a simpler approach was probably better.

I vastly expanded my understanding of *Streptococcus pneumoniae* and pneumococcal diseases. Insightful discussions with Working Group members and OHP staff brought home the realities of running a national surveillance program. Initially, I had not appreciated the difficulties in collating data collected using the different jurisdictions' systems. I was reminded that variations and inconsistencies also occur in systems because they are run by people, who are (thankfully) not standardised, but diverse and idiosyncratic.

PUBLIC HEALTH IMPACT

This was the first evaluation of the program. The EIPDSWG has taken action to address most of its recommendations.

ACKNOWLEDGEMENTS

The members of the Working Group were very generous with their time and expertise during interviews and when providing comments on the draft evaluation report. I was impressed with their level of commitment to the program, which is reflected in its success. I am particularly grateful to Heather Cook, EIPDSWG secretary, and Cindy Toms and Mark Trungove at OHP, who provided useful advice and support. I would like to thank the stakeholders who responded to the evaluation survey; and Nick Pascual, who provided comments on the evaluation report and article.

I'm also grateful to my fellow scholar, Amy Burroughs, who told me "don't overthink things – the best recommendations for system improvements are probably the most simple" and "you don't have to solve all the issues, just highlight them".

Executive summary

Introduction

Australia's Enhanced Invasive Pneumococcal Disease Surveillance Program is a part of the National Notifiable Diseases Surveillance System (NNDSS), and is coordinated by the Enhanced Invasive Pneumococcal Disease Surveillance Working Group (EIPDSWG). Invasive Pneumococcal Disease (IPD) is caused when the bacterium *Streptococcus pneumoniae* invades a normally sterile site, leading to bacteraemic pneumonia, bacteraemia without focus, or meningitis. It has been a notifiable condition in Australia since 2001, and passive surveillance[5] is conducted in all States and Territories ('the jurisdictions'). Pneumococcal vaccination is funded under the National Immunisation Program (NIP) for all infants and for other high risk population groups. This is the first evaluation of the surveillance program. The purpose of the evaluation is to:

- assess the need for enhanced surveillance of IPD in Australia;
- evaluate the program's performance;
- identify ways in which surveillance may be improved; and
- make recommendations to the EIPDSWG.

Methods

I assessed the public health importance of IPD; described the program operation; and collected evidence regarding usefulness and performance against a number of attributes. I used a range of methods, including literature and document reviews; key informant interviews; an online stakeholder survey; and descriptive analyses of a subset of surveillance data. An interim summary of the findings and recommendations was presented to the EIPDSWG for correction and comment.

Findings

Invasive pneumococcal disease remains a disease of public health importance in Australia. It is relatively uncommon, and incidence rates have reduced by around 20% since 2003, remaining relatively unchanged for the past four years. However, disease

[5] Passive surveillance consists of regular reporting of disease data by all institutions that see cases or test specimens, and are part of a reporting network. There is no active search for cases.

can be severe. The case fatality rate for invasive pneumococcal pneumonia is just under 20%; for pneumococcal meningitis is up to 37%, and serious disabilities in meningitis survivors are common. Despite the positive impact of targeted vaccination programs, significant disparities in the incidence of IPD persist, with relatively higher rates among those aged under five and over 65 years, and among Aboriginal and Torres Strait Islander people. Costs of IPD treatment and pneumococcal vaccination are substantial. Continued enhanced surveillance of IPD is vital to detect changes in serotype and resistance profiles, and to inform and evaluate vaccination and treatment strategies. The published surveillance program objectives broadly reflect these goals, but have not been endorsed by the EIPDSWG.

The program is complex, with variation in notification processes, follow-up, data entry and transmission from the jurisdictions to the NNDSS. The case definition for IPD involves laboratory confirmation (Box A), requiring the participation of a large number of public and private diagnostic laboratories, as well as four public health reference laboratories and the communicable disease branches in each jurisdiction (Figure A).

Box A The case definition for a confirmed case of invasive pneumococcal disease (IPD), Australia, 2017. Only confirmed cases are notified.

- Isolation of *S. pneumoniae* from a normally sterile site by culture

OR

- Detection of *S. pneumoniae* from a normally sterile site by nucleic acid testing

While data are collected for all notified cases, some jurisdictions do not routinely collect data on Indigenous status, vaccination history or enhanced data (including risk factors) for cases aged between five and 50 years. Furthermore, data collection in some jurisdictions is hampered by the absence of accessible electronic health records. Summaries of surveillance data are published in regular IPD reports and NNDSS Annual Reports, and selected variables of the IPD dataset from 2009 to 2015 are publically available on the Australian Government Department of Health website. The program is useful for monitoring the effectiveness of the national infant pneumococcal vaccination program from 2005. Surveillance data provided evidence of replacement of vaccine serotypes with a consequent change in the recommended vaccine for infants in 2011. However, the program is less useful for evaluating the effectiveness of targeted vaccination programs in other high- risk groups, due to

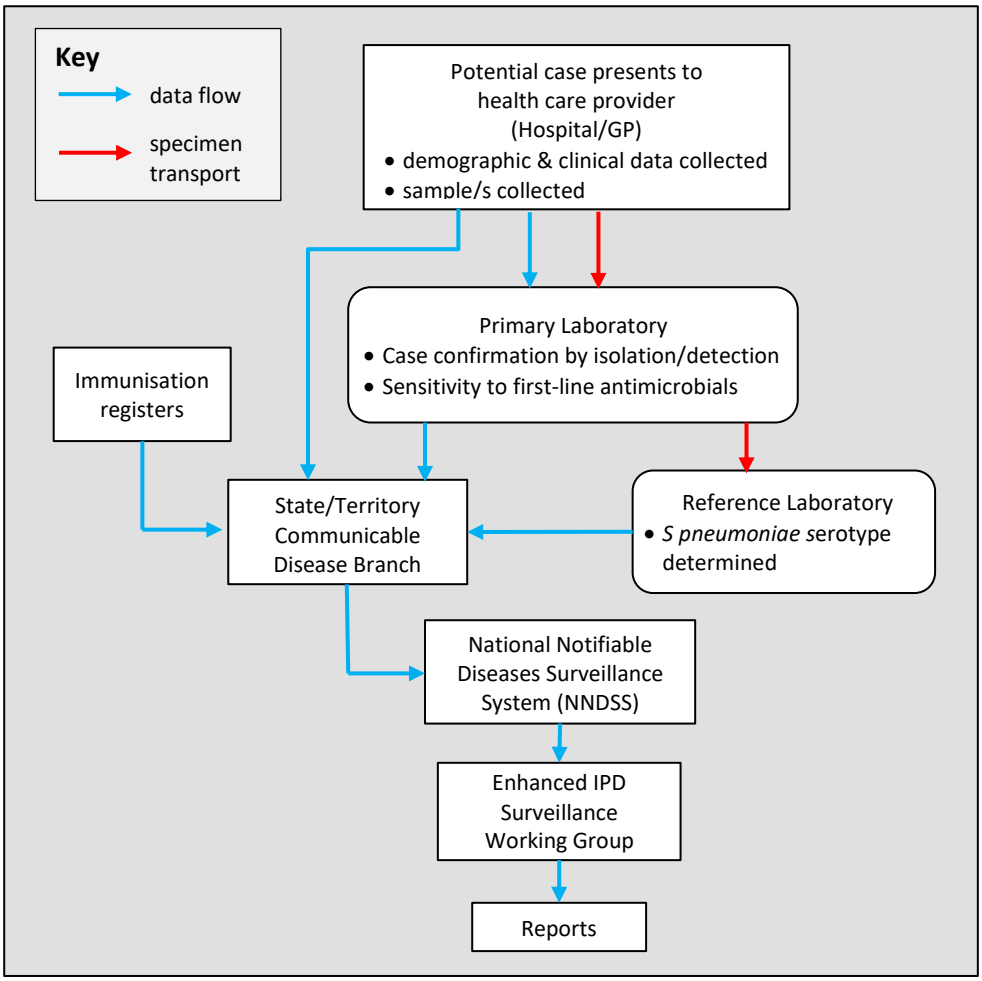

Figure A Simple representation of the operation of Australia's Enhanced Invasive Pneumococcal Disease Surveillance Program, 2017.

missing vaccination and risk factor data for cases aged over five years. There are inconsistencies between risk factor categories in jurisdictional data collection forms, the national dataset, and *The Australian Immunisation Handbook 10th Edition*. Antimicrobial resistance (AMR) data collected during IPD surveillance has been requested by the Antimicrobial Use and Resistance in Australia (AURA) project for monitoring *S. pneumoniae* resistance. Currently, the surveillance data have only moderate utility for this purpose, because reference laboratories are not funded to test susceptibility to the full panel of antimicrobials, and because problems with data entry and transmission in some jurisdictions has led to missing data on sensitivity to first-line antimicrobials. Other stakeholders indicated that the public IPD dataset would be more useful if it included data in greater detail from 2001 onwards. The EIPDSWG has proven a useful forum for rapid communication between jurisdictions and detection of outbreaks.

The quality and completeness of the surveillance data for cases aged under five years of age is excellent, but some issues were identified (Table A). A key factor in the success of this program has been the engagement with the diagnostic laboratory networks during the planning and implementation phases. Ongoing work is required to ensure the commitment of laboratories to forward IPD isolates to the reference laboratories for serotyping and AMR testing.

Table A Issues affecting quality and completeness of data in Australia's Enhanced Invasive Pneumococcal Disease Surveillance Program, 2017.

Issue	Data fields affected	Jurisdictions affected	
		all	some
Cases aged 5-50 years not routinely followed up	Vaccination history*		✓
	Risk factors		✓
	Clinical category		✓
Difficulty accessing medical records	Vaccination history*		✓
	Mortality		✓
	Risk factors		✓
	Clinical category		✓
Testing not performed	Sensitivity to full panel of antimicrobials	✓	
	Serotype (non-culture specimens only)		✓
Data entry/transmission	Sensitivity to first-line antimicrobials		✓
Data field missing from national data collection form	Hospitalisation	✓	
Data entry errors/ illogical data	Date fields	✓	
	Serotype/ Laboratory method		✓

*For cases aged over seven years prior to October 2016 only. The whole-of-life Australian Immunisation Register was introduced in 2016 to record all vaccinations administered under the NIP and most privately-funded vaccines.

The sensitivity of the program for detecting cases of IPD is unknown, but EIPDSWG members and stakeholders felt that it was acceptable. When a specimen was not sought (eg in milder illness), could not be obtained, or was obtained post-mortem, cases are not notified. It is unlikely that false positives are a burden to the dataset. The median time between onset of disease and receipt of notification by the jurisdictions (six days), and between notification and publication of data summaries in Quarterly Reports (three months), was acceptable. However, there is significant delay of transmission of enhanced data from the NNDSS to the National Centre for Immunisation Research and Surveillance (up to 10 months) due to data quality checks.

Over 15 years, the program has been flexible enough to accommodate changes in IPD epidemiology and available vaccines, and to continue to provide relevant data to stakeholders. However, the program needs to accommodate trends in laboratory methods. In particular, the increase in the proportion of cases confirmed by polymerase chain reaction (PCR) only will reduce the program's ability to attain high completeness for serotype and AMR data fields. Predicted moves to whole-genome sequencing for pneumococcal disease diagnosis and surveillance must be managed. Steps must be taken to ensure the succession of EIPDSWG members who, through their passion for IPD prevention, have ensured the stability and longevity of the program. Although complex, the IPD surveillance program is a highly useful, flexible and stable system that is acceptable to users and stakeholders.

Recommendations to the EIPDSWG

Priority Recommendations

- ❖ *Collect complete surveillance data for all cases in all jurisdictions. If resource constraints preclude this in some jurisdictions, consider prospectively following-up a random sample of cases aged five to 50 years.*
- ❖ *Ensure researchers and vaccine developers can access the data at the level of detail they require in the public dataset, while maintaining the privacy of cases. This includes*
  - *finer stratification of age-groups for cases aged less than five years*
  - *data from 2001 onwards*
  - *all available serotype data*
  - *data on vaccine failures.*
- ❖ *Improve the completeness and quality of antimicrobial resistance (AMR) data by*
  - *addressing issues with data transmission in some jurisdictions*
  - *agreeing on the standards for reference laboratory AMR testing*
  - *advocating for funding for reference laboratories to undertake this testing for every case.*

Other Recommendations

- ❖ *Review the program objectives to ensure they reflect the EIPDSWG's aspirations for the program.*
- ❖ *Harmonise notification processes, data collection forms and data transmission from the jurisdictions to the NNDSS. This should include standardising risk factor data domains to ensure they reflect groups at high risk of IPD, as identified in the* Australian Immunisation Handbook 10th Edition.
- ❖ *Advocate for all jurisdictions to implement exclusively electronic laboratory notification systems, ensuring that these collect data consistent with the NNDSS data fields.*
- ❖ *Support jurisdictions to modify their databases to prevent entering non-logical data, and to conduct post-entry logic checks, where these are not already in place.*
- ❖ *Working with relevant partners, plan for the shift to whole genome sequencing by overseeing the development of quality standards for IPD sequencing and bioinformatics, and by auspicing pilot implementation studies.*
- ❖ *Work with the Public Health Laboratory Network to enhance engagement and communication with diagnostic laboratories to ensure their full participation. This should include a review and promotion of the guidelines for forwarding samples to reference laboratories.*
- ❖ *Implement succession planning interventions to ensure there is depth of capacity within the EIPDSWG, reference laboratories and jurisdictions to maintain the program at the current high standard.*

Introduction

Invasive pneumococcal disease (IPD) is caused when the respiratory pathogen *Streptococcus pneumoniae* invades a normally sterile site (4). This Gram-positive bacterium is transmitted person-to-person via respiratory droplets and colonises the nasopharynx of many children within the first year of life, with carriage peaking at around 55% at three years of age and declining to less than 10% in adulthood (5). Determinants of colonisation include overcrowding, childcare attendance, and exposure to tobacco smoke (6).

Local spread of the pathogen can cause non-invasive infections such as otitis media, sinusitis and non-bacteraemic pneumonia (7), often in the presence of viral infections (8, 9). In susceptible people, organisms may migrate to the bloodstream and cerebrospinal fluid (CSF), leading to invasive disease (2). The most common types of IPD are bacteraemic pneumonia, bacteraemia without focus, and meningitis (8). Other sterile sites less commonly infected include the joints, bones, peritoneum, and pericardium (2). Over 90 serotypes of *S. pneumoniae* have been identified, although not all cause disease, and some are more likely than others to be associated with IPD and poorer outcomes following infection (10). IPD cases tend to be sporadic and epidemics—occurring mainly in institutions (11) and disadvantaged populations, including in Aboriginal and/or Torres Strait Islander communities (12, 13)—are now rare.

IPD has been a notifiable condition nationally since 2001, and enhanced passive surveillance is conducted in all jurisdictions (14). This surveillance is a part of the National Notifiable Diseases Surveillance System (NNDSS) and is coordinated by the Enhanced Invasive Pneumococcal Disease Surveillance Working Group (EIPDSWG), a subcommittee of the Communicable Diseases Network Australia (CDNA) (15). Although the NNDSS as a whole was evaluated in 2004 (1), an evaluation focused on the IPD Surveillance Program has not been conducted. The purpose of this evaluation is to:

- assess the need for continued surveillance of IPD in Australia;
- determine whether the stated program objectives are appropriate, and the extent to which they are being met;
- identify ways in which surveillance may be improved; and
- make recommendations to the EIPDSWG.

Methods

For this evaluation, I followed the framework outlined in the Centers for Disease Control and Prevention's Updated Guidelines for Evaluating Public Health Surveillance Systems (16). My objectives were to describe how the program functions and collect credible evidence to evaluate

- the usefulness of the program; and
- its performance against the attributes of simplicity, flexibility, data quality, acceptability, sensitivity, predictive value positive, representativeness, timeliness and stability.

I used literature and document review, key informant interviews, and descriptive analyses of surveillance data (Table 1), along with an analysis of the attributes listed above.

LITERATURE AND DOCUMENT REVIEW

To review the public health importance of IPD, the usefulness of the surveillance system and advances in laboratory methods, I conducted a literature search of the SCOPUS, PubMed and Google Scholar databases using the terms "invasive pneumococcal disease", "Australia", "epidemiology", "surveillance", "whole genome sequencing" and "culture-independent diagnostic tests". I also scanned the reference lists of all review articles and primary studies. I inspected IPD-related content available on the Australian Government Department of Health website, notification forms and procedures published by the jurisdictions, the EIPDSWG's *Explanatory notes for completion of NNDSS Invasive Pneumococcal Disease Enhanced Surveillance data collection form*, and the data notes and caveats for the IPD public dataset and NNDSS data. I also examined the revision history for the dataset field specifications, to determine how these have been changed in response to changes in IPD epidemiology, vaccines and laboratory methods.

Table 1 Summary of methods used for the evaluation of Australia's Enhanced IPD Surveillance Program, 2016 (16).

Task	Rationale/ Description	Method				
		Literature review	Working Group consultation	Stakeholder survey	Surveillance data analysis	Program document review
Describe the public health importance of the disease	Establish an ongoing need for surveillance	✓				
Describe the program & its objectives	Indicate how the surveillance data are collected and used for public health action		✓			✓
Focus the evaluation design	Ensure that time and resources are used efficiently	✓	✓			
Gather evidence of performance:						
Usefulness	Contribution to prevention and control of IPD	✓	✓	✓		✓
Simplicity	Simplicity of structure and ease of operation		✓	✓	✓	✓
Flexibility	Ability to adapt to changing information needs or operating conditions		✓	✓	✓	✓
Data Completeness & Quality	The completeness and validity of the data collected		✓		✓	
Acceptability	Willingness of persons and organisations to participate in the surveillance system			✓	✓	
Sensitivity	Proportion of incident cases detected and the ability of the system to detect outbreaks		✓	✓		
Predictive Value Positive	Proportion of notified cases that truly have IPD		✓			
Representativeness	Ability to accurately describe the occurrence of IPD over time and its distribution in the population by place and person				✓	✓
Timeliness	Time between steps in the system, production of useful data and timeliness for public health intervention		✓	✓	✓	
Stability	Ability to collect, manage and provide data properly without failure; and the ability to be operational when it is needed		✓			✓

COLLECTION OF DATA FROM KEY INFORMANTS

I consulted with members of the EIPDSWG and Office of Health Protection (OHP) data managers at the Australian Government Department of Health between 16 June and 11 August 2016. The EIPDSWG membership consists of representatives from communicable disease control units in all states and territories, the Vaccine Preventable Diseases section of OHP, National Centre for Immunisation Research and Surveillance (NCIRS) and from the four reference laboratories in Sydney, Melbourne, Perth and Brisbane. Interviews were by phone or face-to-face. I asked interviewees to confirm the relevance of the program's published objectives, to describe the operation of the program in their jurisdiction, to assess the program's performance and make suggestions for improvement. I also asked them to suggest questions to include in the stakeholder survey. The interview data collection tool is included in Appendix 4.2.

I emailed a link to an anonymous online survey to individuals and groups identified as surveillance stakeholders (Table 2). The survey was open between 12 October and 14 November 2016, and was tailored to the affiliation indicated by the respondent. Stakeholders were asked to assess the usefulness and performance of the program, to rate and describe their experience of notifying cases or using surveillance data (if applicable), and to make suggestions for improvement. The stakeholder survey is included in Appendix 4.3.

DESCRIPTIVE ANALYSIS OF SURVEILLANCE DATA

I analysed selected fields of the IPD surveillance dataset from 1 July 2013 to 30 June 2016 ('the study period') to assess data completeness and quality. I looked for patterns of data coded as:

- 'blank'
- 'unknown'
- 'not stated'
- 'Followed up – information not available' and 'Not followed up' (vaccine fields)
- 'not typed' and 'not referred' (serotype field).

Table 2 Stakeholder groups and their interest in the IPD surveillance program.

Stakeholder Group	Interest in the IPD Surveillance Program
Australian Technical Advisory Group on Immunisation (ATAGI)	Advises the Minister for Health on vaccines and advises the Pharmaceutical Benefits Advisory Committee on the strength of evidence for existing, new and emerging vaccines (17)
Pneumococcal vaccine manufacturers (Pfizer, Seqirus, GlaxoSmithKline)	Use serotype data to monitor vaccine failure and develop new multivalent vaccines for the Australian market
Antimicrobial Resistance (AMR) Coordination Unit, Australian Commission on Safety and Quality in Health Care	Undertaking the Antimicrobial Use and Resistance in Australia (AURA) Project (development of an antimicrobial resistance surveillance system)
Infectious Diseases Physicians, Paediatricians and other medical officers	Make diagnoses of IPD and may notify, may use antimicrobial resistance data to guide treatment decisions
Department of Prime Minister and Cabinet	Responsible for some areas of Aboriginal and Torres Strait Islander health policy
Commonwealth, state and territory health departments	Conduct surveillance and responsible for vaccination policy and programs
Public and private laboratories	Notify IPD cases
Researchers and academics active in field of pneumococcal disease	Use data to explore changes in pneumococcal disease epidemiology and vaccine effectiveness

To assess the timeliness of the system over the study period, I calculated mean and median days between onset date, specimen date, date the notification was made and the date the notification was received by the jurisdiction. Jajosky and Groseclose (18) recommend assessing a system's ability to detect outbreaks in a timely manner by calculating the percentage of cases that are reported within one and two incubation periods of the disease, surrogate measures for the period of communicability. The incubation period for IPD ranges from one to seven days (19), so I calculated the proportion of case notified within seven and 14 days from disease onset. Cases with missing or invalid date values were excluded from the timeliness analysis.

ETHICAL REVIEW

The stakeholder survey and surveillance data analysis were reviewed and approved by the Australian National University Human Research Ethics Committee (Protocol: 2016/583).

Findings

In this section I present the results of analysis of data from all sources, together with a discussion of their significance and the relevant recommendations. A summary of the conclusions and recommendations is given in the next section.

I conducted twenty interviews with EIPDSWG members and OHP data managers. All jurisdictions and reference laboratories were represented. On average, members had seven years of experience on the Working Group, and six were founder members. There were 28 responses to the stakeholder survey. Most respondents were researchers or from diagnostic laboratories, and five nominated more than one affiliation (Table 3). None of the respondents indicated an affiliation with ATAGI or the Antimicrobial Resistance (AMR) Coordination Unit.

Table 3 Affiliation of stakeholder survey respondents.

Group	Number of respondents*	
Researcher or academic	11	(39%)
Diagnostic laboratory (public or private)	7	(25%)
Vaccine manufacturer	4	(14%)
State/territory policy and programs	4	(14%)
NCIRS	3	(11%)
Infectious Disease Physician	2	(7%)
Paediatrician	1	(4%)
Public Health Practitioner	1	(4%)
Total	**28**	

* Five respondents indicated more than one affiliation (two researchers/academics and NCIRS; one researcher/academic and paediatrician; one researcher/academic and public health practitioner; one researcher/academic and State/Territory policy and programs)

THE PUBLIC HEALTH IMPORTANCE OF INVASIVE PNEUMOCOCCAL DISEASE IN AUSTRALIA

RELATIONSHIP TO NON-INVASIVE PNEUMOCOCCAL DISEASE

The surveillance case definition excludes non-invasive infections. Therefore data from the surveillance program does not capture the true burden of all pneumococcal diseases. It has been estimated that for every bacteraemic pneumonia that is reported, three non-bacteraemic infections occur (10). Isolation of the organism in cases of non-bacteraemic pneumonia is difficult (2), however *S. pneumoniae* may account for around

15% of all community-acquired pneumonia in Australian adults (20). Pneumococcal pneumonia is recognised as a complication of both seasonal and pandemic influenza, and was associated with critical illness during the 2009 influenza A (H1N1) pandemic (10).

Over 520,000 hospital discharges coded for pneumonia in the 2006-07 year were identified in one study (21) , while another estimated the average annual rate of initial general practitioner (GP) visits for pneumonia over the period 2006 to 2009 at approximately 800 per 100,000 population (22).

The most common non-invasive manifestation of pneumococcal disease in children is acute otitis media (AOM), with *S. pneumoniae* implicated in 28 to 55% of cases (23). Otitis media (OM) ranges from effusion behind the eardrum, to suppurative infection with or without perforation (AOM) with ear discharge that may become chronic (24). Estimates of annual episodes of all forms of OM in Australia range from 1.17 million (25) to 2.40 million (26). Most OM is mild and self-limiting (27). However, OM complications include mastoiditis, meningitis, brain abscess and permanent hearing loss (28).

FREQUENCY

When national notification came into full effect in 2002, IPD notification rates were 11.5 per 100,000 population (29). Rates dropped markedly to 7.0 per 100,000 population in 2006 following the introduction of a universal seven-valent pneumococcal conjugate vaccine (7vPCV) program for infants in 2005 (30). Since then, rates have been generally stable (Figure 1) (31, 32), with an increase in 2011 which can be largely attributed to an outbreak of disease due to Serotype 1 (33). The 13-valent pneumococcal conjugate vaccine (13vPCV) replaced the 7vPCV in 2011 (34). Approximately 1,500 cases were reported in 2015, representing a notification rate of 6.7 per 100,000 (15). Notifications of IPD are highest during the winter months (15). The burden of IPD is borne predominantly by those aged under five years and over 65 years (Figure 2), and rates have declined in both these age groups since 2002 (14).

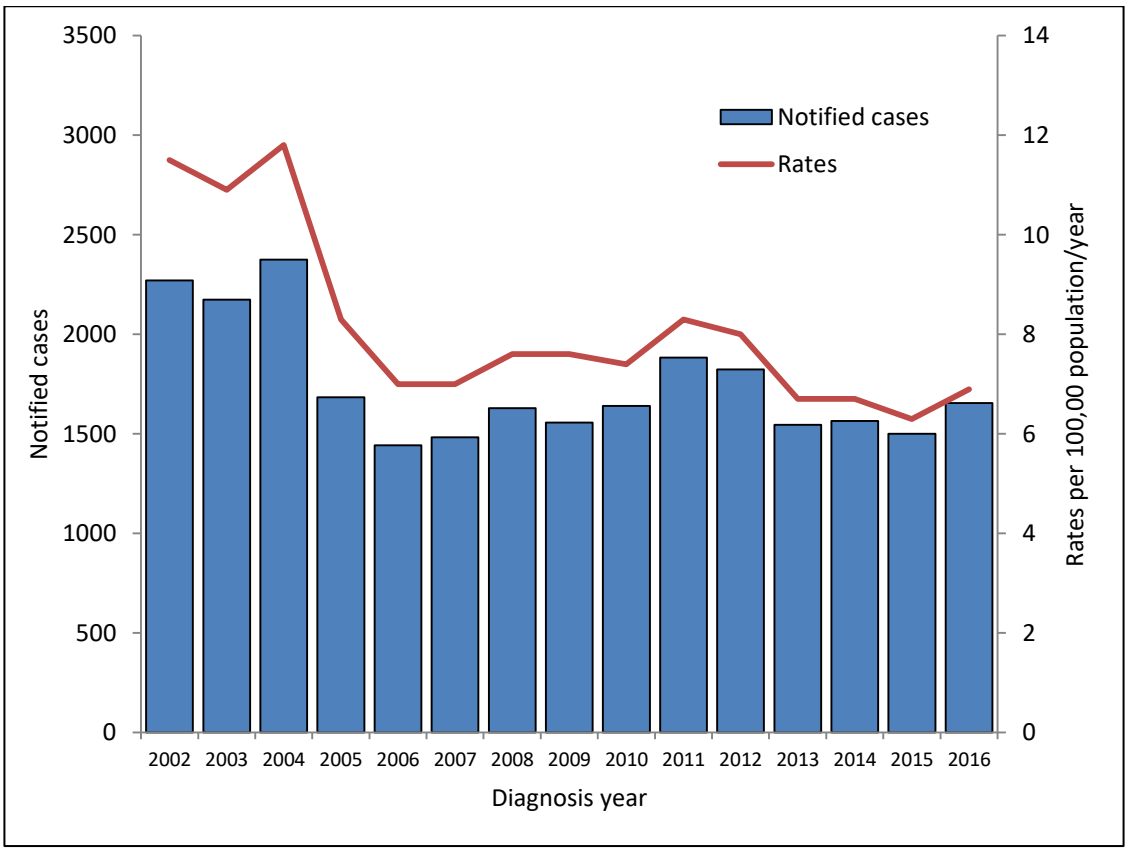

Figure 24 Notified cases and rates of IPD, Australia, 2002 to 2016 (32, 35).

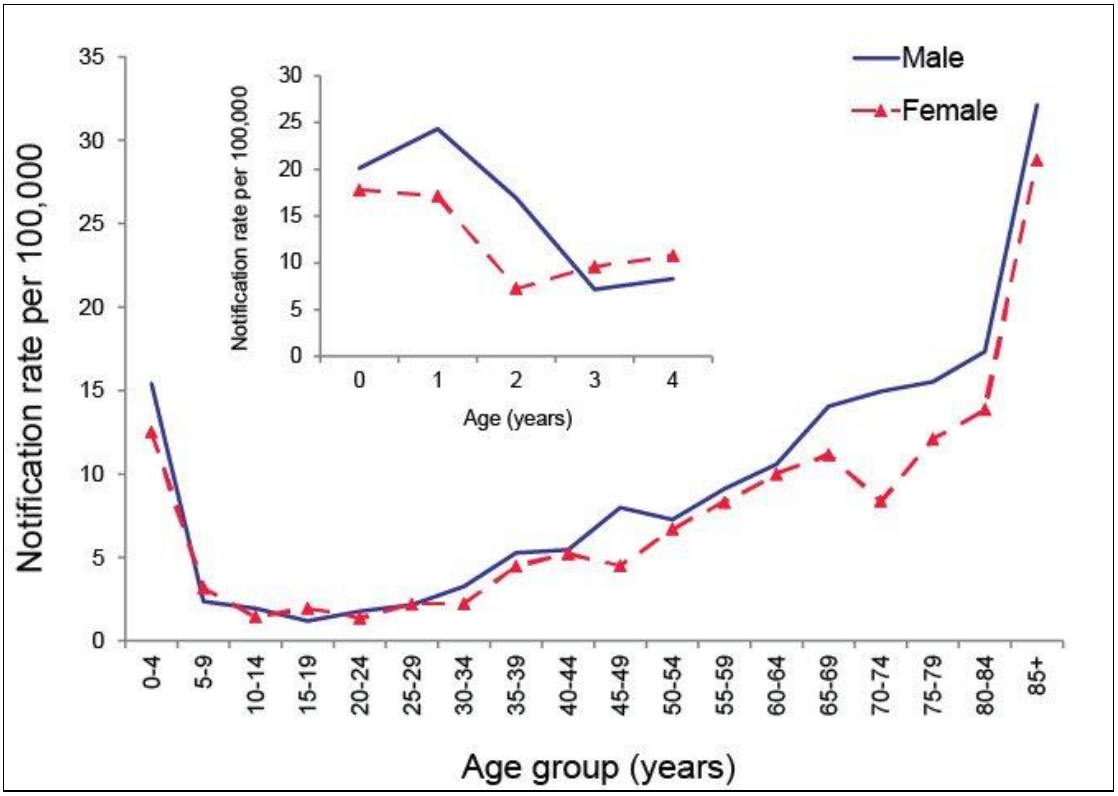

Figure 25 Notification rates of IPD, Australia, 2014, by age group and sex (31).

Risk factors for developing IPD following colonisation are shown in Table 4. The combination of diabetes, chronic heart disease and chronic obstructive pulmonary disease in people over age 19 years places them in the highest category of risk (36). In Australia, common risk factors in 2009 and 2010 for notified cases aged less than five years included prematurity (<37 weeks gestation), childcare attendance and immunocompromise (14). Common risk factors for cases aged 65 years or older and Aboriginal and Torres Strait Islander cases aged 50 years or older included chronic illness and immunocompromise (14).

Table 4 Conditions associated with an increased risk of IPD in children and adults, by severity of risk (23).

Highest Increased Risk	Functional or anatomical asplenia
	Immunocompromising conditions: • congenital or acquired immune deficiency • immunosuppressive or radiation therapy • haematological and other malignancies • solid organ or haematopoietic stem cell transplant • HIV (including AIDS) • chronic renal failure, or relapsing or persistent nephrotic syndrome
	Cerebrospinal fluid leak
	Cochlear implants
	Intracranial shunts
Increased Risk	Chronic cardiac disease: • cyanotic heart disease or cardiac failure in children • excluding hypertension only (in adults)
	Chronic lung disease: • chronic lung disease in preterm infants • cystic fibrosis • severe asthma in adults
	Diabetes and other metabolic diseases
	Autoimmune conditions (eg systemic lupus erythematosus, rheumatoid arthritis and multiple sclerosis)
	Down syndrome
	Alcoholism
	Chronic liver disease
	Preterm birth at <28 weeks gestation
	Tobacco smoking

SEVERITY

Invasive pneumococcal pneumonia has a 30-day mortality of 17-19% (37, 38). Cases may present first with symptoms of meningitis, sepsis, pericarditis or peritonitis (39). A common complication is pleural effusion with empyema; less common are lung abscess,

necrotising pneumonia and acute respiratory distress syndrome; and haemolytic uraemic syndrome is rare (2).

Bacteraemia without focus accounts for around 70% of IPD in children (23). Signs and symptoms in the absence of focal disease are usually non-specific, and may include fever, lethargy and irritability, with febrile convulsions occurring in some children (40). Complications include the development of focal infection, sepsis and septic shock (40).

Mortality from pneumococcal meningitis in developed countries ranges from 16 to 37% (41). It usually occurs after pneumococcal bacteraemia (2), and presents with symptoms and signs including headache, irritability, fever, lethargy, vomiting, neck stiffness, seizures and coma (41). Cerebrovascular complications, including stroke and venous thrombosis, are common (41). Serious neurological sequelae are common, and include cognitive and motor deficits in around 25% of cases and hearing loss in around 32% (2). Severe lifelong sequelae occur in nearly 10% of infant meningitis and moderate sequelae in an additional 14% (42).

In 2015, 83 deaths from IPD were reported[6], although mortality data was provided for less than two thirds of notified cases (14). There were 3,615 hospitalisations for IPD meningitis and bacteraemia only from 2005 to 2010, which is an annual rate of 18.9 per 100,000 population for Aboriginal and Torres Strait Islander people, and 3.2 for others (43).

PREVENTABILITY

The 23-valent pneumococcal polysaccharide vaccine (23vPPV) contains polysaccharides from the serotypes causing the majority of IPD in Australian adults (23). It induces a significant antibody response in adults, but is poor at generating an immune response in young children and immunocompromised adults, and has little effect on nasopharyngeal carriage as it does not induce an immune memory response (6). The 23vPPV has been available and recommended for people with specified high risk medical conditions since before 1991 (23). Pneumococcal conjugate vaccines contain

[6] deaths within the first two weeks of diagnosis

fewer serotypes but are immunogenic in young children and induce an immune memory (23). Introduction of pneumococcal conjugate vaccination programs in infants also leads to a decrease in IPD and pneumococcal carriage in unvaccinated people (44). The 7vPCV was funded by the NIP for all infants at two, four and six months of age from 2005 and was replaced by the 13vPCV in 2011 (34). This change was made in response to an increase in non-7vPCV serotypes observed in notified cases. The 10-valent pneumococcal conjugate vaccine was funded for all children in the NT aged two, four, six and 18 months from 2009 and replaced by 13vPCV in 2011 (34). Current pneumococcal vaccination practice in Australia, and the serotypes targeted by vaccines are shown in Table 5. In July 2016, the Pharmaceutical Benefits Advisory Committee recommended a change in the schedule to a single 13vPCV dose for pneumococcal vaccine naïve non-Indigenous adults aged 65 years and over and pneumococcal vaccine naïve Aboriginal and/or Torres Strait Islander adults aged 50 years and over (45), although this has not yet been implemented.

Table 5 Pneumococcal vaccines, recommendations and serotypes targeted, 2016 (23).

Vaccine type	Recommendation	Serotypes targeted by the vaccine
13-valent pneumococcal conjugate vaccine (13vPCV)	• Infants at 2, 4 and 6 months of age • Aboriginal and/or Torres Strait Islander children at 12-18 months of age living in NT, QLD, SA and WA • Adults with a medical condition(s) associated with the highest increased risk of IPD (see Table 4)	1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.
23-valent pneumococcal polysaccharide vaccine (23vPPV)	• Aboriginal and/or Torres Strait Islander people aged ≥50 years • Adults aged ≥65 years • Children aged >5 to <18 years with chronic medical condition(s) associated with increased risk of IPD (see Table 4) • Adults with a condition(s) associated with an increased risk of IPD (see Table 4)	1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F and 33F.

Invasive pneumococcal disease notifications have decreased since the introduction of pneumococcal conjugate vaccines, but there has been an associated increase in the proportion of serotypes not covered by the 7vPCV (Figure 3) (15). There were also marked reductions in all-cause pneumonia hospitalisations for children (38% for children aged <2 years; 28% for children aged 2 to 4 years) in the 30 months following the introduction of the 7vPCV program (21). A recent study estimated that over the five year period of the 7vPCV program, 162 IPD deaths, 5 783 IPD hospitalisations and 60

cases of moderate or severe disability from meningitis were averted (46). The program also prevented nearly 12 000 myringotomies with ventilation tube insertion, and over 22 000 hospitalisations and 5 100 deaths from non-invasive community-acquired pneumonia (46). The trend of lower rates of notifications has shown a decline since the introduction of the 13vPCVin 2011 (47). Data from 2014 indicates that 60-70% of IPD in age groups targeted by the 23vPPV program is caused by serotypes included in this vaccine (15). Ongoing surveillance of IPD is vital to detect serotype replacement and emergence of disease-causing serotypes, and to identify and evaluate vaccination programs (43).

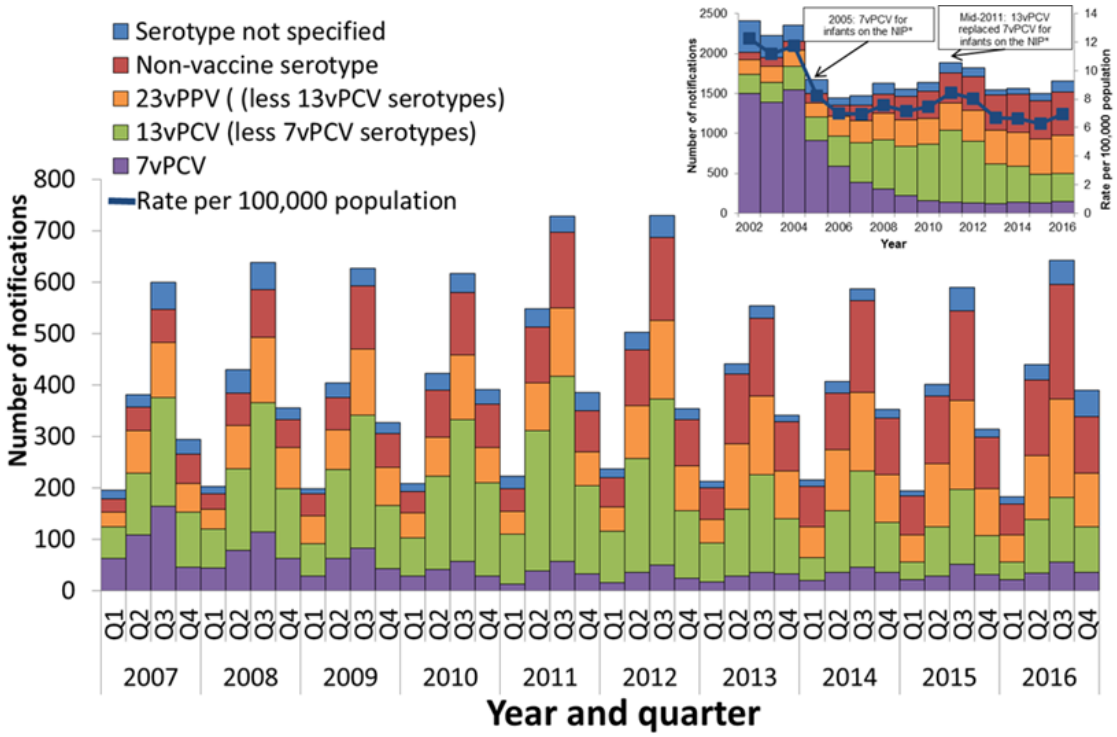

Figure 26 Notifications of invasive pneumococcal disease, Australia, 2002 to 2016, year and quarter, by vaccine serotype group (32).

Tertiary prevention for IPD includes antimicrobial treatment, general supportive care and intensive care (2). Surveillance data indicates that the rate of resistance to penicillin and ceftriaxone/cefotaxime increased to 16% in 2010, with resistance mainly evident in serotypes 19A (the serotype that accounted for the highest number of deaths) and 19F (14). Continued surveillance will provide data on prevalence of resistant serotypes in the population, and inform treatment choices for invasive and non-invasive disease.

COST

The estimated costs (to the health care system) and quality-adjusted life years (QALYs) lost for each case of pneumococcal disease in children aged under 5 years in 2011 are shown in Table 6 (42). The estimated cost of treating pneumococcal pneumonia and invasive bacteraemia and meningitis in people aged 65 years and over was $56.9 million in 2012 (48). The annual average general practitioner-related cost of all-cause pneumonia over 2006 to 2009 in all age groups were approximately $20 million per year (22). Treatment costs for OM in 2008 were estimated to be between $100 million and $400 million (26). The net cost to the NIP of the 13vPCV program was estimated at less than $10 million in 2015 (49). The cost of the 23vPPV to the Pharmaceutical Benefits Scheme was $611,310 in 2011 (50).

Table 6 Estimated costs and QALY loss for each case of pneumococcal disease in children aged under 5 years, 2011 (42). This table includes non-invasive pneumonia and otitis media (OM).

Parameter		Cost/Loss per case
Cost	**Hospitalisation**	
	Meningitis	$10 132
	Bacteraemia	$8 666
	Pneumonia*	$3 788
	OM	$1 641
	Hearing loss (meningitis)	
	Hearing aid/s (every 5 years):	
	21–64 years (private)	$2 000
	Others ages (public)	$500
	Fitting (every 5 years)	$500
	Maintenance (per year)	$137
	Cochlear implant	$27 505
	Moderate disability	
	5–17 years	$9 540
	18+ years	–
	Severe disability	
	5–17 years	$23 353
	18+ years	$82 500
QALY loss	**Hospitalisation**	
	Meningitis	0.0232
	Bacteraemia	0.0079
	Pneumonia*	0.006
	OM	0.009
	Outpatient cases	
	Pneumonia*	0.004
	OM	0.005
	Moderate disability (per year)	0.09
	Severe disability (per year)	0.54

*Includes non-bacteraemic pneumonia

DISPARITIES

In 2014, the incidence rate of notification for Aboriginal and Torres Strait Islander people was around six times higher than for other Australians (Figure 4) (14). There was an 87% reduction in notifications of IPD caused by 7vPCV serotypes between 2001 (when the 7vPCV program among Aboriginal and Torres Strait Islander children began) and 2010 (43). However, the reduction was not as steep as for other children, due to a lower proportion of IPD caused by 7vPCV types before vaccine introduction (43). Prevalence of OM among Aboriginal children is 42%, the highest rate in the Asia-Pacific (25).

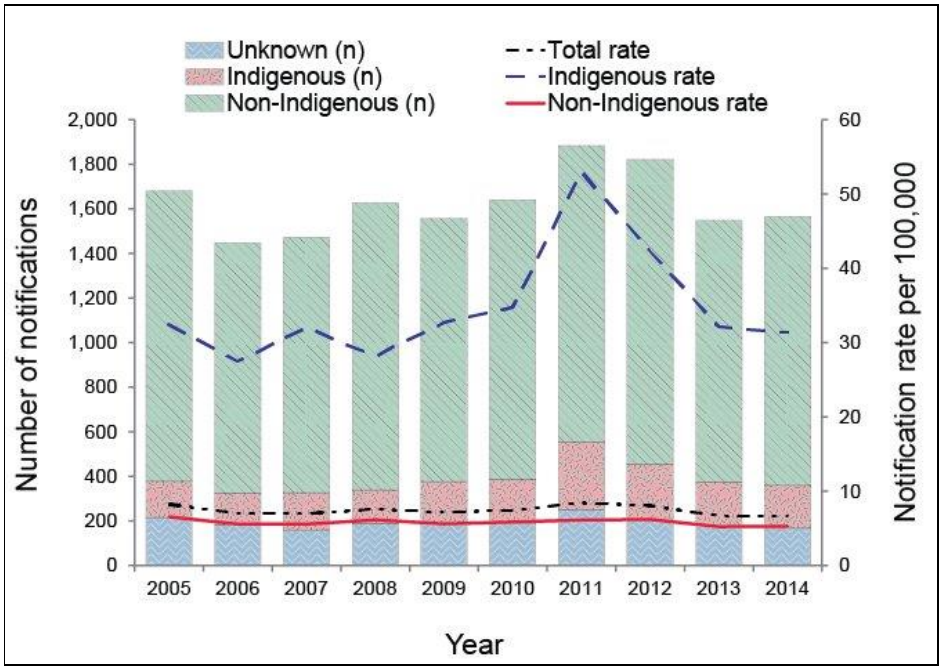

Figure 27 Notifications and notification rates of invasive pneumococcal disease, Australia, 2005 to 2014, by year and Indigenous status (31).

PUBLIC AND POLITICAL INTEREST

As a disease with limited outbreak potential, IPD is unlikely to generate the public and political interest garnered by some other communicable diseases. However, in 2008 the Council of Australian Governments agreed to six targets to address Aboriginal and Torres Strait Islander disadvantage, including closing the gap in life expectancy by 2031 and halving the gap in mortality rates for children under five by 2018 (51). Given the disparity in pneumococcal disease burden between Aboriginal and Torres Strait Islanders and other Australians, addressing this disease is important politically and ethically.

CONCLUSION

IPD is a severe disease with high rates of mortality, incidence of disability in survivors and costs to the health system. Non-invasive pneumococcal disease, while less severe, has high incidence. Vulnerable groups—particularly the very young, elderly and Aboriginal and Torres Strait Islander people—are over-represented in pneumococcal disease incidence. The World Health Organization recommends routine surveillance of IPD, on the grounds of the disease's severity and the availability of vaccines (52).

While significant gains in pneumococcal disease incidence have been made as result of vaccination programs, these have not been shared equally among all groups at risk, and the emergence of serotype replacement and antimicrobial resistance continues to threaten primary and tertiary prevention strategies. Continued national surveillance of this disease of public health importance will inform the development and evaluation of vaccination programs and contribute to closing the gap on Aboriginal and Torres Strait Islander disadvantage.

PROGRAM OPERATION

In this section, I present the findings related to the surveillance program operation, including the surveillance case definition, management and flow of data, and the human resources required to operate the program. This provides the context in which to discuss the objectives of surveillance.

The legislative basis for the collection of data required for the functioning of the IPD surveillance program and the other systems in the NNDSS is provided by the public health legislation of each state and territory (53). States and territories voluntarily forward these data to the Australian Government Department of Health for the purpose of surveillance. The exchange of this information, including personal information, between jurisdictions and the Commonwealth is authorised by the *National Health Security Act 2007*. The National Health Security Agreement supports this legislation, and is a policy and administrative arrangement that outlines the operational procedures and mandatory data (unique record number, notifying State or Territory, disease code, and date of receipt of notification) to be provided to the Australian Government (54). Under this agreement, "additional data may be provided as defined in the NNDSS Core

and Enhanced Datafield Specifications". Governance of the enhanced data fields is the responsibility of the EIPDSWG, which meets by teleconference quarterly and

- assures data quality, for example through the development and review of explanatory notes for all fields of the national IPD dataset
- provides a network for a coordinated response to changes in IPD epidemiology, the NIP and laboratory methods.

SURVEILLANCE CASE DEFINITION

The national case definition for a confirmed case of IPD is

- Isolation of *S. pneumoniae* from a normally sterile site by culture

or

- Detection of *S. pneumoniae* from a normally sterile site by nucleic acid testing (4).

Only confirmed cases are notified. This case definition has not essentially changed since 2001 (55), although the method of detection was explicitly articulated later, in 2004 (56).

DATA MANAGEMENT, FLOW AND REPORTING

Data collection for the program is integrated into the systems set in place for the NNDSS. The components of the program are described in Table 7. Dataset fields for core and enhanced data are specified and have undergone several revisions since 2001. Enhanced data collection is supported by detailed explanatory notes which define dataset fields, indicate acceptable data sources, and provide explanations or examples for each field (57). Figure 5 illustrates how surveillance data flows through the system.

Laboratories and pathologists are required by law to notify cases of IPD in all jurisdictions. All medical practitioners are required to notify cases in SA, Victoria, NT and ACT. Each jurisdiction uses a different form for notification. Most notifications are received by the state or territory Communicable Diseases branch passively from the primary diagnostic laboratories (public or private). Occasionally notifications are received directly from a medical practitioner. Some primary diagnostic laboratories do not have the ability to perform nucleic acid testing (polymerase chain reaction, PCR), so

must forward these samples to a secondary laboratory. Isolates are forwarded to a reference laboratory for serotyping using the Quellung reaction (for culture-positive specimens) or, in around 5% of cases, molecular typing (for PCR-positive specimens) (35). Serotype data are usually received by the jurisdictions from the reference laboratories some weeks after the initial notification, and are cross-checked against the notification data. While susceptibility to first-line antimicrobials is assessed by the diagnostic laboratory, susceptibility to the full panel of antimicrobials is only routinely conducted on suitable specimens from Queensland and NT.

While data are collected for all notified cases, Victoria and NSW—the jurisdictions with the largest populations— do not routinely collect data on Indigenous status, vaccination history or enhanced data (including risk factors) for cases aged between five and 50 years. In 2015, this subgroup consisted of 29% and 25% of notifications in Victoria and NSW respectively, which is over 13% of cases nationally. Routine collection of enhanced data on these age groups in Queensland is not universal, and varies by local public health unit (PHU). If cases were admitted to a public hospital, the epidemiologist collects enhanced data from the integrated electronic inpatient medical record. In smaller jurisdictions (eg ACT and NT) all follow-up and enhanced data collection is conducted by the Public Health Nurse (PHN), surveillance officer or epidemiologist in the Communicable Diseases Branch. In larger jurisdictions, case follow-up is delegated to officers in the local PHU. Direct access to clinical data varies widely between jurisdictions and PHUs. For example, in the NT, the PHN has access to all electronic hospital, laboratory and (all-ages) vaccination data, and quite often contacts the case or their family directly to obtain data. In contrast, public health officers in Victoria must request copies of hospital discharge summaries and GP vaccination records, and only have electronic access to childhood vaccination data via the Australian Childhood Immunisation Register[7] (ACIR). In all jurisdictions, entered data are checked for errors and missing data by the epidemiologist or PHN.

Deidentified data are automatically transmitted daily to the NNDSS. The exceptions are in WA, Tasmania and ACT, where all data are sent manually and the enhanced data are transmitted quarterly or annually rather than daily. Extra transmissions are made on

[7] The Australian Immunisation Register was introduced in October 2016.

request. Core data are collated into a fortnightly report for the CDNA, and published on the Department of Health website (58). Every quarter, the NNDSS data officer emails a spreadsheet of line-listed cases back to the jurisdictional officer for checking. Once checked, the core data are collated into a quarterly report for review and public release (59).

Complete core data and enhanced data are sent to NCIRS approximately monthly and annually, respectively. These data form the basis of NCIRS' advice to ATAGI regarding vaccines to be included in the NIP. The EIPDSWG also aims to publish an annual report, but the latest combines the 2011 and 2012 reports (35). Annual IPD data are included in the NNDSS annual reports, most recently 2014 (60). Every year, the EIPDSWG sends a report to all laboratories, outlining the epidemiological status of IPD nationally and in the laboratory's jurisdiction. Selected surveillance data from 2009 to 2014 are available publicly on the Department of Health's website (59).

Table 7 Components of Australia's Enhanced IPD Surveillance Program, 2016.

Component	Description	
Population under surveillance (14)		
Core data	All Australian residents • Indigenous status & vaccination history are not routinely collected for cases aged 5-49 years in NSW & Victoria	
Enhanced data	All ages	ACT, NT, TAS, SA & WA
	Under 5 years & 50 years and over	QLD* (61), Victoria† (62) & NSW
Who is required to notify	• Laboratories: all jurisdictions • Medical practitioners: NT‡, SA, VIC, ACT • Authorised Nurse Practitioners & hospitals: ACT	
Data collected		
Core data	• State/Territory • Notification ID • Disease code • Organism code and Name • Serogroup subtype • Confirmation status • Laboratory diagnosis method • Vaccination history (status, validation and doses) • Resident postcode and location • Dates of onset, specimen collection, notification made and notification received	• Date of birth • Age at onset • Sex • Indigenous status • Died • Outbreak reference • How the notified case was identified • Place of acquisition • Hospitalised • Date of last vaccination • Details of up to five vaccinations

* Follow-up of enhanced data in Queensland varies between Public Health Units. Since 2014, the epidemiologist has been able to follow up all cases admitted to public hospitals through the integrated electronic health record system. (61)

† Prior to 30 June, 2012, Victoria followed up the collection of enhanced data on all ages. Between 1 July 2012 and 31 December 2012, and from 2014 to the present, Victoria only followed up the collection of enhanced data in the under 5 years and the 50 years and over age groups (62, 63).

‡ In the NT, medical practitioners are required to notify cases, but IPD is not included in the doctors' notification form (64).

Component	Description
Data collected	
Enhanced data	• Risk factors • Gestational age • Clinical category of IPD (bacteraemia, meningitis, pneumonia, or other) • Date died • The specimen from which the organism was obtained • Susceptibility to first-line antimicrobials • Susceptibility to full panel of antimicrobials
Data sources	
Core data (except serotype and vaccination history)	• Primary public and private laboratories • Clinicians: general practitioners, hospital medical officers, infection control nurses and/or discharge summaries
Serotype data (and full panel susceptibility in QLD and NT only)	Reference laboratories: • Microbiological Diagnostic Unit Public Health Laboratory, University of Melbourne (VIC, TAS & SA cases) • NSW Health Pathology (NSW & ACT cases) • Pathwest Laboratory Medicine (WA cases) • Queensland Health Forensic & Scientific Services (QLD & NT cases)
Vaccination history	• Australian Immunisation Register (prior to October 2016: Australian Childhood Immunisation Register for cases under 7 years of age only) • clinical record, general practitioner or the case/family • NT: Northern Territory Immunisation Register (NTIR) – all adults and children • QLD: Vaccination Information and Vaccination Administration System (VIVAS) – for children up to age 10 years, adult refugees, and 23vPPV for Indigenous adults (65)
Other enhanced data	• Obtained from clinicians by jurisdictional surveillance officers or local public health officers • In some jurisdictions, officers have direct access to electronic clinical records, and/or contact cases or their families directly

Component	Description

Data Management systems (entry, transfer, storage etc)	• Notifications and reference laboratory data are received by jurisdictions via online reporting, fax, post, or (less commonly) phone calls
	• Various methods of data entry, including
	  ○ hand-written notification/case report forms or laboratory log entries, later transcribed into web-based databases or spreadsheets
	  ○ direct data entry into databases or spreadsheets
	• Predominantly, core data are automatically transmitted to NNDSS nightly. Enhanced data are transmitted daily or quarterly. Some jurisdictions manually email a spreadsheet of core and enhanced data quarterly.
	• Each quarter, a spreadsheet of cases notified to NNDSS are emailed to each jurisdiction for checking, cleaning and further follow-up
	• Data transmitted to NCIRS from NNDSS monthly (core data) and annually (enhanced data)

Data privacy and security systems	• All electronic databases are backed up on departmental servers • Data transmission either automatic or through secure fax or email • Only de-identified data transmitted to NNDSS

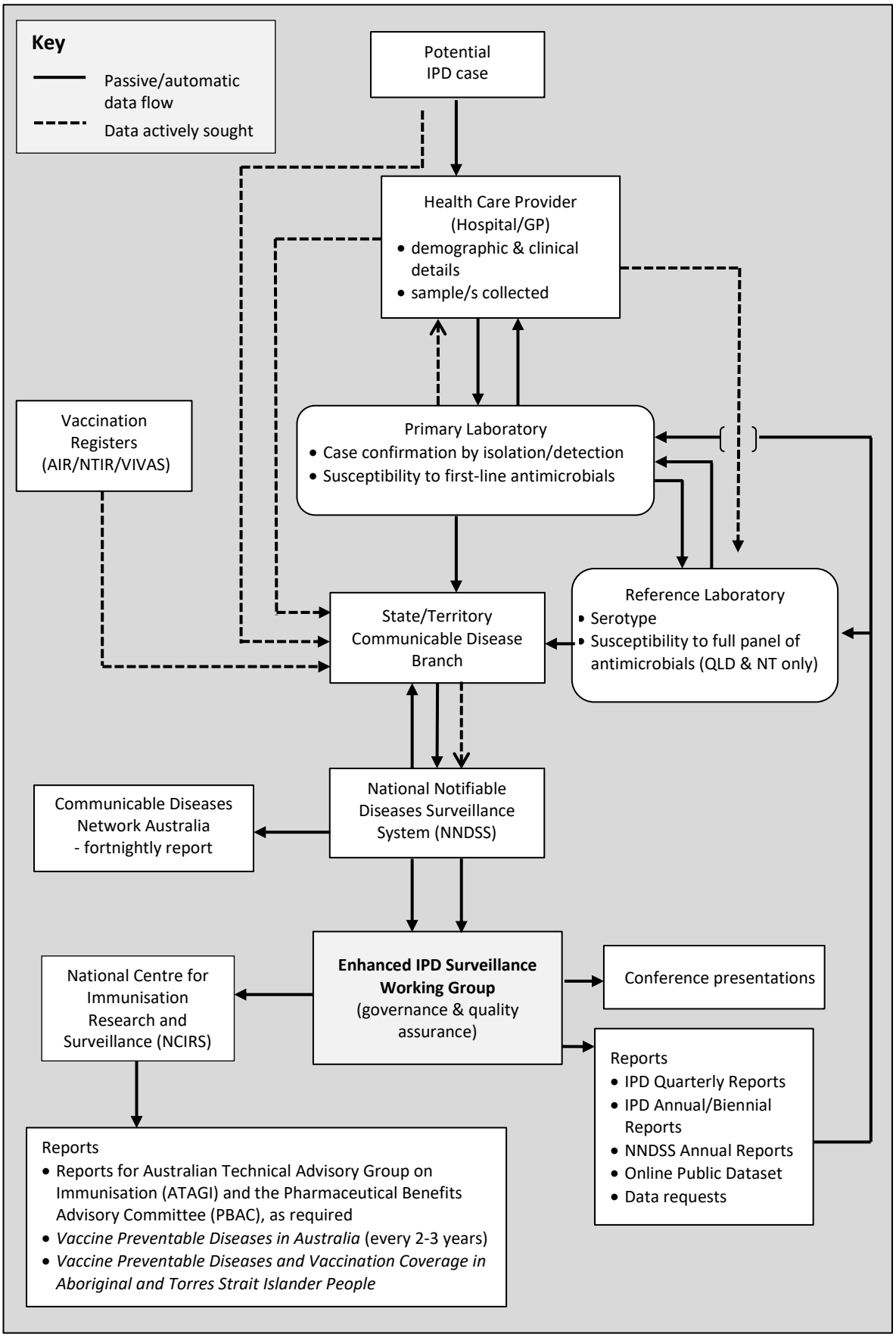

Figure 28 IPD case notification and reporting of surveillance data, 2016.

Resources

Members of EIPDSWG report that 181 staff are involved in IPD surveillance data collection nationally, including reference laboratory staff, but all have other duties. Reference laboratories stated that testing, data entry and reporting for each case took an average of 30 minutes, but sometimes up to an hour. Members from jurisdictional health departments reported a wide variation in estimates of the time spent on data collection for each case. Generally, data collection in jurisdictions with electronic access to clinical records takes 90 minutes or less per case, but three to 10 hours per case in jurisdictions without electronic access.

The costs of conducting IPD surveillance include those related to reference laboratory testing, case follow-up, data entry, reporting, and information technology technical support and maintenance. Under the *Project Agreement for Vaccine Preventable Diseases Surveillance Program* the Australian Government will provide the States and Territories with $845 000 for reporting of surveillance data on the 15 nationally notifiable vaccine-preventable diseases (including IPD) during the 2016-17 financial year (66). This includes payments to the Northern Territory for provision of secretariat services to the EIPDSWG.

Program Objectives

There are five objectives for the surveillance program published on the Department of Health's website (Table 8) (53). These have not been endorsed by the EIPDSWG. I asked EIPDSWG members comment on each objective and indicate whether they were still relevant and being achieved.

Overall, EIPDSWG members thought that the objectives were appropriate, although not all were currently being met. Members thought that surveillance was capturing as high a proportion of cases as was possible (Objective 1), but that it was still important to strive for 100% sensitivity. Although enhanced data are not currently collected for all age groups in some jurisdictions, 90% of members thought that they should be (Objective 2). As it is important to gain a national picture of IPD epidemiology, inclusion of IPD surveillance within the NNDSS is still appropriate (Objective 3). There was consensus that the epidemiological impact of conjugate vaccination must be measurable using data collected by the program (Objective 4), and some members

suggested that polysaccharide vaccination should be included in this objective. However, the capacity to achieve this objective is limited by missing vaccination, serotype and AMR data. The former is due to the difficulty in collecting vaccination data on adults, while the latter relates to laboratory methods. Many EIPDSWG members felt that the wording of Objective 5 was unhelpful and did not reflect the likelihood that deaths associated with IPD vaccine failure or AMR may have multiple causes, particularly for the elderly. Again, achievement of this objective has been hampered by missing vaccination and AMR data, and also by problems with mortality data that will be discussed in later sections.

Sixty per cent of members thought that there was no need for further objectives to be added. Suggestions for additional objectives centred on the need for the program to report high quality data that would allow other organisations to

- monitor epidemiology (including the types of presentations and risk factors)
- develop vaccination policy and write the *Australian Immunisation Handbook*
- estimate the economic burden of IPD.

Table 8 EIPDSWG members' assessment of the stated objectives of the surveillance program, 2016.

Objective (53)	**Proportion of EIPDSWG members who thought this objective was…** …relevant	…being met	**Selected Respondent Comments** (Key: **J** – state or territory health department**; L** – reference laboratory; **O/N** – OHP or NCIRS)
1. To record every case of IPD occurring in Australia	100%	80%	*Not sure that we are hearing about every case – particularly the less severe ones. I think we are doing it for all the severe cases. This is an aspirational objective, but still appropriate* – J *Out of all the diseases, this is the most likely to capture all cases* – O/N *We're meeting this to a large extent, as most cases in Australia are hospitalised* – O/N *I feel that the reference lab is getting 95% of cases for serotyping* - L
2. To collect detailed information on each case of IPD as set out in the NNDSS Invasive Pneumococcal Infection Enhanced Surveillance Form	90%	40%	*Antibiotic susceptibility is incomplete, and we're missing some age groups in some jurisdictions, but in terms of reflecting the higher risk groups and targeted populations, we have it covered* – O/N *Data managers work hard, but it's hard to get the original data from clinicians and[diagnostic] labs* – O/N *I think it has been a pragmatic policy decision of the [EIPDSWG] not to follow up every case. Those not followed up are a smallish number of relatively healthy adults* – O/N *All fields are relevant for all cases* – O/N *It's disappointing that we can't do it in the biggest jurisdiction for a big group that are at risk of disease and death and is our largest Indigenous population. And there are so few cases they could be doing it all as they have per-capita resources* – J *We have seen serotype completeness drop for the over five- and under fifty-year-olds. These are often the most interesting cases – quite a few deaths, but we are often missing serotype, Indigenous status and comorbidities for these cases* – J *Ideally, in Victoria and NSW we would take a random sample of the over five- and under 50-year-olds* – L

Objective (53)	**Proportion of EIPDSWG members who thought this objective was…** …relevant	…being met	**Selected Respondent Comments** (Key: **J** – state or territory health department**; L** – reference laboratory; **O/N** – OHP or NCIRS)
3. To collate nationally this information in the NNDSS dataset for enhanced IPD surveillance	95%	80%	*It absolutely has to be national, especially for serotypes, as they differ geographically. I see a lot of things published with data from bigger cities and results are extrapolated to all of Australia. Life's not like that!* – J *The NNDSS is the most appropriate place to collate it* – O/N *It's not necessary for all the enhanced data to be collated and reported nationally as a part of NNDSS. For example, we may only need serogroups rather than serotypes* - L
4. To measure the impact of conjugate pneumococcal vaccination on the rates and types of pneumococcal disease, the prevalence of circulating pneumococcal serotypes and levels of antibiotic resistance	100%	40%	*This is one of the uses of the data, not an objective of the system. These assessments are mostly done as separate projects by OHP or NCIRS* – O/N *This is the main aim. We are not getting full [antibiotic] susceptibility data, but we should* – L *We have issues now with PCR-positive cases. It's selective as to which ones are being serotyped: only certain labs send samples for PCR serotyping, usually the under 5s, those with low suspicion of IPD and a small amount of genetic material will not be typed* - L *We have uniform collection practices for rates and types of disease and for serotypes, but it's not the best for levels of antibiotic resistance. We don't use a common reference lab so we don't have the uniform data we hoped for* – J *We probably should include the polysaccharide vaccine in the objective, or as a separate objective* – J
5. To assess whether cases or deaths in children under 5 years and adults over 65 years are due to IPD vaccine failure or antibiotic resistance	85%	40%	*[This objective] should include high risk and high comorbidity groups so we can adjust the NIP to target people with risk factors and provide more evidence for modifying risk factors* – J *Unless we follow up later, we may not know if someone has died. We could do a study linking data from the NNDSS and the mortality database* – J *Vaccination and susceptibility data are often missing* – L *We need an 'all-of-life' vaccination register* – L *It should be 'associated with', not 'due to'* – J

Table 9 Examples of additional objectives for the Enhanced IPD surveillance program suggested by EIPDSWG members, 2016.

Selected Respondent Comments (Key: **J** – state or territory health department**; L** – reference laboratory; **O/N** – OHP or NCIRS)
*Possibly one about data feeding into vaccination policy and clinical guidelines, like the [*Immunisation*]* Handbook – O/N
Should be an objective about regular reporting and provision of data for transparency…and include one about measuring the impact of polysaccharide vaccination – J
Something to do with 'characterising the type of presentations' caused by the pathogen. For example, there is a new type of meningococcal in Australia with an atypical presentation. It would be good to be able to pick this up to warn people. So, there seems to be an increase in empyema cases in certain [IPD] serotypes, but there's not enough data to be sure – L
We need to think about whether we want to understand better the rates of hospital admissions and length of stay—so, healthcare costs. This could be used to build a business case for funding surveillance – L

Recommendation 1

Review the program objectives to ensure they reflect the EIPDSWG's aspirations for the program.

PROGRAM PERFORMANCE

In this section I assess the performance of the program and make recommendations for improvement for each of the attributes listed in Table 1. Recommendations may apply to more than one attribute.

USEFULNESS

Over 90% of respondents in EIPDSWG interviews and the stakeholder survey indicated that the program was very or extremely useful (Figure 6). Those who indicated that the program was moderately useful were representatives from reference laboratories, who reported that the discussions held at EIPDSWG meetings were not usually relevant to them. Table 10 lists some of the comments made by respondents about the usefulness of the program.

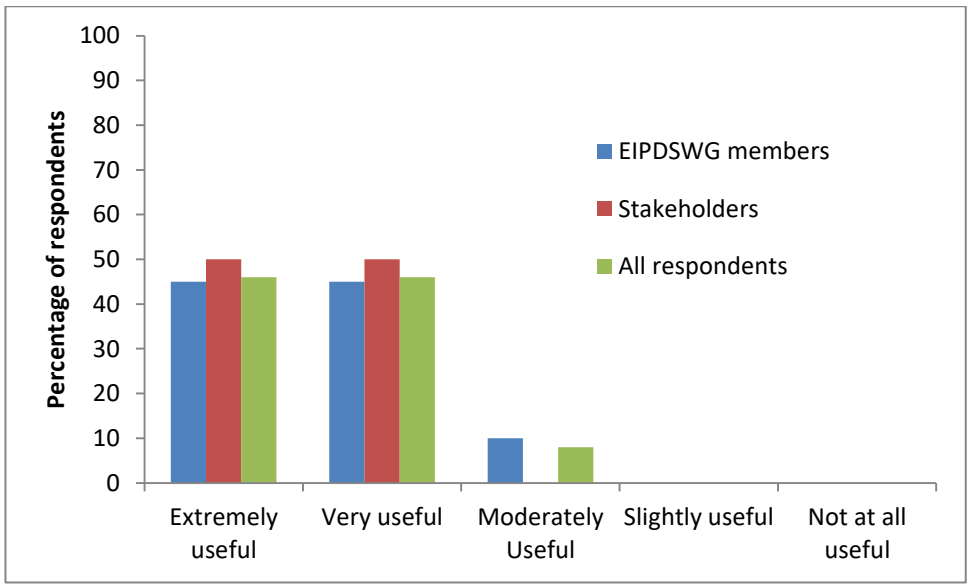

Figure 29 EIPDSWG member and stakeholder ratings of the overall usefulness of the enhanced IPD surveillance program, 2016.

Table 10 Examples of comments on the usefulness of the enhanced IPD surveillance program from EIPDSWG members and stakeholders, 2016**.**

Selected Respondent Comments (Key: **J** – state or territory health department**; V** – vaccine manufacturer; **O/N** – OHP or NCIRS)
The surveillance has been used to guide child and adult vaccination programs. We have the evidence to take to ATAGI to inform a change. – J *Publically available surveillance information is essential to inform the development of new vaccines and for the evaluation of the performance of current vaccines* – V *There is a 10 month delay in the dump of enhanced data from NNDSS to NCIRS. There is a reason why it takes so long—all the checking and confirmation is time consuming—but it reduces the utility of the system for us (OHP/NCIRS).* ***– O/N***

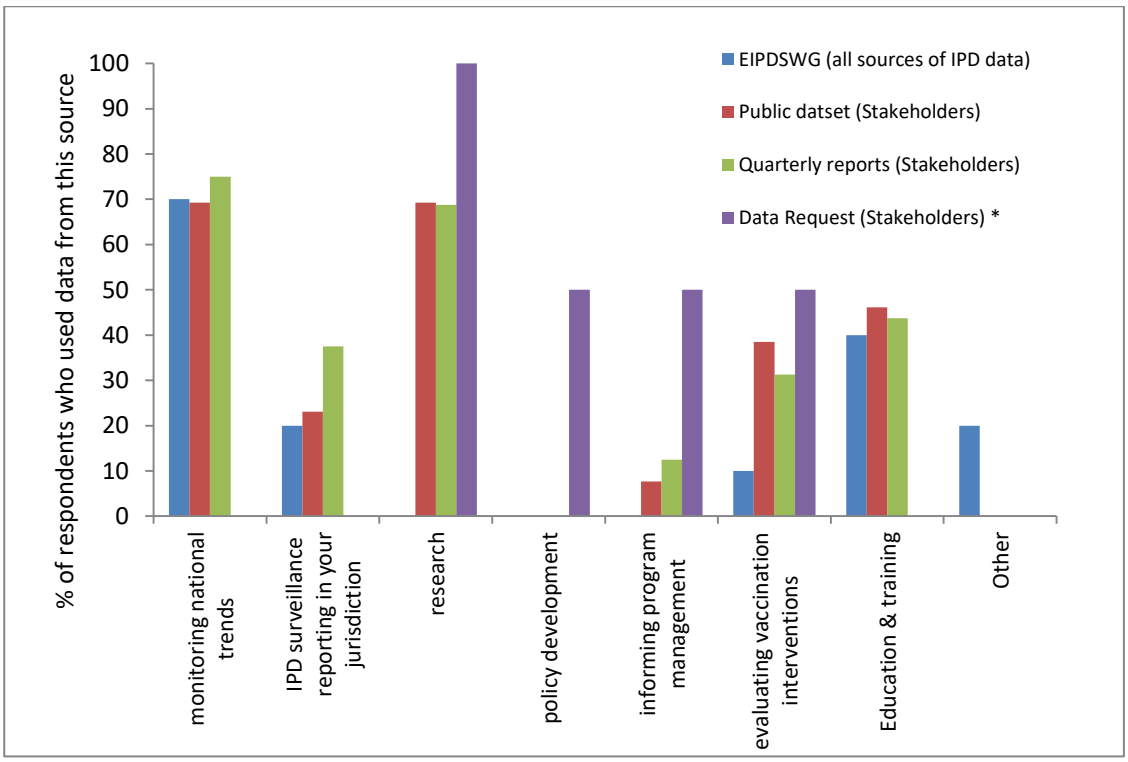

Figure 30 Purposes for which EIPDSWG interview and stakeholder survey respondents reported using various sources of IPD surveillance data, Australia, 2016. (*Only two stakeholder survey respondents indicated they had requested line-listed data from OHP).

Usefulness for evaluating and informing vaccination policy and programs

The complete national dataset (including dates of birth and residential location) is only available for analysis within OHP and by NCIRS. It is clear that this national surveillance data has provided evidence for effective changes to the infant conjugate vaccination program. However, the program has less utility for evaluating the impact of the targeted 23vPPV program, as less than three quarters of cases aged over 50 years had complete vaccination data over the study period (data not shown). A lack of data for cases aged over five years also hinders the estimation of the herd effects of childhood vaccination, and thus economic evaluations (46).

It is difficult to assess the impact of the NIP on other high-risk population groups targeted by immunisation programs. This is because of lack of adult vaccination data, and inconsistencies between the risk groups listed in the *Australian Immunisation Handbook 10th Edition* (23) and categorisation of 'risk factor' data in the national enhanced IPD dataset (67)—and there are further variations between these and the risk factor data collected in Victoria (68) and Queensland (69) (Table 11). In other jurisdictions, notification forms allow at most a free-text field for 'clinical comments' or

'risk factors', and detailed risk factor data are sought by PHNs, public health officers or epidemiologists and entered directly into their database. The explanatory notes for the national dataset do provide excellent guidance as to the types of conditions to be included in each domain. However, grouping of risk factors (eg into 'chronic conditions') and the fact that data on the specific type of condition is held at the state and territory level (if at all) means that it may be difficult to extract useful risk factor data from the dataset. For example, while it would be simple to assess changes in IPD epidemiology and the impact of vaccination programs on people with functional and anatomical asplenia, it would be difficult to do the same for people with cochlear implants, intracranial shunts, Type 2 diabetes, or for transplant recipients (Table 11). Notable inconsistencies also exist for exposure to smoke and excessive alcohol use.

Usefulness of the public dataset

Several EIPDSWG members indicated that the provision of surveillance data in the public dataset had reduced the requests to OHP for data and felt that this dataset contained everything stakeholders required for their purposes. Nearly half of survey respondents indicated that they had used the IPD public dataset, including all who were affiliated with pharmaceutical companies. Most stakeholders reported that serotype (92% of respondents), demographic data (92%) and vaccination history (75%) were the most useful data fields in the public dataset. Overall, they found the data caveats and interpretation notes useful for understanding these data fields.

Vaccine developers and researchers identified currently unavailable surveillance data that they would find useful for their work (Table 12). To adequately assess the impact of the NIP, stakeholders wanted access to data from before 2009. Two respondents from vaccine manufacturers emphasised their need for finer stratification for children aged under five years to reflect the timings of 13vPCV immunisation in the NIP. Currently, the age of cases included in the public dataset is provided in five year age groups to prevent re-identification of cases. However, it is notable that quarterly reports published since March 2016, and the annual report for 2011-2012 have provided age in months (for cases aged under one year) and years (for cases aged one year to under five years) as well as Indigenous status, serotype, clinical category and risk factor data. One respondent suggested age stratification bands of zero to six months, seven to 23 months and two to five years for the public dataset.

Table 11 Risk factors for IPD infection (and therefore groups targeted for vaccination) compared with data domains for Victorian and Queensland IPD data collection forms and the national enhanced IPD surveillance dataset, 2016.

Risk factors for infection (red=highest increased risk; blue=increased risk) (23)	Victorian IPD notification form (68)	Queensland IPD case report form (69)	National dataset risk factor data domains (57, 67)
Functional or anatomical asplenia	Anatomical or functional asplenia	Anatomical or functional asplenia	Anatomic or functional asplenia
Immunosuppressive or radiation therapy	Immunosuppressive therapy	Immunocompromised; specify	Immunocompromised (eg transplant*, HIV, lymphoma, multiple myeloma, nephrotic syndrome, HTLV-1, IgA deficiency, chronic pancytopaenia, active SLE, other autoimmune disease, recent or current immunosuppressive therapy,) *included in dataset field specifications, but not in the explanatory notes
Haematological and other malignancies	Multiple myeloma Other cancer		
Solid organ or haematopoietic stem cell transplant	Organ transplantation		
HIV (including AIDS)	HIV infection		
Relapsing or persistent nephrotic syndrome	Nephrotic syndrome		
Autoimmune conditions (eg systemic lupus erythematosus, rheumatoid arthritis and multiple sclerosis)	Other immuno-compromising condition (including chronic pancytopaenia, IgA deficiency, active SLE, other autoimmune disease)		
Congenital or acquired immune deficiency, including symptomatic IgG subclass or isolated IgA deficiency			
Cochlear implants	-	-	-
Intracranial shunts	-	-	-
Chronic renal failure	Chronic renal failure	Chronic disease; specify	Chronic illness, including • chronic renal failure with reduced function • CSF leak • cardiac disease (ischaemic heart disease but not uncomplicated hypertension)
Cerebrospinal fluid leak	CSF leak		
Chronic cardiac disease: • particularly cyanotic heart disease or cardiac failure in children • excluding hypertension only (adults)	Cardiac disease (but not uncomplicated hypertension)		

Risk factors for infection (red=highest increased risk; blue=increased risk) (23)	Victorian IPD notification form (68)	Queensland IPD case report form (69)	National dataset risk factor data domains (57, 67)
Chronic lung disease, including: • chronic lung disease in preterm infants • cystic fibrosis • severe asthma in adults	Bronchiectasis Emphysema Chronic airway limitation (due to scarring/severe asthma requiring hospitalisation or chronic treatment)	Chronic disease; specify	• pulmonary disease (bronchiectasis, emphysema and other chronic airway limitations due to scarring, or severe asthma requiring hospitalisations/ regular treatment in the last 12 months) • chronic liver disease with reduced function • diabetes (types 1 & 2) • carcinoma not recorded under immunocompromised • Chronic or recurrent infections (eg chronic otitis media, pancreatitis) • any chronic condition that impairs physical functioning (eg cerebral palsy, significant dementia or other neurological deficit, malnutrition)
Chronic liver disease	Other chronic conditions impairing physical functioning (eg cerebral palsy, neurological deficit, malnutrition)		
-	Chronic or recurrent infections (incl pancreatitis, chronic otitis media)		
Diabetes or other metabolic disease	Diabetes (Type 1 or 2)	Chronic disease [as above] Metabolic abnormalities (case <15 years old only)	
Down syndrome	Congenital or chromosomal abnormality	Congenital or chromosomal abnormality	Congenital or chromosomal abnormality
Preterm birth at <28 weeks gestation	Gestational age	Premature (<37 weeks gestation)	Premature (<37 weeks gestation); specify gestational age
Tobacco smoking	Smoking status (current, ex, never)	Smoking status (current, ex, never)	Risk factors not identified elsewhere: • excessive alcohol consumption • smoke exposure (smoker or ex-smoker; passive household exposure to smoke even if a person smokes outside only) • exposure to campfire/cooking smoke >1 per week at time of illness • History of previous pneumonia
	Smoker in household	Smoker in household (case <15 years old only)	
Alcoholism	Alcohol-related problems	Alcohol excess	
-	Attended grouped care outside home for >4 hrs within 4 weeks of onset	Childcare attendee	Attended grouped childcare (>4 hrs cumulative) within the preceding 4 weeks
-	Previous diagnosis of IPD	Previous episode of IPD	Previous episode of IPD

Table 12 Extant surveillance data (not currently available in the public dataset) that vaccine manufacturers and researchers who responded to the stakeholder survey would find useful, 2016.

Vaccine manufacturers	Researchers/Academics
• Finer age stratification for <5 years • Serotype data for WA • ACT data (combined with NSW) • Pre-2009 data • Data updated quarterly • Vaccine failures • Timing of vaccinations • Clinical risk factors	• Deaths • Specimen site (if not in the clinical category) • Pre-2009 data

Individual identification of vaccine failures would also be useful. These data are collected by jurisdictions for discussion at EIPDSWG meetings and included in the Quarterly reports, but are not explicitly included in the NNDSS (57). One stakeholder, who is involved in research, indicated that data on other vaccines received by the cases would be useful. This respondent may have been interested in the role of influenza vaccination on the risk of IPD (9, 70, 71).

Usefulness for monitoring antimicrobial resistance (AMR)

Qualitative susceptibility to first-line antimicrobials used in clinical management of IPD (penicillin and cefotaxime/ceftriaxone) is routinely tested by diagnostic laboratories. However, completeness of this field for cases diagnosed by culture over the study period was low, at 78% nationally— a result largely due to completeness of only 3% in Western Australia (Figure 8). This is due to problems with transmission of data from the primary laboratories, and the Western Australian database not containing a data field for minimum inhibitory concentration.

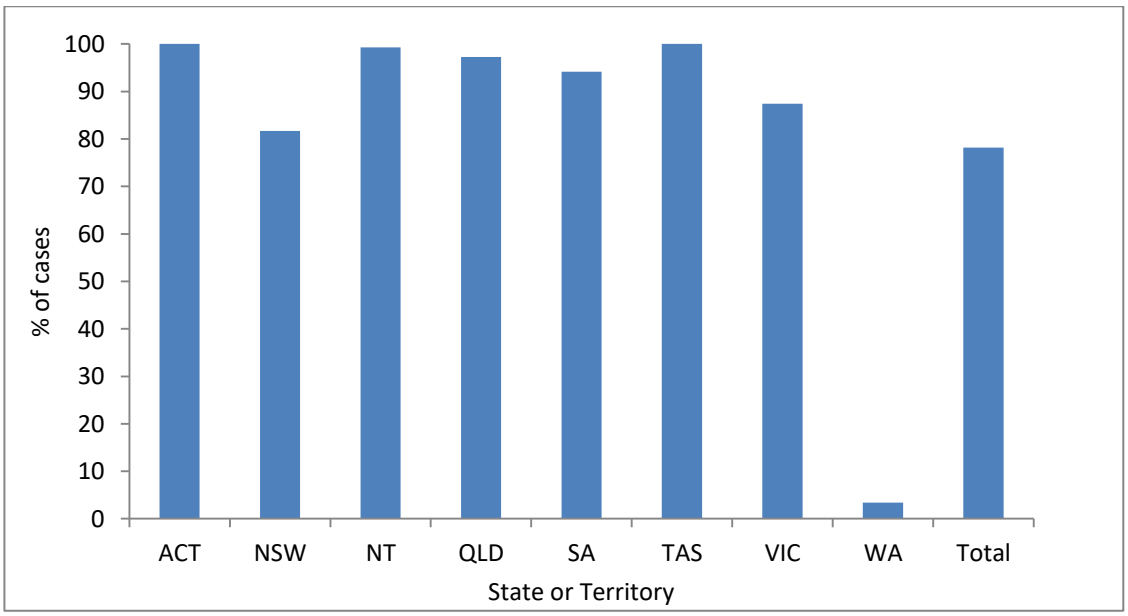

Figure 31 Proportion (%) of notified IPD cases diagnosed by culture for which qualitative susceptibility to first-line antimicrobials (penicillin and cefotaxime/ceftriaxone) is reported, by State or Territory of residence, Australia, 1 July 2013 - 30 June 2016.

The surveillance program was set up to also collect quantitative susceptibility to the full panel of 14 antimicrobials (including penicillin and cefotaxime) tested under standard conditions in a reference laboratory. However, reference laboratories do not receive funding from the Australian Government for this, as they do for serotype testing (72). There is reference laboratory susceptibility data in the IPD dataset for only 7% of cases nationally over the study period (data not shown), and these include information for, at most, four antimicrobials. The method of susceptibility testing and the panel of antimicrobials tested are not uniform across the four reference laboratories. Some laboratories do test samples and forward the data to the jurisdictions, but these data are not necessarily routinely entered for transmission to the NNDSS.

The Australian Group on Antimicrobial Resistance (AGAR) conducted six surveys of AMR in *S. pneumoniae* in invasive and non-invasive infections between 1989 and 2007 (73), assessing quantitative susceptibility to up to eight antimicrobials in 20 laboratories. These surveys demonstrated steadily increasing rates of AMR, including an increase in multi-resistant strains. However, the group is not planning to conduct further surveys (74).

According to the World Health Organization, AMR

> *…threatens the very core of modern medicine and the sustainability of an effective, global public health response to the enduring threat from infectious diseases …Without harmonized and immediate action on a global scale, the world is heading towards a post-antibiotic era in which common infections could once again kill. (75)*

Under the implementation plan for Australia's First National Antimicrobial Resistance Strategy 2015 – 2019, the Australian Government has made a commitment to "minimise the development and spread of antimicrobial resistance and ensure the continued availability of effective antimicrobials" (76). One objective included in this plan is to develop nationally coordinated surveillance of AMR. Monitoring of AMR is additionally important for *S. pneumoniae* to allow comprehensive evaluation of immunisation programs. This is because vaccination can reduce circulation of resistant serotypes (eg as seen the reduction in IPD caused by serotype 19A following the introduction of the 13vPCV (35)), and also by reducing the need for antimicrobial prescribing for both invasive and non-invasive disease (73). This topic is one that has been discussed at EIPDSWG meetings and arose repeatedly in interviews for this evaluation. For example

> *…we need a consensus on how this will be approached. Is the clinical management susceptibility data adequate?—and what is its quality?—or will we move to reference labs? This has funding implications…*

Surveillance data has been requested by the AURA project for monitoring *S. pneumoniae* resistance. Establishing a parallel system for monitoring AMR would capture data about non-invasive disease, but would lack the richness of the enhanced data provided by the IPD surveillance program. Therefore, it is essential that reference laboratory AMR surveillance is conducted as a part of the existing enhanced IPD surveillance program.

Usefulness for informing clinical practice

Providing reliable data to inform clinical decision-making is not a direct objective of the program, but there is evidence that the IPD data is used this way. For example, an EIPDSWG member representing a reference laboratory reported:

> *I direct people to the data and reports frequently. For example, a clinician had a patient with an unusual serotype. They wanted to know how common it was, I could direct them to the online reports and dataset. Also,*

paediatricians want to know about AMR trends to inform their treatment decisions – (Reference laboratory)

One survey respondent, who identified themselves as a paediatrician and researcher/academic made the following suggestion for additional reporting from surveillance data:

Provide an easy to access website that you can access on your phone to review IPD condition frequency, serotype distribution, and antibiotic resistance profile of IPD in your region. Ideally, this should allow the user to access results according to different time frames and according to different age groups at the bedside. It would be most helpful if this was part of a larger database that allow access to this information for all important invasive infections rather than just limited to IPD.

Usefulness of the Working Group as a communication network

Several interviewees noted the importance of the working group as a means of rapid communication between jurisdictions, for example:

Queensland saw breakthrough cases of 19A after PCV13 6-8 months before other jurisdictions. The Working Group forum allowed us to keep others on the look-out

Another EIPDSWG member noted

I've been on five committees over the years and this one is the most productive—a big focus on high quality and accurate data.

However, one member stated the Working Group would function better if members met face-to-face once a year, and another thought that there was opportunity for more collaborative projects involving all members.

Recommendation 2

Collect complete surveillance data for all cases in all jurisdictions. If resource constraints preclude this in some jurisdictions, consider following-up of a random sample of cases aged five to 50 years in these jurisdictions.

This is a priority recommendation

Recommendation 3

Ensure researchers and vaccine developers can access the data at the level of detail they require in the public dataset, while maintaining the privacy of cases. This includes

- *finer stratification of age-groups for cases aged less than five years*
- *data from 2001 onwards*
- *all available serotype data*
- *data on vaccine failures.*

This is a priority recommendation

Recommendation 4

Harmonise notification processes, data collection forms and data transmission from the jurisdictions to the NNDSS. This should include standardising risk factor data domains to ensure they reflect groups at high risk of IPD, as identified in the Australian Immunisation Handbook 10th Edition*.*

Recommendation 5

Improve the completeness and quality of antimicrobial resistance (AMR) data by

- *investigating the poor completeness for first-line AMR data from Western Australia*
- *agreeing on the standards for reference laboratory AMR testing*
- *advocating for funding for reference laboratories to collect these data for every case*

This is a priority recommendation

SIMPLICITY

One EIPDSWG member described the program as "a fine system – not the easiest to use…and intricate…but not too bad for a complex disease". Confirmation of IPD cases is more straightforward than for some other notifiable conditions (for example, Hepatitis B), and of the five stakeholder survey respondents who

indicated that they had notified a case of IPD, three described the process as ‘extremely easy’ and the remainder described it as ‘somewhat easy’. However, the surveillance program is not a simple system. This is largely due to the collection of enhanced data. The flow of data is complicated (Figure 5), and this is compounded by the fact that data collection systems are not harmonised across jurisdictions.

The two stakeholder survey respondents who had requested line-listed surveillance data described the request process as ‘somewhat difficult’ and ‘neither easy nor difficult’, but did not elaborate. This process is currently under review by OHP.

DATA COMPLETENESS AND QUALITY

Results of the completeness of AMR data is presented under the findings related to usefulness in Section 3.3.1

Serotype and Vaccination History

In the 2014 *Project Agreement for Vaccine Preventable Diseases Surveillance Program* (66), the Commonwealth of Australia agreed to provide a financial contribution to the states and territories for the reporting of surveillance data on nationally notifiable vaccine preventable diseases. The Agreement specifies performance indicators against which the jurisdictions must report annually. I do not have access to these reports, but have assessed performance against the indicators relevant to IPD using surveillance data collected during the evaluation study period (1 July 2013 to 30 June 2016).

The first indicator is that “the Serogroup Subtype field is completed (where lab [sic] diagnosis method allows) for…cases younger than 5 years or older than 50 years for equal to or greater than 80% of notified cases” (66). As shown in Figure 9, all the jurisdictions other than South Australia (64% serotype data for age less than five years) are achieving above this target.

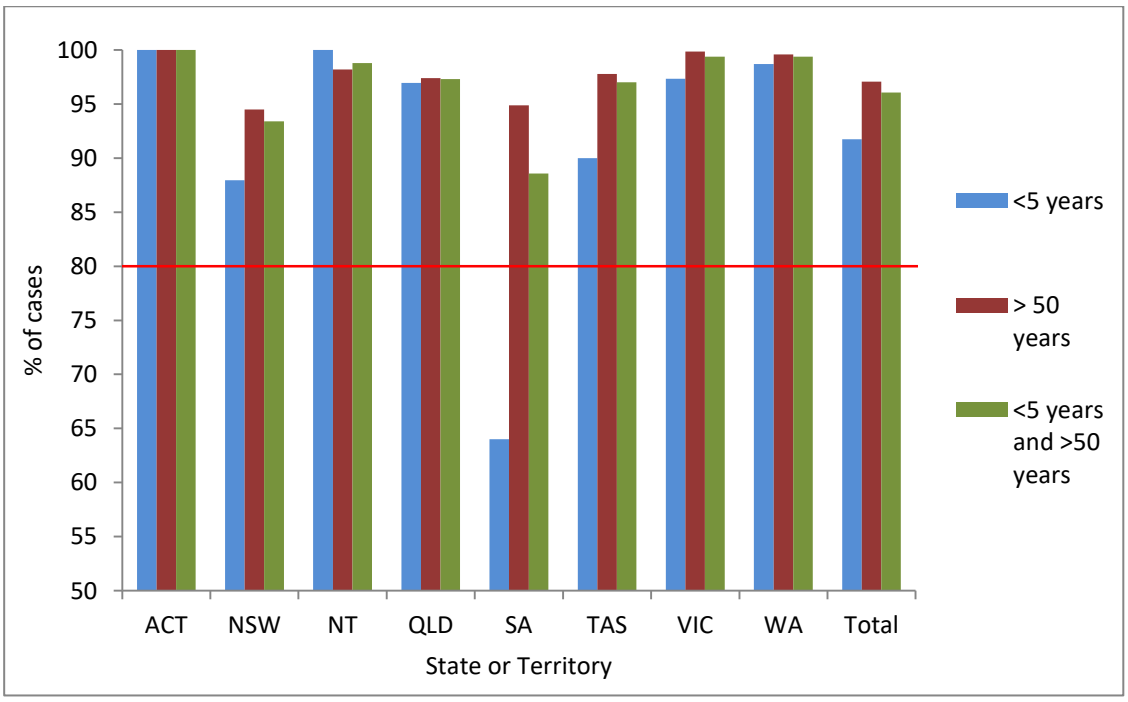

Figure 32 Proportion (%) of notified IPD cases in age groups targeted for vaccination for whom serotype data is complete, by State and Territory, Australia, July 2013 to 30 June 2016. This does not include for cases for which the isolate could not be tested. The red line (at 80%) indicates the performance target specified in the *Project Agreement for Vaccine Preventable Diseases Surveillance Program* (66).

Availability of serotype data for all ages is also markedly lower in South Australia compared with other jurisdictions (Table 13). Working group interviewees perceived this to be a problem of South Australian diagnostic laboratories not forwarding a large proportion of PCR-positive isolates to the reference laboratory for typing, because they do not think there is sufficient genetic material. Among cases aged under five years in South Australia over 37% of diagnoses are made by PCR alone, compared with 0.4% in cases aged over 50 years. This is the likely cause of the poor performance of this state against the above target.

The second indicator is "vaccination information is completed for children aged less than 7 years…for equal to or greater than 95% of notified cases where their vaccination status is recorded on the Australian Childhood Immunisation Register" (66). Nationally, this target is not being reached, due to only 87% completeness in NSW, the state with 30% of cases in this age group (Figure 10). This state also achieved only 91% completeness for cases aged less than five years. All other jurisdictions have met this target over the study period. Upon further investigation, this appears to be a problem of transmission of data to the NNDSS.

Table 13 Proportion (%) of all notified IPD cases for which serotype data is provided, by State and Territory, Australia, 1 July 2013 - 30 June 2016.

State or Territory *	Serotype data available (%)	Isolate not typable, not viable or result pending (%)	Typing not attempted (PCR) (%)	Untyped (%)	Not referred for typing (%)
ACT	100.0	0	0	0	0
NSW	94.0	0	0	0.5	6.0
NT	98.0	0.7	0	0	1.0
QLD	94.0	0.3	3.0	0.8	2.0
SA	84.0	4.0	3.0	0	9.0
TAS	94.0	0.8	0.8	0	5.0
VIC	97.0	2.0	0	0.7	0.7
WA	98.0	1.0	0.5	0.4	0
Australia	94.0	1.0	0.7	0.5	3.0

** Row totals may not sum to 100% due to rounding*

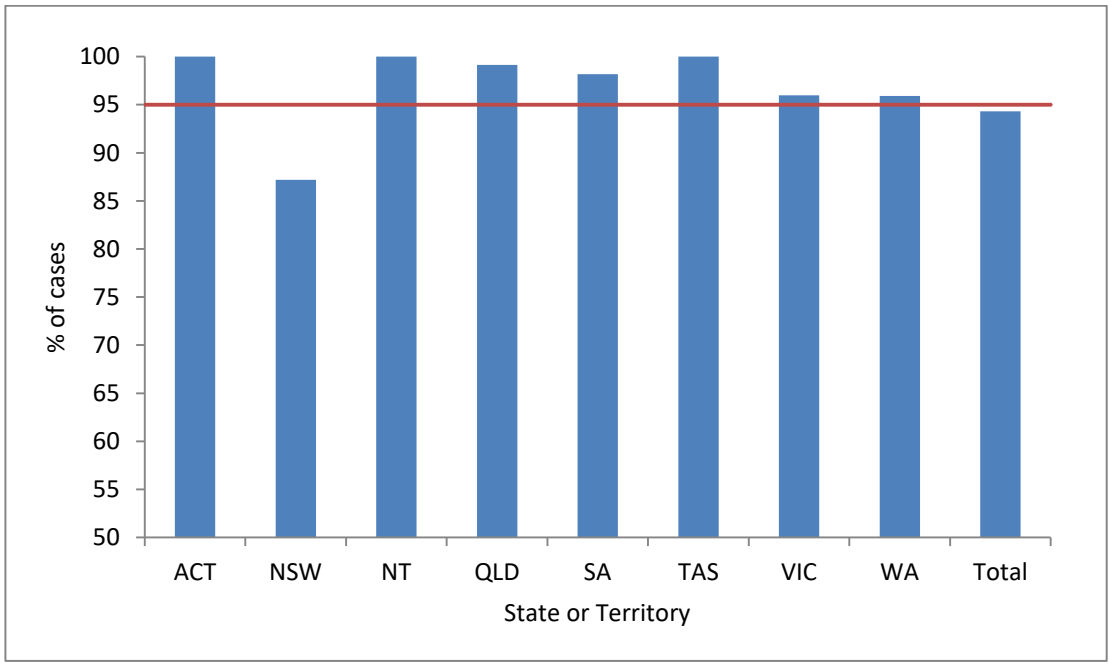

Figure 33 Proportion (%) of notified IPD cases aged under 7 years for whom vaccination data are complete, by State and Territory, Australia, July 2013 to 30 June 2016. This does not include cases whose data was sought but was not available. The red line (at 95%) indicates the performance target specified in the *Project Agreement for Vaccine Preventable Diseases Surveillance Program* (66).

When the vaccination completeness data for all ages is examined, there is a much greater variation between jurisdictions (Figure 11). In 2016, the ACIR was expanded to become the whole-of-life Australian Immunisation Register (AIR) for all NIP and most privately-funded vaccines (77). As a result, I would expect a

marked improvement in the completeness of vaccination fields in the future. However, the degree of improvement in NSW, Victoria and Queensland would depend upon the commitment of these jurisdictions to follow-up every case.

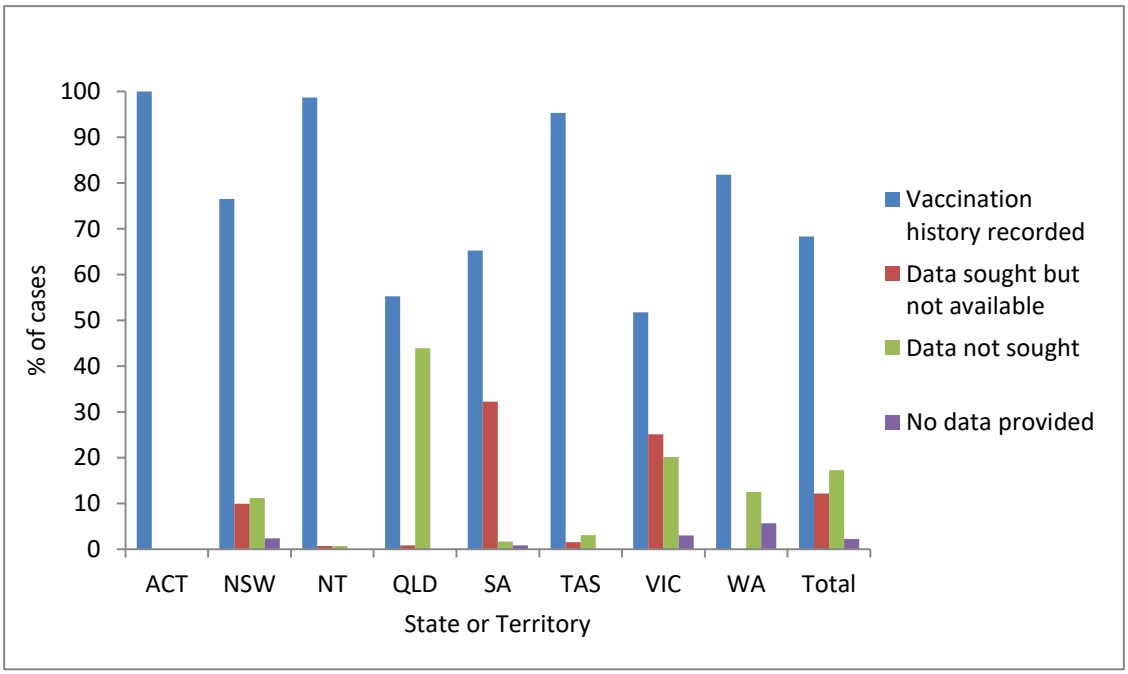

Figure 34 Proportion (%) of all notified IPD cases for which vaccination history data are provided, by State and Territory, Australia, 1 July 2013 - 30 June 2016.

Hospitalisation and mortality

Hospitalisation and mortality are the only measures of severity and cost burden of IPD cases collected in the surveillance dataset. Hospitalisation (which includes admission to an emergency department for more than four hours) is one of the least complete fields in the enhanced IPD dataset (Figure 12A). Only ACT and Western Australia provide data for this field. The hospitalisation status of a case was ratified as a core data field of the NNDSS in March 2016, and included in the IPD data collection form in April 2016, so it was not routinely collected before this date.

Deaths from IPD are defined as "those due to a current invasive pneumococcal infection even if the case has a pre-existing terminal condition or other co-morbidities that contributed to their death" (57). The EIPDSWG provides a flowchart with clear guidance for recording IPD deaths (57). Although mortality is recorded in over 90% of notified cases nationally (Figure 12B), IPD deaths may be misclassified, particularly if they occur many weeks after the notification was received, were not hospitalised, or died after discharge. Again, access to electronic

records would improve the completeness and accuracy of death data, as noted by one EIPDSWG member who represented a jurisdiction:

> *...perhaps getting access to all digital medical records will allow us to systematically follow-up cases to find out who has died from their IPD. We don't have the resources to keep ringing up, and staff change in hospitals, making it difficult.*

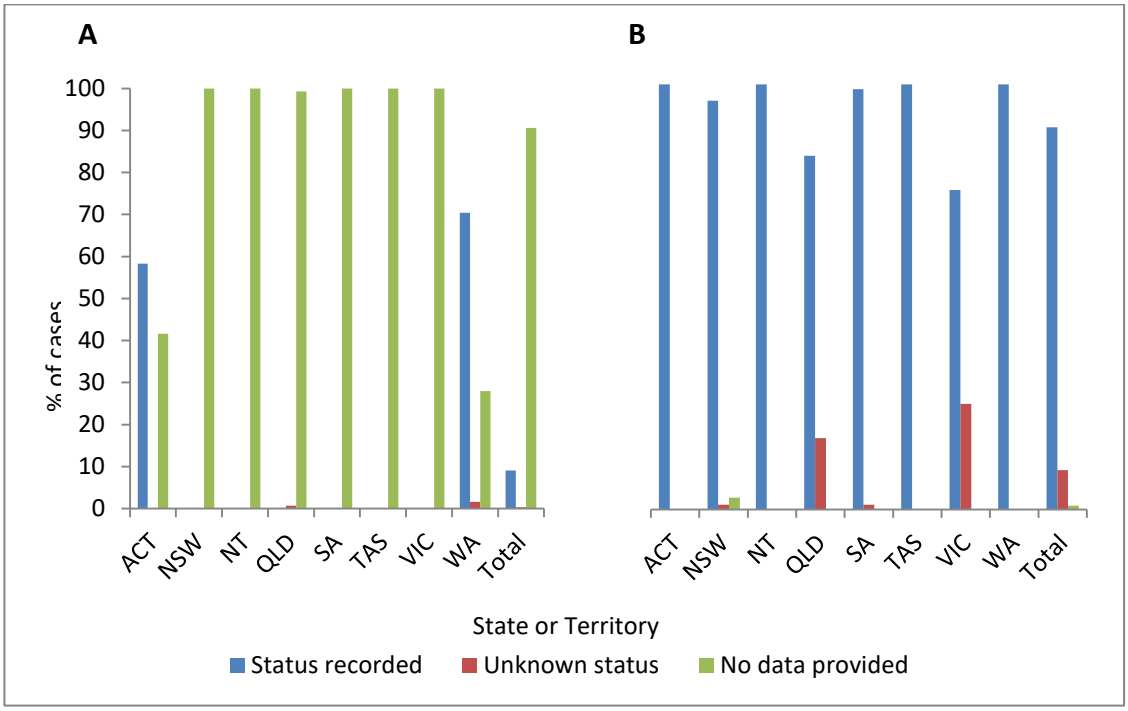

Figure 35 Proportion (%) of all notified IPD cases for which (**A**) hospitalised and (**B**) mortality data are provided, by State and Territory, Australia, 1 July 2013 - 30 June 2016.

Indigenous Status

In 2004, the year that recommendations were made in the *Improving Indigenous Identification in Communicable Disease Reporting Systems* report (78), Indigenous status was recorded in slightly under 80% of IPD cases nationally. Over the evaluation period, recording of Indigenous status was higher at 90% (Figure 13). This is an excellent result when compared with NNDSS data as a whole, which had only 45% completeness for this field in 2014 (31). Reporting in the ACT improved dramatically (6% in 2004 versus 100% in the evaluation study period), but worsened in Victoria (93% versus 77%). Further improvements in completeness and quality of this data field can be expected with continued promotion and implementation in hospitals, GP practices and diagnostic laboratories of the National Best Practice Guidelines for Collecting Indigenous Status in Health Data

Sets (79). In a small study in one PHU in NSW, staff were able to increase the completeness for this field to 99% in IPD cases by referring to the electronic hospital admissions database (80). This process took less than five minutes per case.

Figure 36 Proportion (%) of notified IPD cases for which Indigenous status data were provided in 2004 (56) and the period 1 July 2013 - 30 June 2016, by State and Territory, Australia. Completeness data for all diseases recorded in the NNDSS in 2014 is provided for comparison (31).

Clinical data

The completeness of the clinical category and risk factor data fields over the study period is shown in Figure 14. Cases for which clinical category data are missing include those coded as 'Other' (neither bacteraemia, meningitis, nor pneumonia), but with no further details. Nationally, completeness was 86% for clinical category and 74% for risk factor data. The poorest performance was in jurisdictions where all age groups are not routinely followed-up and where surveillance staff do not have access to electronic medical records.

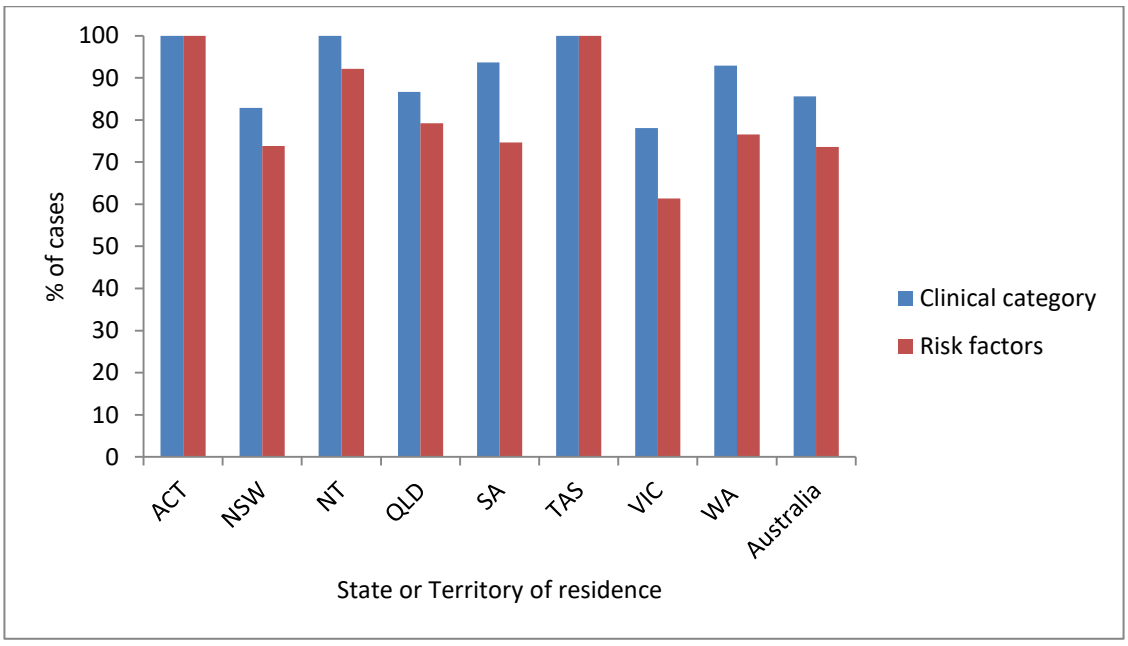

Figure 37 Proportion (%) of notified IPD cases for which data on clinical category and risk factor data is provided, Australia, 1 July 2013 - 30 June 2016.

It is clear that enhanced data collection for IPD surveillance would be greatly improved through access to a single electronic health record. Integrated state-wide electronic medical inpatient record systems are being implemented across public (but not private) hospitals in NSW (81) and Queensland (82). Unfortunately, although electronic records systems are being rolled out in Victorian hospitals, these systems are not integrated across the state, so the access to enhanced data will vary across PHUs. Currently, only Queensland has an exclusively electronic laboratory notification system. All private and public laboratories participate in this system and there is a governance structure to ensure notifications are made to standard. Two other jurisdictions have electronic notification systems, but they also receive notifications by fax and mail, and in one jurisdiction the data from the electronic form must be manually entered into the surveillance database.

Data Quality

Overall members of the EIPDSWG reported that the quality of data had improved over the last few years, to the point where the data is now highly reliable. This is particularly the case since OHP has been sending extracts from the NNDSS back to the jurisdictions for checking prior to the preparation of the quarterly report. Logic checking of NNDSS entries has also helped.

In analysing the surveillance data, I encountered a number of errors in the chronology of dates, and also logical inconsistencies between 'laboratory diagnosis method' and 'serotype'. These errors (in date and other field types) could be avoided by ensuring jurisdictional databases have controls that prevent entering non-logical data, and by conducting post-entry logic checks at the jurisdictional level, when data verification is easiest.

Recommendation 6

Advocate for all jurisdictions to implement exclusively electronic laboratory notification systems, ensuring that these systems collect data consistent with the NNDSS data fields.

Recommendation 7

Support jurisdictions to update their databases to prevent entering non-logical data and to conduct post-entry logic checks, where these are not already in place.

FLEXIBILITY

EIPDSWG members almost universally agreed that the program is flexible enough to accommodate changes in IPD epidemiology and available vaccines. Most stakeholders also thought the program could do this very or extremely well. Examination of the core and enhanced data fields revision history indicates multiple changes to both datasets since 2001, including changes to reflect the introduction of the 13vPCV and the identification of new serotypes. Representatives from the jurisdictions and OHP data managers indicated that, technically, it was easy to alter dataset fields or domains, although the bureaucratic process to obtain permission may be lengthy.

In contrast, both EIPDSWG members and stakeholders had less confidence in the program's ability to adapt to changes in laboratory methods. The proportion of notified cases confirmed by PCR only has increased from 0.1% in 2001 and 2002 to

6.8% in the 2015-16 financial year. This has likely resulted in a slight increase in sensitivity and decrease in specificity, as presence of the pathogen's genetic material does not necessarily indicate disease. Also, isolates obtained for PCR are less useful than cultures for determining serotype and AMR. Data on laboratory methods are reported in the IPD annual reports, but not the quarterly reports or public dataset.

Several EIPDSWG members foreshadowed the emergence of whole-genome sequencing (WGS) for diagnostic and surveillance purposes. In a study in Canada, public health laboratories assessed the utility of WGS for routine pneumococcal surveillance by testing a random sample of surveillance isolates collected over a four year period (83). Overall, the researchers demonstrated 95% sensitivity and 100% specificity of genomic prediction of susceptibility to erythromycin, clindamycin, chloramphenicol and tetracycline; and a 98% success rate for predicting sequence type. In a similar study in the US, the Active Bacterial Core surveillance (ABCs) team subjected over 80% of *S. pneumoniae* surveillance isolates collected in 2015 to WGS using a bioinformatics tool, or "pipeline", to predict antimicrobial phenotypes (84). The authors concluded that

> *the capability of our WGS pipeline to accurately and reliably predict antimicrobial testing results for currently recovered IPD isolates to six different β-lactam antibiotics, erythromycin, clindamycin, cotrimoxazole, tetracycline and chloramphenicol. In addition, the pipeline detected rare instances of fluoroquinolone-resistance and [rifampicin]-resistance. This sampling of recent national surveillance IPD isolates gives an accurate assessment of the pipeline's reliability for detecting and measuring individual resistance phenotypes, and for determining the frequencies of different resistance mechanisms. WGS-based methodology is an effective substitute for [broth dilution testing] that also serves for concurrent determination of other critical pneumococcal strain features. As technical advancements continue, WGS technology may be employed in future clinical settings for deducing key pathogen parameters relevant to patient care. The high concordance of WGS-based predictions with pneumococcal antimicrobial phenotypes is compatible with this goal.*

The move towards WGS for diagnosis and surveillance appears inevitable and will lead to profound advances in the understanding of communicable disease epidemiology (85) and enhance outbreak detection (86, 87). The speed of change

in next-generation sequencing indicates that WGS may soon be comparable to conventional laboratory methods in terms of time and cost (85, 88). However, the shift to WGS is not without its challenges, and will require clear guidelines, robust protocols and standard operating procedures not only for sample preparation and sequencing (wet laboratory), but also for the computational assessment (dry laboratory) of the results. The interpretation of billions of sequence reads is by no means trivial, and improvements in the availability of 'user-friendly' software and enhancements in computer and data storage infrastructure will be of paramount importance for the realization of the potential of these technologies.(89)

The European Centre for Disease Prevention and Control expects that, in the next five years, it will have standards and systems in place to allow WGS to replace all other typing methods used for microbial surveillance across the European Union (88). Following this lead, now is the time for the EIPDWG to initiate work with OHP, the Public Health Laboratory Network, and other relevant parties to plan for such a change in Australia, ensuring that standards and formats allow data to be shared and synthesised internationally. The EIPDSWG may also wish to initiate or auspice pilot implementation studies of WGS using Australian IPD surveillance data.

Recommendation 8

Working with relevant partners, plan for the shift towards whole genome sequencing by overseeing the development of quality standards for IPD sequencing and bioinformatics, and by auspicing pilot implementation studies.

ACCEPTABILITY

From the interviews with EIPDSWG members, it is clear that the program is highly acceptable. As one interviewee noted

> *Because of the buy-in of the Working Group who are passionate (especially in the NT), this leads to a commitment to collecting useful data to inform decisions. Overall, all parties want to collect the info—it's not like pulling teeth to get it (OHP/NCIRS).*

As a system reliant upon laboratory diagnosis, the success of this program has also been largely a result of engagement with diagnostic laboratory networks during the planning and early implementation phases in 2000 and 2001. However, one representative of a reference laboratory gave the following warning:

> *We hear more and more from our colleagues in primary labs that they have more and more work to do and they feel it is not their business to do surveillance...the increase in work is leading to missing data/missing isolates/missing cases. The weight of gathering the info is shifting from reference lab to public health unit to collect.*

Ongoing work is required to ensure the commitment of laboratories to forward isolates to the reference laboratories for serotyping and AMR testing. This is particularly the case for South Australia, where many PCR-positive isolates are not forwarded. The EIPDSWG and the Public Health Laboratory Network have published guidelines for collection, storage, and transport of PCR-positive specimens (90). However, these guidelines are verbose and would benefit from a review. A simple, colourful flowchart, highlighting the value of serotype data and distributed to laboratories through an appropriate method may assist. Direct engagement with laboratory networks may also be required.

Although the EIPDSWG provides an annual report, tailored by jurisdiction, to all laboratories, only one of the six survey respondents from diagnostic laboratories was certain that they had ever received such a report. Respondents indicated that they would like to receive summary reports, with serotype data reported at the national and regional level. One respondent emphasised that they would like the serotyping method to be reported in both the laboratory summary and in the public dataset.

Recommendation 9

Work with the Public Health Laboratory Network to enhance engagement and communication with diagnostic laboratories to ensure their full participation in the program. This should include a review and promotion of the guidelines for forwarding samples to the reference laboratories.

SENSITIVITY

Sensitivity refers to the proportion of cases of disease detected by the program. Eighty percent of EIPDSWG members thought that the sensitivity of the program was excellent, with the remainder rating it as good. They felt that the severity of the disease meant that most cases were detected. Stakeholders' ratings were slightly less favourable, with most rating the sensitivity as good.

According to the objectives of the program, it should identify every case of IPD in Australia (sensitivity of 100%). The true sensitivity of the program could only be estimated through methods such as a capture-recapture analysis. The factors affecting the ability of the system to capture every case (shown in *Figure 15*) are generally outside of the control of the EIPDSWG. As IPD is usually not a mild disease, there will be only a small proportion of true IPD cases who do not present for health care. However, obtaining specimens from sterile sites is not straightforward, and in some cases (e.g. meningitis with raised intracranial pressure) may be contraindicated (2). As one EIPDSWG member noted, "clinical management should always determine whether or not a specimen is collected". Blood culture methods may detect *S. pneumoniae in* as few as 10% to 20% of pneumococcal pneumonia cases (91). Failure to detect or isolate *S. pneumoniae* may be due to the sporadic nature of bloodstream invasion, poor handling of the specimen, and prior administration of antimicrobial treatment (3). The availability of PCR, the results of which are unaffected by antimicrobial treatment, has improved sensitivity, although serotyping from PCRs is less sensitive. According the one EIPDSWG member, some cases are missed by surveillance "because the clinician and primary laboratory forget that certain sites should be sterile, like pleural fluid or the brain".

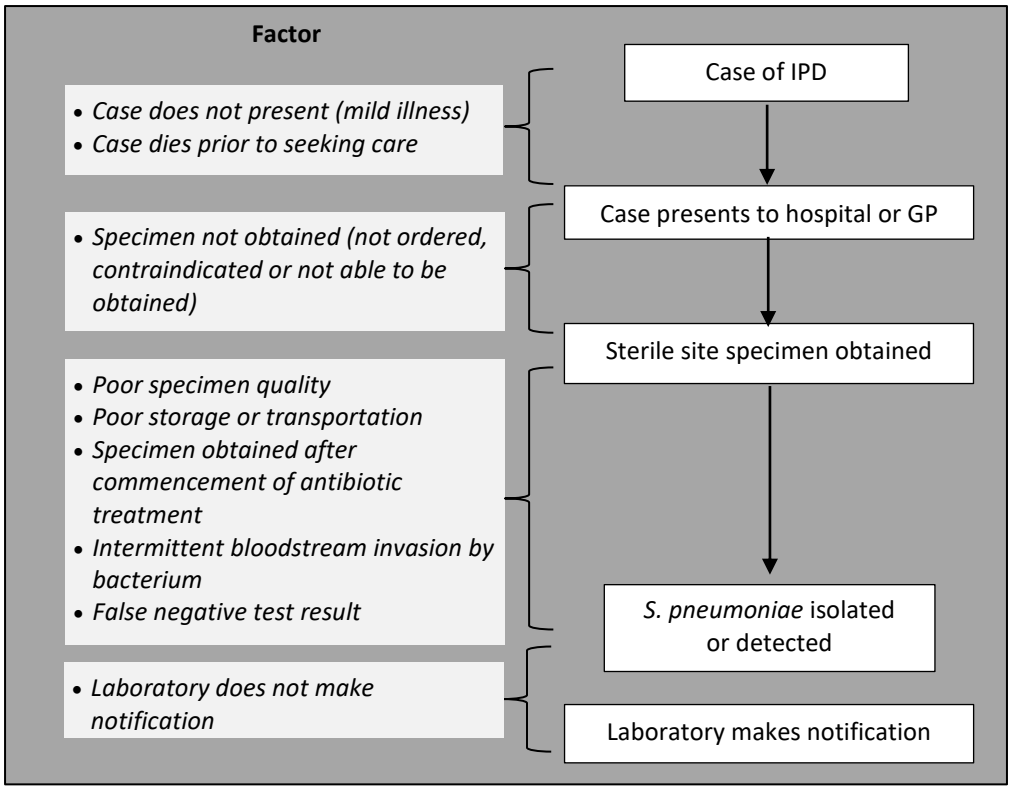

Figure 38 Factors affecting sensitivity of the IPD surveillance Program (1-3)

Some EIPDSWG members suggested that the case definition could be broadened to include detection of *S. pneumoniae* antigen in urine. Urinary antigen testing is increasingly used in clinical practice due to the ease of obtaining a sample and because (as for PCR) administration of presumptive antimicrobials will not affect the result. The EIPDSWG has previously referred this question to the Public Health Laboratory Network.

The sensitivity of a surveillance system also refers to its ability to detect an outbreak. This is discussed below. As enhanced data on clinical category of IPD is collected, the program's sensitivity to changes in IPD epidemiology in terms of types of clinical presentation is reasonably high. However, as discussed above, missing data for cases aged five to 50 years reduces its sensitivity.

REPRESENTATIVENESS

As the true sensitivity of the program is unknown, it is difficult to determine if there is any pattern to missed cases that would reduce the program's ability to accurately describe the occurrence of IPD over time and its distribution in the population by place and person. However, it is clear that there is relatively lower completeness for cases

aged between five and 50 years of vaccination history, Indigenous status, and enhanced data fields (including risk factors), compared with other cases.

PREDICTIVE VALUE POSITIVE

The predictive value positive of the surveillance program is the proportion of notified cases that truly have IPD. As only laboratory-confirmed (not suspected) cases are notified, it is rare for non-IPD cases to be notified, and so it is likely that the PVP is high. EIPDSWG members representing jurisdictions reported that the handful of notified cases that turn out not to be IPD are mainly due to

- laboratories or clinicians notifying detection or isolation of *S. pneumoniae* from
    - a non-sterile site (eg sputum, bronchial washings, ear swabs)
    - urinary antigen testing
    - post-mortem collection; or
- rarely, the reference laboratory identifies the isolate as a bacterium other than *S. pneumoniae*, despite a positive culture in the diagnostic laboratory.

Post-mortem cases are sometimes included, following review by the EIPDSWG.

TIMELINESS

The median time between the onset of disease and receipt of notification by the jurisdiction was six days nationally (Figure 16). Fortnightly lists of new cases are produced for the CDNA and published within a week on the Department of Health's website (92). The median time to publication of a year's IPD surveillance data in an annual report is four years (93), but was as long as seven years for 2009 data (14). Both EIPDSWG members and stakeholders indicated that the introduction of the quarterly reports has improved the timeliness of publically-available data. Over the study period 75% of quarterly reports were published three months after the end of the reported quarter, with the remainder published six months after. However, survey respondents representing vaccine developers indicated that the quarterly reports—although timely—did not have the level of detail they required. They wished to have access to the data behind the figures and aggregated tables in these reports. For these respondents, the annual reports and public dataset were not updated frequently enough to be of use.

Two-thirds of stakeholders and 90% of EIPDSWG members thought that the national data are analysed and reported frequently enough to inform prevention programs and policy. However, it appears that ensuring the high quality of enhanced data has come at some cost to timeliness, with one EIPDSWG member noting that:

> *There is a 10 month delay in the dump of enhanced data from NNDSS to NCIRS. There is a reason why it takes so long—all the checking and confirmation is time consuming—but it reduces the utility of the system (OHP/NCIRS).*

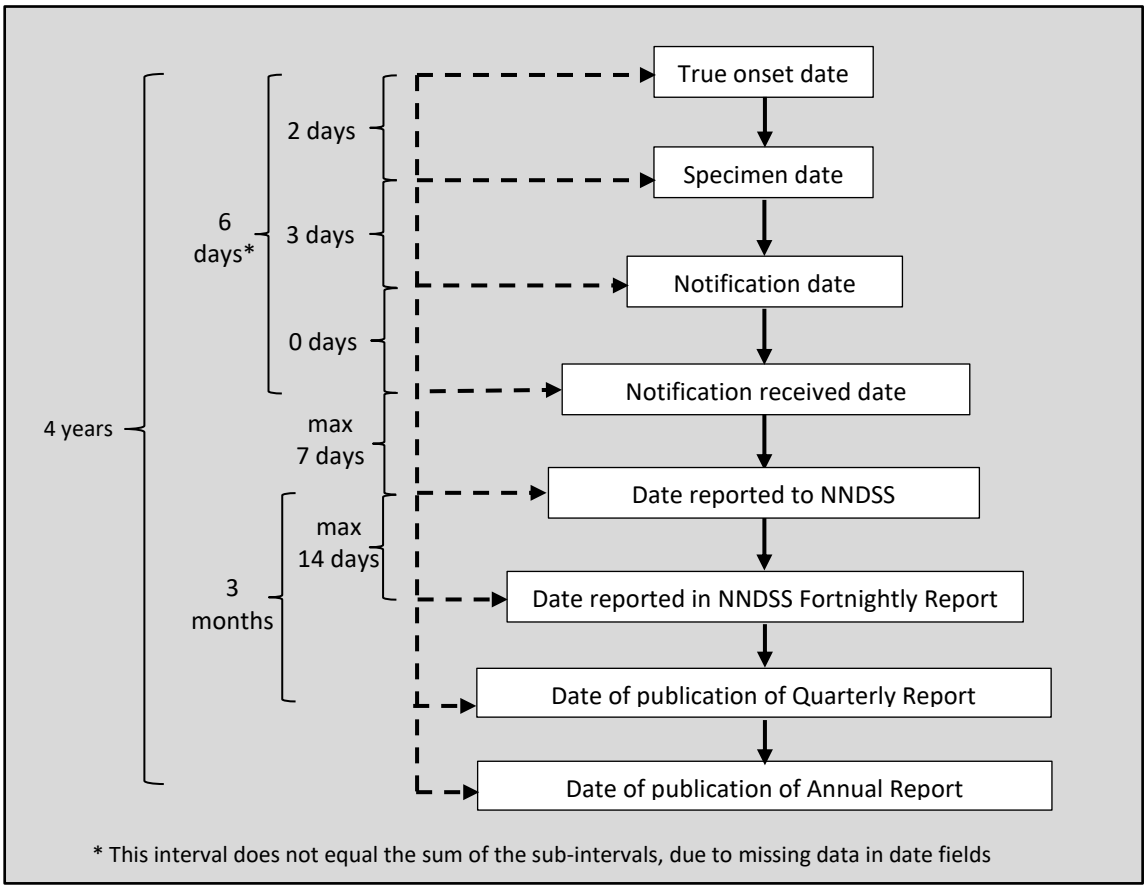

Figure 39 Median intervals between elements of case notification (1 July 2013 to 30 June 2016) and reporting (2001 – 2016) in Australia's enhanced IPD surveillance program.

EIPDSWG interviews revealed that delays in obtaining and verifying data are due to

- lack of access to electronic clinical records;
- delays in the production of hospital discharge summaries;
- absence of an 'all-of-life' vaccination register;
- batching of serotype testing and reporting by reference laboratories;
- diagnostic labs requiring prompting to forward isolates for typing (particularly for cases confirmed by PCR); and

- data cleaning and checking.

The detection of outbreaks of IPD is not an objective of IPD surveillance, and less than a quarter of stakeholders thought the program was capable of this. In contrast, three quarters of EIPSWG members thought that through the communication network of the EIPDSWG, surveillance was timely enough for jurisdictions to detect an outbreak. Several interviewees pointed to the experience of the multi-jurisdictional serotype 1 outbreak from 2010 to 2012 as an example:

> *An outbreak was identified in the NT using [jurisdictional] data. When we looked at data obtained through the Working Group we could see that the outbreak started some time earlier in WA.*

Nationally, 54% of cases with available and valid date data are notified within seven days and 80% within 14 days. However, it must be noted that it usually takes several weeks after notification for the jurisdictions to receive data on serotype for a case, making early identification of linked cases unlikely. One EIPDSWG member indicated that South Australia would have difficulty identifying linked cases due to this jurisdiction's difficulty in obtaining serotype data. Another indicated that they would find it helpful if the Working Group developed guidelines about what to do in case of a suspected outbreak.

STABILITY

Forty percent of EIPDSWG interviewees rated the stability of the program as 'excellent', and half rated it as 'good'. None indicated that there had been any significant periods during which the program could not function. The exception was one reference laboratory which became overwhelmed during the 2009 H1N1 influenza pandemic, and was unable to type about 20% of cases. These favourable responses reflect the fact that the program has operated for over 15 years without major problems, and that the NNDSS is a stable system. Again, the utility of the EIPDSWG as a governance and communication mechanism has been important in this regard. However, some members indicated they were concerned about the program's ability to function at the current level when long-term members left. They suggested that the high quality of enhanced data was heavily reliant upon the involvement of passionate members of EIPDSWG who have been a "driving force". Some jurisdictions and the OHP indicated there would be problems in data collection and quality if key public health staff left their

positions with no succession plan. One jurisdiction reported that they had already addressed this issue:

> *It used to be just one person in [jurisdiction] looking after IPD data, now it is spread across a few people. We often do training sessions on how to use the [data collection] form and using the metadata*

Some interviewees felt that the program was somewhat vulnerable to changes in funding priorities from the Australian Government, for example

> *It takes a lot of manpower to collect detailed information on not many cases. It may look to some as if [the program] has little bang for buck and is a good candidate for cost-savings (OHP/NCIRS).*

One member suggested that more work needed to be done to quantify the economic costs arising from IPD hospitalisations and deaths in order to demonstrate the "business case" for continued enhanced surveillance. To this end, it is important that useful IPD surveillance data, including high quality hospitalisation and death data, be readily available for such work.

Recommendation 10

Implement succession planning interventions to ensure there is depth of capacity within the EIPDSWG, reference laboratories and jurisdictions to maintain the program at the current high standard.

Conclusion

This evaluation verifies that the enhanced IPD surveillance program is one of Australia's most useful and stable disease surveillance systems. Nonetheless, the program is not performing to its full potential, particularly in terms of data collection for cases aged between five and 50 years to inform targeted vaccination programs, AMR monitoring, and providing easily accessible and useful surveillance data. The declining number of cases, the increasing availability of vaccination data for all ages on the AIR, and the continued move towards electronic medical records should put complete data collection for all cases within the reach of all jurisdictions. Ongoing work is required of the EIPDSWG to ensure complete AMR testing; to harmonise notification, data entry and transmission processes; and to plan for the shift to whole-genome sequencing.

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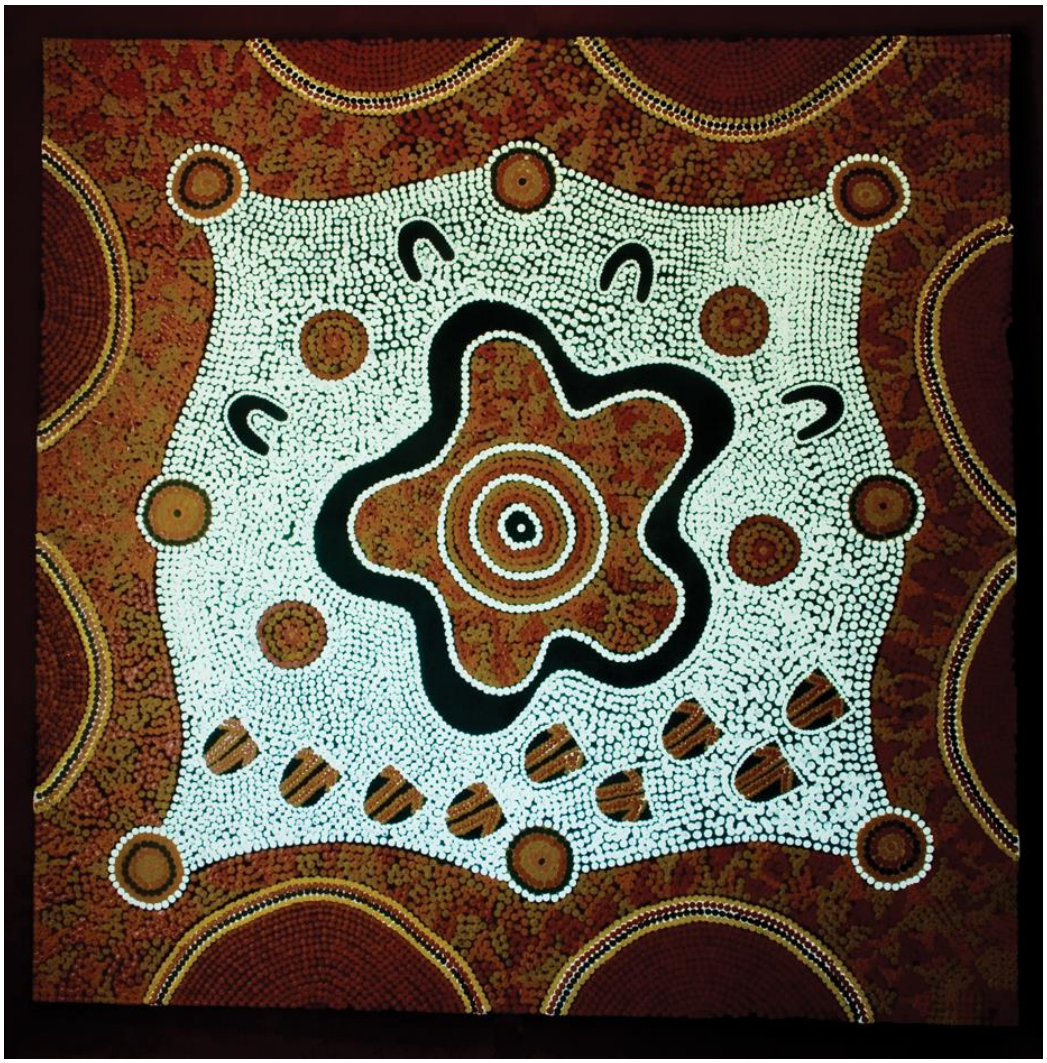
CHAPTER 5 – NEW DIRECTIONS: MOTHERS AND BABIES SERVICES: AN EVALUATION OF THE PROGRAM USING AUSTRALIAN EARLY DEVELOPMENT CENSUS DATA 2009 - 2015



Alex Marmor, Dr David Harley and Nick Pascual

Australian Government
Department of Health

Australian National University

We have a catchy mantra of 'Closing the Gap', which in many ways suggests that as blackfullas we are here; other Australians are there; with a big gap in the middle that leaves us blackfullas with some catching up to do if we are to be as good as the average Australian. When in fact the truth is reflected in the less catchy notion of 'shifting the bell curve to the right', a notion that reminds us all that many Aboriginal people are as exceptional as our fellow Australians.

Dr Chris Sarra

Artwork: Making Two Worlds Work Project, developed by Mungabareena Aboriginal Corporation and Women's Health Goulburn North East, 2008. www.whealth.com.au/mtww

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ABBREVIATIONS

AEDC	Australian Early Development Census
AIHW	Australian Institute of Health and Welfare
ANAO	Australian National Audit Office
IARE	Indigenous Area
MSI	Multiple Strengths Indicator
NAPLAN	National Assessment Program – Literacy and Numeracy
NDMBS	New Directions: Mothers and Babies Services

DISCLAIMER

This report uses data from the Australian Early Development Census (AEDC). The AEDC is funded by the Australian Government Department of Education and Training. The findings and views reported are those of the author and should not be attributed to the Department or the Australian Government.

Prologue

The New Directions: Mothers and Babies Services (NDMBS) program is a key responsibility of my Section at the Department of Health. Although it has been in operation since 2008, it has not been evaluated for effectiveness. This was the first project commenced during my field placement, but the last completed. The main reason for this was that the geographical locations in which NDMBS had already been delivered was uncertain as a result of an amalgamation of the program into a broader primary health care program. This information took many months and much effort by staff in the Section to obtain. While these data were gathered, the project aims changed from informing the expansion of the NDMBS to new locations, to baseline analysis for later evaluation, and finally an evaluation of the program outcomes after release of the 2015 Australian Early Development Census (AEDC) data in 2016.

MY ROLE

For this project I

- developed the data analysis plan
- developed the program logic model for NDMBS
- drafted the ethics application
- conducted the analysis
- drafted the report for the Department of Health, and the accompanying technical summary
- wrote the Minute to obtain clearance for publication from the Branch Manager
- presented the evaluation findings to the Indigenous Health Division forum.

My academic supervisor, David Harley, provided ongoing feedback and guidance.

LESSONS LEARNT

In developing the program's logic model, I gained a deeper understanding of program planning and evaluation. I learnt about the difficulty that funding agencies face in balancing the need to implement programs quickly, with minimal burden to the funded organisations, and the need to collect useful data from those organisations. I also learnt the value of keeping a detailed record of commands used in a data analysis. My methods were questioned by the AEDC data team, and by checking my annotated Stata do files, I was able to quickly justify my analysis.

PUBLIC HEALTH IMPACT

This was the first outcome evaluation of a $278 million national program. Its usefulness was hindered by problems with allocation to exposure groups, as it was difficult to determine the geographical reach of the NDMBS program accurately and with a high enough resolution. However, in the report and presentation to the Division, I aimed to highlight the need for development of logic models during program planning, and to ensure that appropriate data is collected to facilitate later evaluation. Several staff members from within the Indigenous Health Division have since approached me to discuss logic models and evaluation for other programs.

ACKNOWLEDGEMENTS

I am grateful to

- Dr Annie Dullow and Maria Luteria, who suggested the use of AEDC data to evaluate the program
- Andrew Apperley and Shaun O'Sullivan (Child and Family Health Section, Indigenous Health Division), for their work on identifying the areas serviced by NDMBS-funded organisations
- Rachelle Nevin (Geospatial Analysis, Research Data and Evaluation Division), who created the map shown in Figure 2
- my placement supervisor, Nick Pascual, who facilitated access to the AEDC data and reviewed the analysis plan, and draft and final reports.

Summary of findings and recommendations

New Directions: Mothers and Babies Services (NDMBS) aims to increase access to antenatal, postnatal and child and maternal services for Aboriginal and Torres Strait Islander families to ensure children are healthy and ready to learn when they start school. Over $224 million was invested in NDMBS from 2007-08 to 2014-15. A further $53.96 million has been committed for 2015-16 to 2017-18 to expand the program to a further 51 sites.

In this first evaluation of the program, we assessed the effect of NDMBS investment between 2007 and 2015 on school readiness of Aboriginal and Torres Strait Islander children. Using data from the Australian Early Development Census (AEDC) collected in 2009 and 2015, we analysed whether measures of early development in the first year of school improved for children who lived in an area serviced by an NDMBS-funded organisation, compared with children who did not.

Overall, the results show improvements in areas that were serviced by NDMBS-funded organisations. However, comparisons with non-NDMBS areas suggest that the contribution of the NDMBS program to these improvements have been modest on a national scale. At most, only two percentage points of the improvement in early child development indicators could be attributed to living in an area serviced by an NDMBS-funded organisation. In some indicators, improvements in NDMBS-serviced areas were exceeded by the improvements in the rest of Australia.

As the program has targeted areas of highest need, it is possible that child development indicators in these areas may have worsened in the absence of investment. Problems with maternal and child health staff recruitment and retention in remote areas may also have limited the effectiveness of the NDMBS.

The AEDC indicators relate only to the school readiness of children, not to the ability of schools to engage children in high quality teaching and learning. The accuracy of this evaluation was reduced by the limitations of using population-level outcome indicators, and by the low geographical resolution of the data.

Recommendations

1. Enhance support for NDMBS-funded organisations that deliver services in remote and very remote areas. Focus should be on strategies that develop the remote maternal and child health workforce, particularly Aboriginal and/or Torres Strait Islander Workers/Health Practitioners and Aboriginal and Torres Strait Islander midwives and nurses.

2. Require organisations that receive NDMBS funding to regularly report the postcodes of children and families who receive services to allow future evaluations of effectiveness.

Introduction

New Directions: Mothers and Babies Services (NDMBS) is part of the Australian Government's commitment to close the gap in infant mortality rates between Aboriginal and Torres Strait Islander and non-Indigenous Australian children (Figure 1). The program is based on international and Australian research that indicates the importance in investing in the early years for children and their families. The objective of NDMBS is to increase access to antenatal, postnatal and child and maternal services for Aboriginal and Torres Strait Islander families. The areas serviced by organisations that received funding to deliver New Directions Mothers and Babies Services between 2007 and 2015 is shown in Figure 2, and listed in Appendix 5.1.

NDMBS is a child and maternal health care program that supports Aboriginal and Torres Strait Islander families and early childhood development to support children to be healthy and ready to learn when they start school, through providing access to services in five priority areas:

1. antenatal and postnatal care;
2. standard information about baby care;
3. practical advice and assistance with breastfeeding, nutrition and parenting;
4. monitoring of developmental milestones, immunisation status and infections; and
5. health checks and referrals to treatment for Aboriginal and Torres Strait Islander children before starting school.

The program is flexible to local needs and provides access to a range of child and maternal health functions as part of a broader primary healthcare service.

Over $224 million was invested in NDMBS from 2007 to 2015. A further $53.96 million has been committed for expanding the program in 2015to 2018. Three assessments of the program have already been completed:

- a performance audit conducted by the Australian National Audit Office (ANAO) in 2011-12 (1);
- a Descriptive Analysis commissioned by the Department of Health ("the Department") in 2013 (2); and
- an assessment of the program conducted by the Australian Institute of Health and Welfare (AIHW) in 2014 (3).

The performance audit concluded that the Department had been effective in establishing and implementing the program, but more performance data needed to be collected by the program in order to monitor and evaluate its effectiveness. The Descriptive Analysis consisted of a review of the funded organisations' NDMBS action plans, a survey of 64% of funded organisations, and interviews with staff at 17% of organisations. Services reported they were mostly using the NDMBS funding to employ midwives, child and family health nurses, and Aboriginal and/or Torres Strait Islander Health Workers/Health Practitioners to provide care in clinic and home settings. Overall, organisations were providing services consistent with the program's priority areas, and there had been increased activity as a result of the program. However, organisations were challenged by difficulties in recruiting and retaining staff, lack of patient transport, limited funding, and difficulties related to remote service delivery. Only one quarter of the organisations indicated they had capacity to meet demand for maternal and child health services.

The AIHW assessment used national Key Performance Indicator (nKPI) data from 2012 and 2013 that is collected from primary health care organisations funded by the Australian government. The data used included measures of outcome (proportion of normal birthweight children, and proportion of women who attended their first antenatal visit before 13 weeks gestation) and processes-of-care (completeness of birthweight data; immunisation coverage at one, two and five years of age; and child and women's health check coverage). The change in these measures over a six or twelve month period in organisations that received NDMBS funding was compared with the change in organisations that did not. Organisations funded by NDMBS improved to a greater degree in five of the eight measures, but no tests of statistical significance were performed.

In this analysis, we aimed to evaluate the effect of NDMBS investment between 2007 and 2015 on school readiness, and to make recommendations to the Department. Specifically, we wished to determine if indicators derived from the Australian Early Development Census (AEDC) improved for Aboriginal and Torres Strait Islander children who lived in NDMBS-serviced areas, compared with children who did not. This report is accompanied by a technical summary (Appendix 5.2).

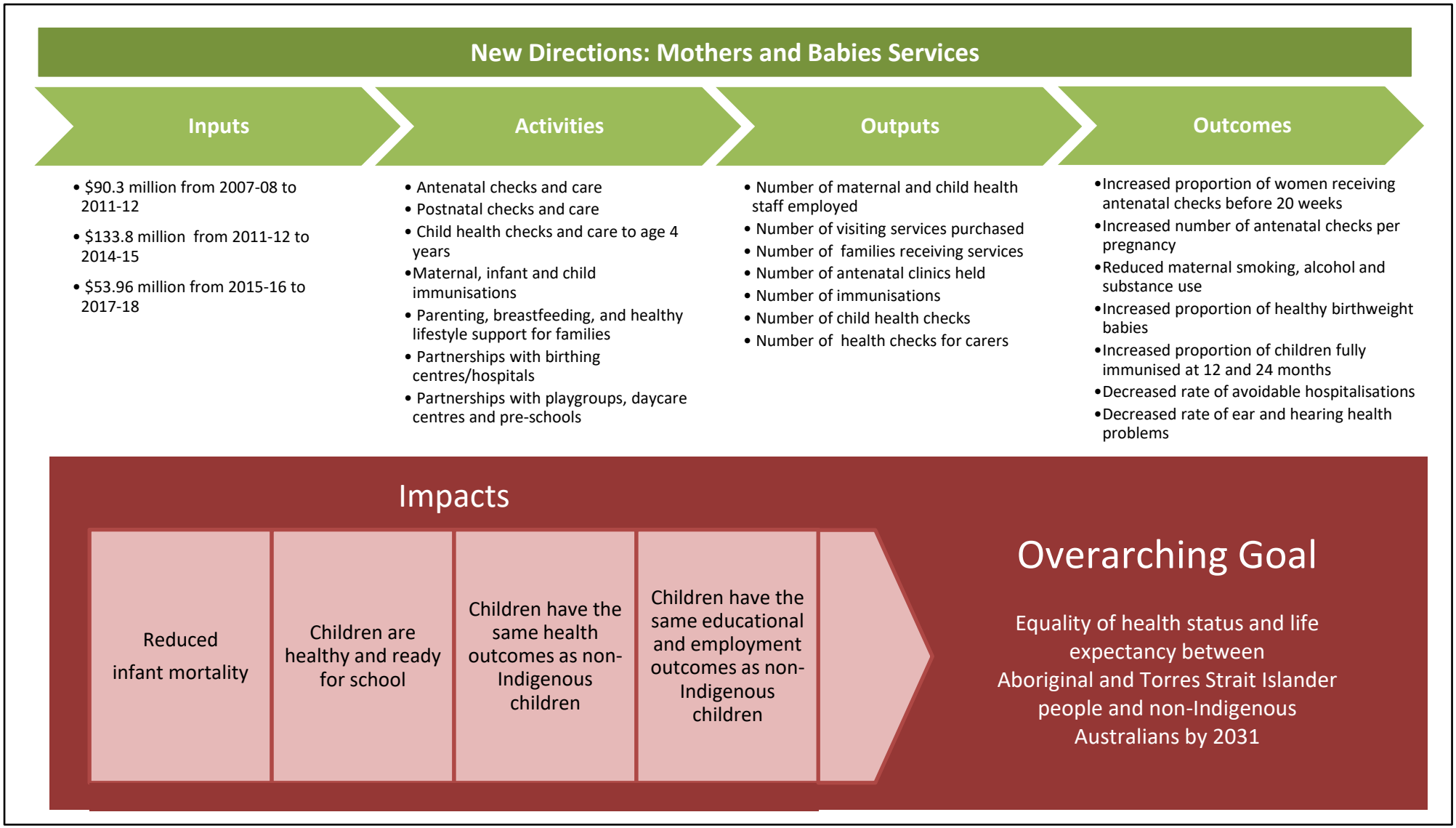

Figure 40 Program logic for the New Directions: Mothers and Babies Services (NDMBS) program.

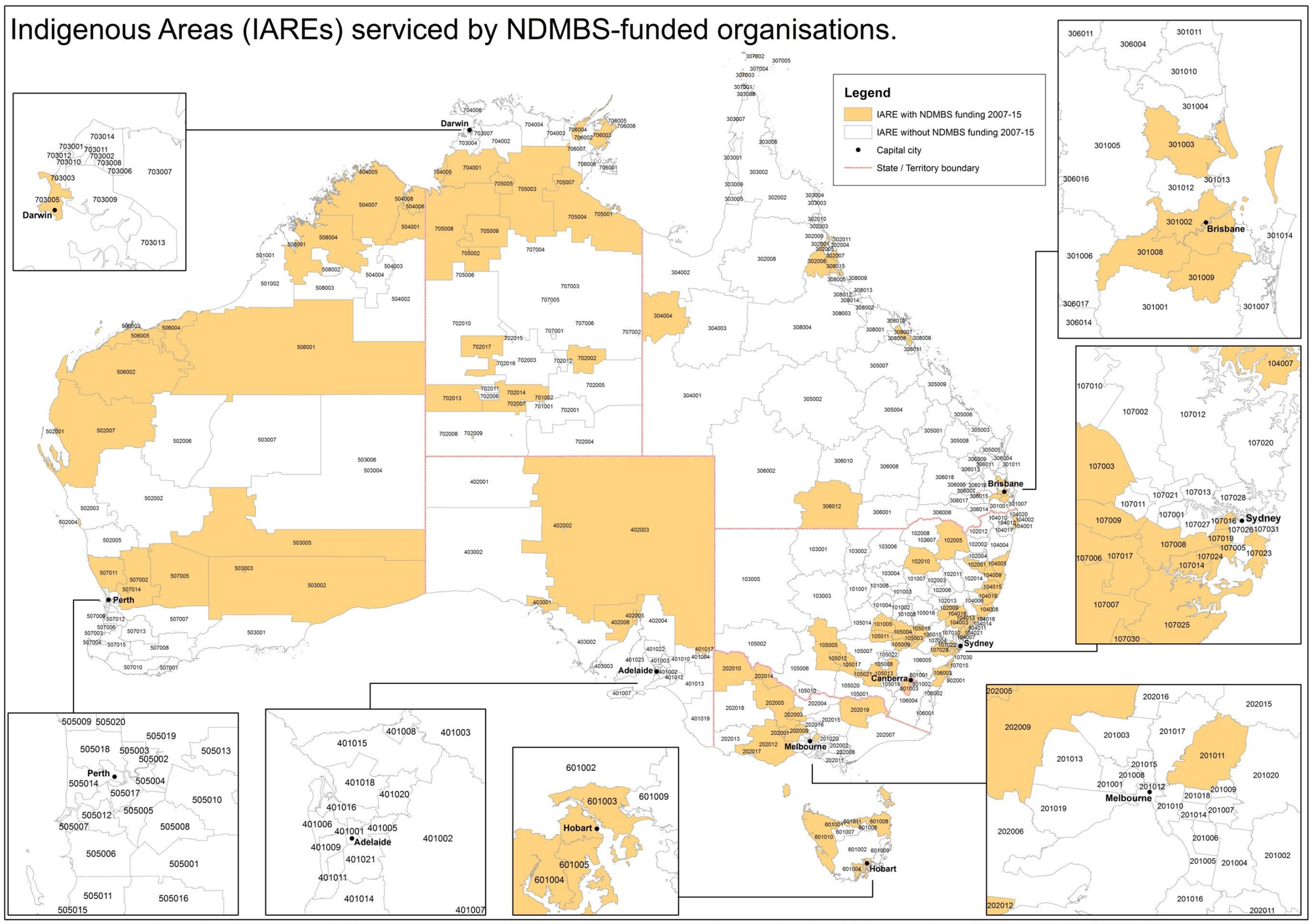

Figure 4.1 Indigenous Areas (IAREs) serviced by organisations that received funding to deliver New Directions Mothers and Babies Services (NDMBS), 2007-2015.

Methods

CHILD DEVELOPMENT MEASURES

We used data from the Australian Early Development Census (AEDC, previously the Australian Early Development Index), which is a population measure of early childhood development (4). It is often used as a measure of school readiness. It covers five domains of child development: physical health and wellbeing; social competence; emotional maturity; language and cognitive skills; and communication and general knowledge. All five of these domains have been found to predict National Assessment Program – Literacy and Numeracy (NAPLAN) outcomes at Years 3, 5 and 7 (5). Children who start school with good early development will generally maintain superior educational trajectories compared with children who have poor early development, regardless of their socio-economic status (6).

Scores for AEDC domains are calculated for each Australian child during the first year of full-time school, based on teacher responses to 96 developmental questions. If the teacher of an Aboriginal and Torres Strait Islander child is not of Indigenous descent, the questions are completed in consultation with an Indigenous cultural consultant, where available. The census was taken in 2009, 2012 and 2015, and the dataset includes over 96.5% of all children registered to start school in those years. While AEDC data is collected for each child, data is aggregated at a community level based on the communities where children live.

Results from the AEDC are reported as proportions of children regarded as 'on track', 'developmentally at risk' and 'developmentally vulnerable' in each domain (Table 1), Summary indicators reported are the proportion of children vulnerable in one or more domain, and vulnerable in two or more domains. Results are also reported using the Multiple Strengths Indicator (MSI, Table 2). Unlike the vulnerability summary indicators, which are based on the challenges children face when they start school, the MSI combines information from all five domains to summarise the strengths they have developed (7). As these summary indicators are capturing different information about child development, communities may have both a high proportion of children with developmental vulnerabilities and a high proportion of children with well-developed or highly-developed strengths.

Table 1 Characteristics of children considered 'developmentally on track', or 'developmentally vulnerable' for each of the four AEDC domains (4).

Domain	Children developmentally on track	Children developmentally vulnerable
Physical health & wellbeing	Almost never have problems that interfere with their ability to physically cope with the school day. These children are generally independent, have excellent motor skills, and have energy levels that can get them through the school day.	Experience a number of challenges that interfere with their ability to physically cope with the school day. This may include being dressed inappropriately, frequently late, hungry or tired. Children are usually clumsy and may have fading energy levels.
Social competence	Almost never have problems getting along, working, or playing with other children; is respectful to adults, is self-confident, and is able to follow class routines; and is capable of helping others.	Experience a number of challenges with poor overall social skills. For example children who do not get along with other children on a regular basis, do not accept responsibility for their own actions and have difficulties following rules and class routines. Children may be disrespectful of adults, children, and others' property; have low self-confidence and self-control, do not adjust well to change; and are usually unable to work independently.
Emotional maturity	Almost never show aggressive, anxious, or impulsive behaviour. Children will have good concentration and will often help other children.	Experience a number of challenges related to emotional regulation. For example problems managing aggressive behaviour being prone to disobedience and/or is easily distracted, inattentive, and impulsive. Children will usually not help others and are sometimes upset when left by their caregiver.
Language & cognitive skills (school-based)	Children will be interested in books, reading and writing, and basic mathematics; capable of reading and writing simple sentences and complex words. Will be able to count and recognise numbers and shapes.	Experience a number of challenges in reading/writing and with numbers; unable to read and write simple words, will be uninterested in trying, and often unable to attach sounds to letters. Children will have difficulty remembering things, counting to 20, and recognising and comparing numbers; and usually not interested in numbers.
Communication skills & general knowledge	Children will have excellent communication skills, can tell a story and communicate easily with both children and adults, and have no problems with articulation.	Children will have poor communication skills and articulation; have limited command of English (or the language of instruction), have difficulties talking to others, understanding, and being understood; and have poor general knowledge.

Table 2 Characteristics of children in each Multiple Strengths Indicator (MSI) category (7).

Category	Characteristics
Emerging strengths	Children may be meeting developmental expectations when they start school but they do not demonstrate a high number of strengths. Children in this category range from those with strengths in none of the 39 MSI items, to children with strengths in about half of the MSI items.
Well-developed strengths	Children are showing strengths in 50-70% of the following skills: relating to peers and teachers, self-control, curiosity about the world, working independently, reading and writing simple words, communicating effectively with peers and teachers, and storytelling.
Highly developed strengths	Children have strengths in most of the 39 MSI items. These children are likely to be on track on all five AEDC domains, and show strengths in their social and emotional, literacy and communication skills.

DATA ANALYSIS

We used data for all Aboriginal and Torres Strait Islander children who did not have special needs, were aged over three years, and who had available geographical data from the 2009 and 2015 censuses (Figure 3). As the NDMBS program rolled out in 2007, most of the children in the 2009 census were too old to receive NDMBS services, so these data were used as the baseline for the evaluation. Follow-up data was taken from the 2015 AEDC. Most children in this census were born in 2010, so NDMBS services were available throughout their antenatal and early childhood periods. We divided the data from both census years into two groups: all children living in areas that were serviced by a NDMBS-funded organisation, and all other children. Children were allocated to either group based upon the Indigenous Area (IARE) they lived in at the time of the census. Indigenous Areas generally have a minimum of 250 Aboriginal and Torres Strait Islander residents (8). We calculated the percentage point change in child development indicators between 2009 and 2012 for both groups nationally and by state and territory. Each of these calculations excluded children who did not have a valid score for the indicator.

As the NDMBS program has been targeted at areas of high need for maternal and child health services, we expected that children in these areas would have relatively poorer development indicators. However, if the NDMBS program has been effective, we would expect to see a greater improvement in these areas between 2009 and 2015, compared with areas that did not receive NDMBS investment.

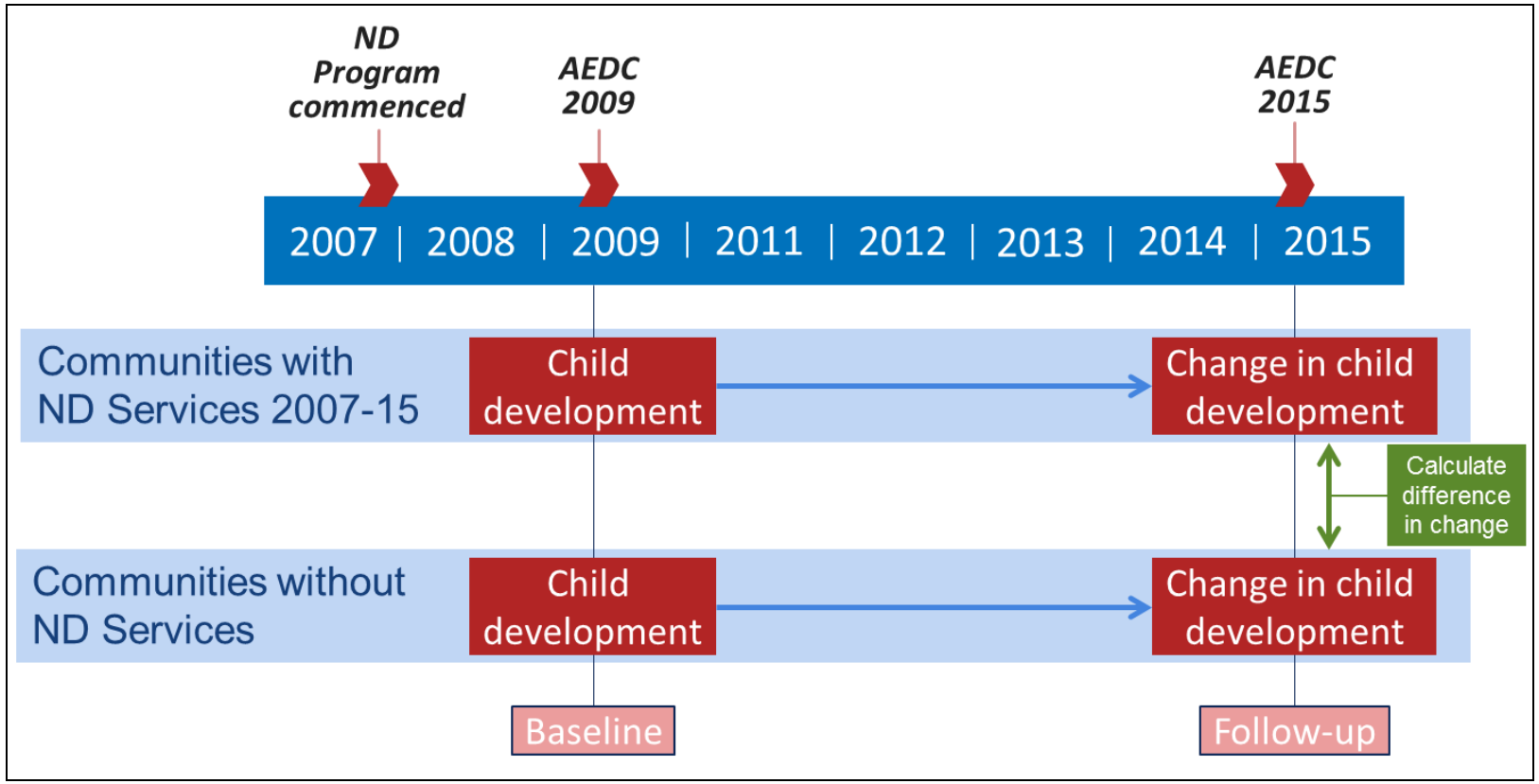

Figure 42 Method for evaluation of New Directions: Mothers and Babies Services from 2007 to 2015 using AEDC data.

Results

DESCRIPTION OF CHILDREN INCLUDED IN THE EVALUATION

In 2009 and 2015, there were 12 459 and 16 197 Aboriginal and Torres Strait Islander children who were eligible for this study and for whom census data were available. Just over 45% of these children lived in IAREs serviced by organisations that received NDMBS funding between 2007 and 2015. The age and sex of this group of children did not differ from other Aboriginal and Torres Strait Islander children, and their distribution across areas of relative socio-economic disadvantage was similar (Table 3). A greater proportion of children who lived in non-NDMBS areas were in remote or very remote areas, had a language background other than English[8], and spoke English as a second language. While 86% of all Aboriginal and Torres Strait Islander children were assessed in the AEDC by a non-Indigenous teacher, a greater proportion of assessments of children living in non-NDMBS areas were completed with the assistance of an Indigenous cultural consultant.

Two-thirds of children in the NDMBS-serviced areas lived in New South Wales or Queensland in 2009 (Figure 4). All of the IAREs in the ACT were serviced by a NDMBS-funded organisation, so no comparison could be made in this jurisdiction.

[8] Children who speak a language other than English in the home or whose parent(s)/guardian(s) speak a language other than English in the home.

Table 3 Characteristics of children included in the analysis (Aboriginal and Torres Strait Islander children in the first year of school), by NDMBS service areas, 2009.

Characteristic	Area received NDMBS (5 674 children)	Area did not receive NDMBS (6 785 children)	All Aboriginal & Torres Strait Islander children (12 459 children)
Mean age (years)	5.5	5.5	5.5
Female	2 889 (51%)	3 369 (50%)	6 258 (50%)
Language background other than English[1]	1 405 (24%)	1 966 (29%)	3 371 (27%)
English as a second language	1 132 (20%)	1 658 (24%)	2 790 (22%)
Lived in least socio-economic disadvantage area	364 (7%)	335 (5%)	699 (6%)
Lived in most socio-economic disadvantage area	2 685 (48%)	3 106 (46%)	5 791 (47%)
Remote or very remote location	1 345 (24%)	2 058 (30%)	3 403 (27%)
Indigenous teacher	763 (14%)	951 (14%)	1 714 (14%)
Non-Indigenous teacher who was assisted by an Indigenous cultural consultant	1 440 (29%)	2 151 (37%)	3 591 (33%)
Attended a preschool program	3 266 (69%)	4 196 (72%)	7 462 (71%)

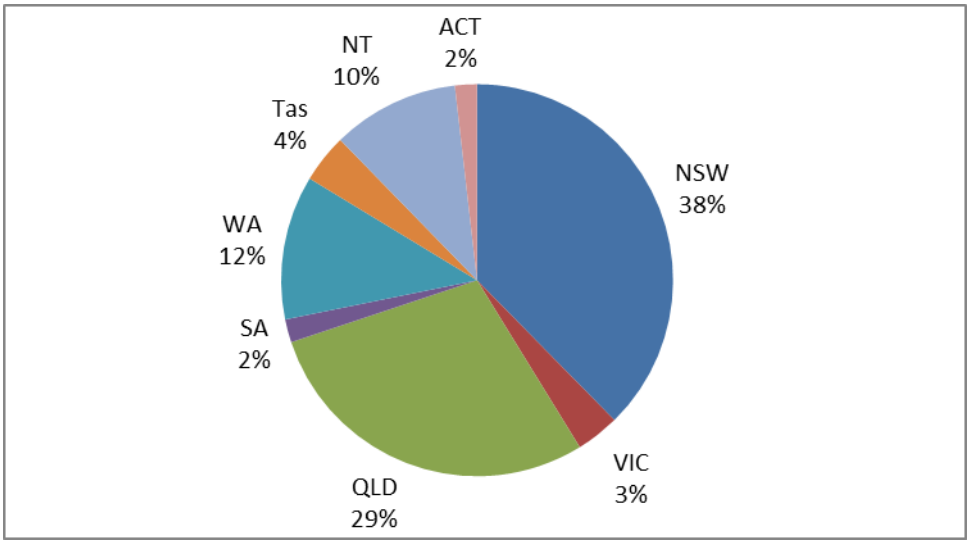

Figure 43 State or territory of residence of Aboriginal and Torres Strait Islander children living in NDMBS-serviced areas, 2009.

DEVELOPMENTAL DOMAINS

In the NDMBS-serviced areas, the proportion of children who were on-track in each AEDC domain increased between 2009 and 2015. Over 60% of children in these areas were on track in each domain in 2015. There were remarkable improvements in the 'language and cognitive skills' domain (Figure 5 and Table 4). However, reductions in developmental vulnerability in other domains were much smaller or negligible.

Overall, the improvements observed in the NDMBS-serviced areas were also observed in the rest of Australia (Table 4 and Figure 6). The greatest relative improvements in early child development that could be attributed to the NDMBS program were in the proportion of children on-track in the 'emotional maturity' domain, and the proportion of children vulnerable in the 'physical health and wellbeing' domain. However, these differences were small. In some indicators—in the 'communication & general knowledge' domain, for example—improvements in NDMBS-serviced areas were exceeded by the improvements in the rest of Australia.

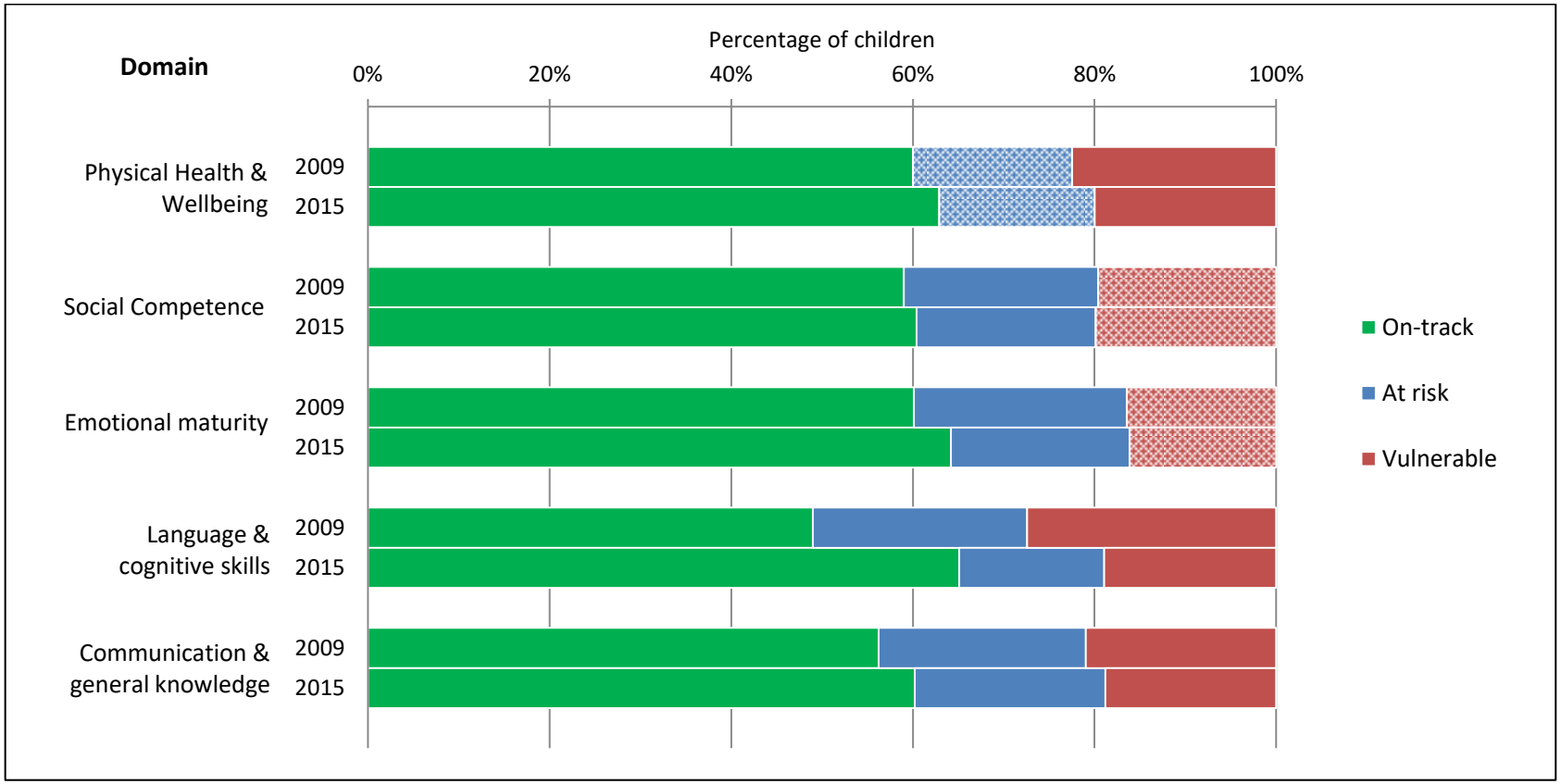

Figure 44 Proportion of Aboriginal and Torres Strait Islander children living in areas serviced by New Directions Mothers and Babies Services (Wave 1), in each AEDC domain category, 2009 and 2015. Hatched bars indicate that the change between 2009 and 2015 was within the margin of error.

Table 4 Change in proportion of Aboriginal and Torres Strait Islander children on-track and vulnerable in each developmental domain, from 2009 to 2015, by NDMBS service area. A negative change in the vulnerable categories indicates an improvement.

NDMBS services		Physical health & wellbeing		Social competence		Emotional maturity		Language & cognitive skills (school-based)		Communication & general knowledge	
		On-track	Vulnerable	On track	Vulnerable	On track	Vulnerable	On track	Vulnerable	On-track	Vulnerable
Yes	2009 (%)	60.0	22.5	59.0	19.6	60.1	16.5	49.0	27.4	56.2	21.0
	2015 (%)	62.9	20.0	60.4	19.9	64.2	16.1	65.1	18.9	60.2	18.8
	change (%)	2.9	-2.5	1.4	0.3*	4.1	-0.3*	16.1	-8.5	4.0	-2.1
No	2009 (%)	60.1	22.4	56.9	21.5	58.9	18.1	45.6	31.3	53.8	23.2
	2015 (%)	61.8	22.0	58.1	21.0	61.0	17.5	60.9	21.2	59.0	19.8
	change (%)	1.7	-0.5*	1.2	-0.5*	2.1	-0.6*	15.3	-10.1	5.2	-3.4
Difference in change (%)		1.2	-2.0	0.2	0.8	2.0	0.3	0.8	1.6	-1.3	1.3

* The change between 2009 and 2015 was within the margin of error.

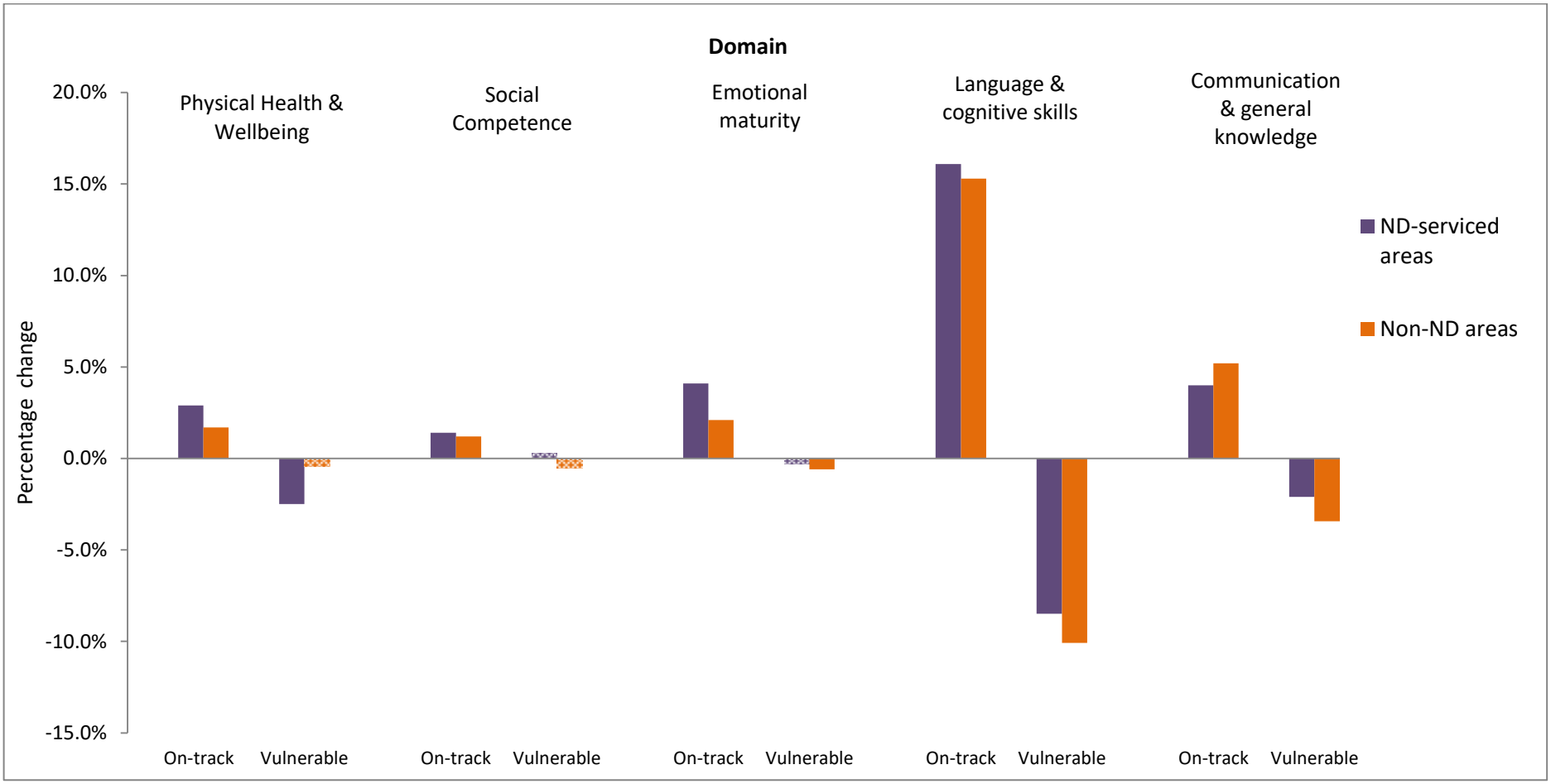

Figure 45 Change in the proportion of Aboriginal and Torres Strait Islander children in AEDC domain categories, NDMBS-serviced areas versus non-NDMBS areas, 2009-2015. A negative change in the vulnerable categories indicates an improvement. Hatched bars indicate that the change was within the margin of error.

SUMMARY INDICATORS – AUSTRALIA

There were substantial improvements in the summary indicators for children in NDMBS-serviced areas from 2009 to 2015 (Table 5, Figure 7 and Figure 8), particularly in the proportion of children who had highly-developed strengths. However, these changes were similar to the improvements observed in all Aboriginal and Torres Strait Islander children over this period (Table 5 and Figure 9), with less than one percentage point difference between the groups on each indicator.

Table 5 Change in summary early child development indicator categories for Aboriginal and Torres Strait Islander children, from 2009 to 2015, by NDMBS service area. A negative change in the vulnerable and 'emerging strengths' categories indicates an improvement.

NDMBS services		Vulnerable in 1 or more domains	Vulnerable in 2 or more domains	Multiple Strengths Indicator		
				Highly-developed strengths	Well-developed strengths	Emerging strengths
Yes	2009 (%)	46.9%	29.0%	30.6%	24.9%	44.5%
	2015 (%)	40.8%	25.2%	38.6%	23.5%	37.9%
	change (%)	-6.1%	-3.8%	8.0%	-1.4%	-6.6%
No	2009 (%)	49.7%	31.8%	27.8%	25.0%	47.2%
	2015 (%)	43.2%	27.1%	34.8%	23.7%	41.5%
	change (%)	-6.5%	-4.7%	7.0%	-1.3%	-5.7%
Difference in change (%)		0.4%	0.9%	0.9%	-0.1%	-0.9%

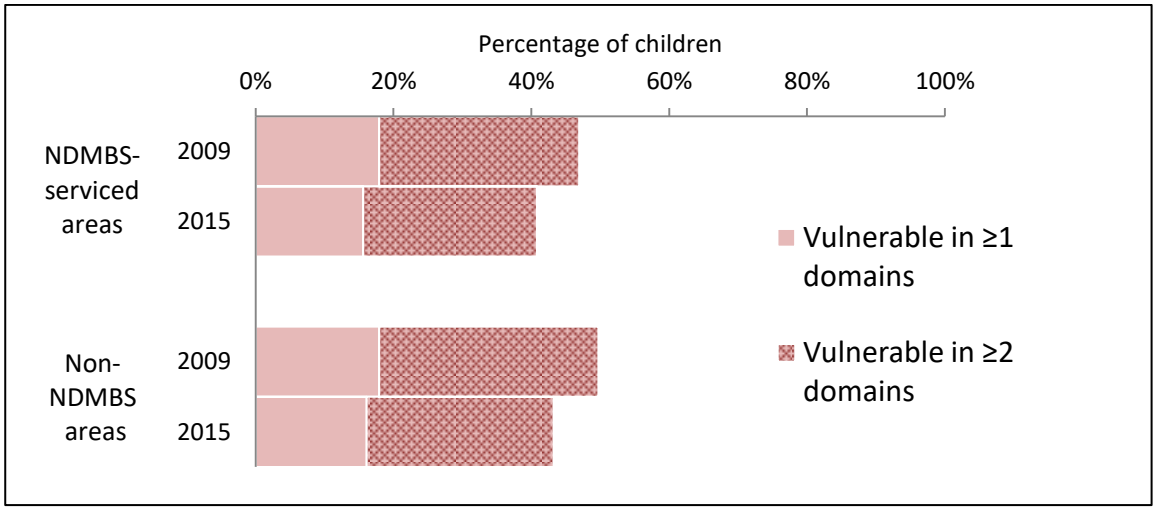

Figure 46 Proportion of Aboriginal and Torres Strait Islander children who were vulnerable in one or more, or two or more domains, 2009 and 2015, by NDMBS service area.

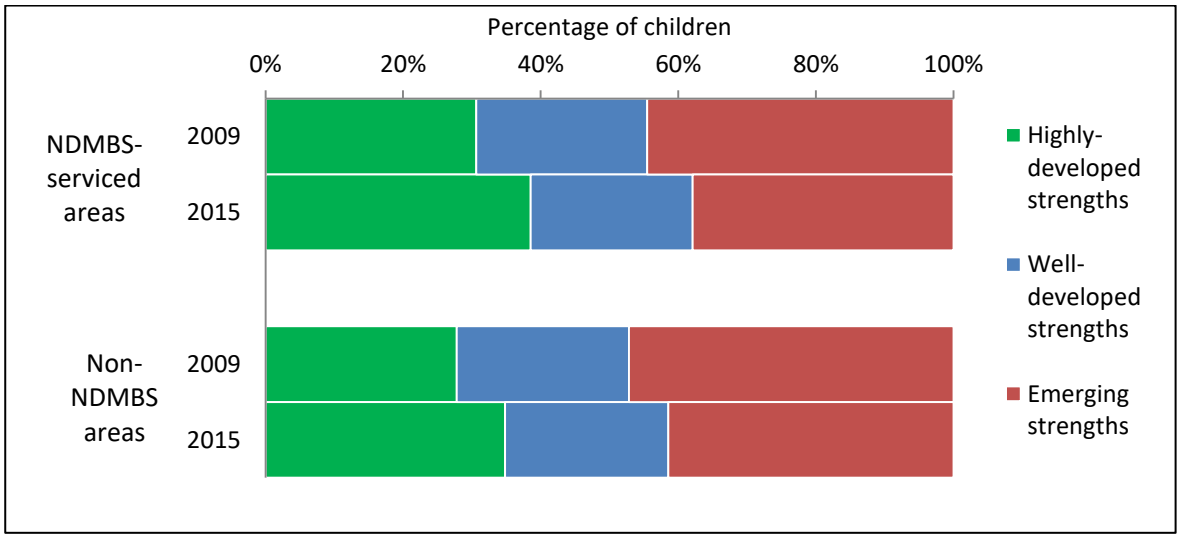

Figure 47 Proportion of Aboriginal and Torres Strait Islander children who were in Multiple Strengths Indicator categories, 2009 and 2015, by NDMBS service area.

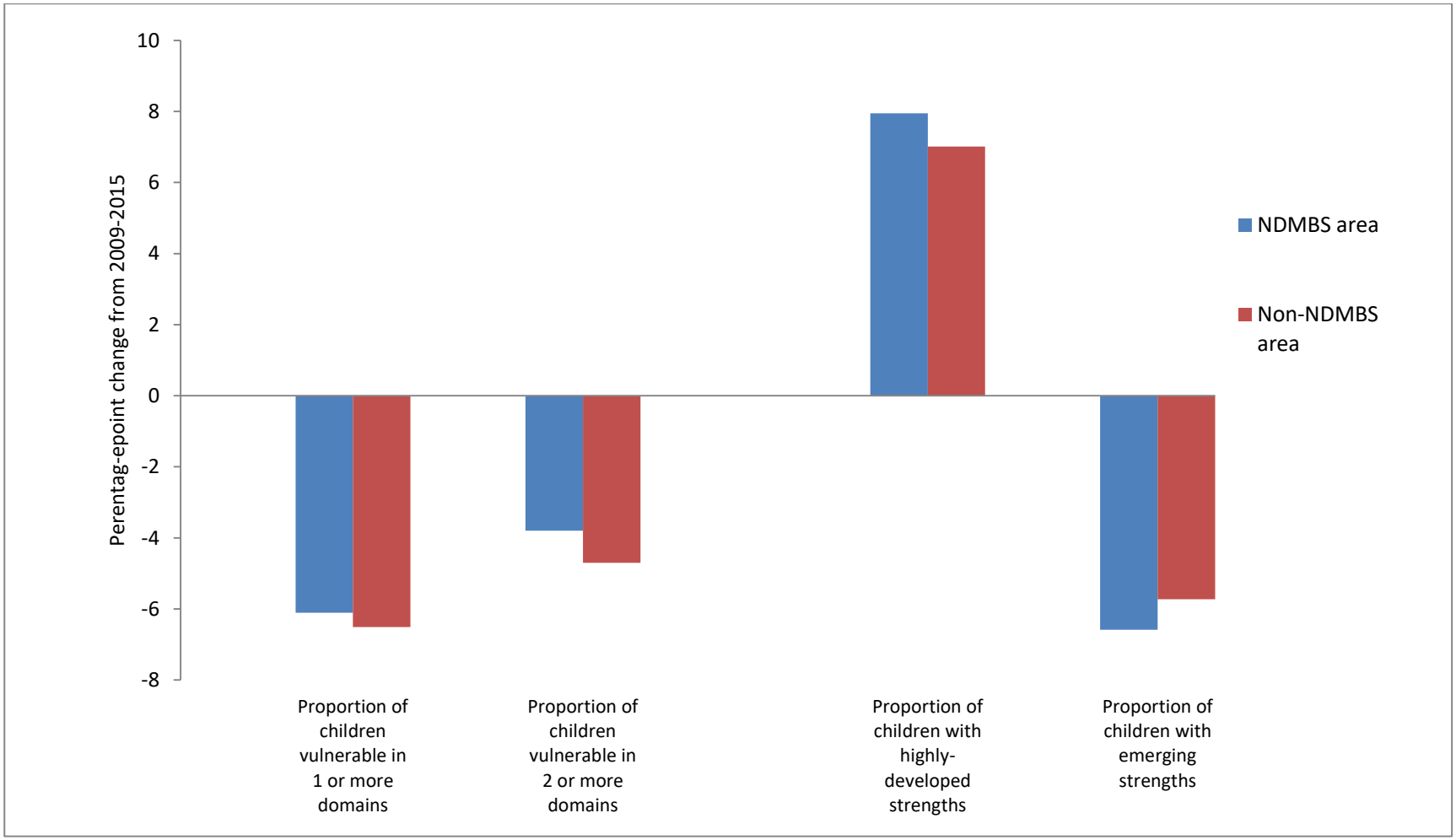

Figure 48 Change in summary early child development indicator categories for Aboriginal and Torres Strait Islander children, from 2009 to 2015, by NDMBS service area. A negative change in the vulnerable and 'emerging strengths' categories indicates an improvement.

SUMMARY INDICATORS – STATE AND TERRITORY

Notable improvements in summary indicators in NDMBS areas were observed in New South Wales and Queensland (Table 6 and Figure 10). Western Australia experienced more modest improvements overall, and an increase in the proportion of children who were vulnerable in two or more domains. The changes observed in the other States and Territories were within the margin of error for the vulnerability indicators.

Table 6 Change in summary child development indicators, NDMBS-serviced areas only, 2009-2015, by State and Territory.

State/Territory	Number of children in 2009	Percentage point change			
		Highly developed strengths	Emerging Strengths[#]	Vulnerable in ≥1 domains[#]	Vulnerable in ≥2 domains[#]
NSW	2 136	7.8%	-5.7%	-4.3%	-2.6%
VIC	203	5.2%	-7.3%	-2.1%*	-3.1%*
QLD	1 626	8.8%	-8.8%	-7.5%	-5.1%
SA	108	0.5%	-4.5%	0.8%*	-3.5%*
WA	675	3.8%	-0.9%	-1.1%*	4.1%
TAS	228	5.0%	-2.0%	-4.8%*	-4.6%
NT	595	1.4%	0.7%	-1.9%*	1.4%*
ACT	101	-3.6%	2.7%	2.9%*	6.1%*
Australia	5 672	8.0%	-6.6%	-6.1%	-3.8%

*The changes observed in these indicators were within the margin of error.
[#] As these are indicators of deficit, a negative change represents an improvement.

New Directions investment appears to have had a positive but modest effect upon children with emerging strengths or who were developmentally vulnerable in New South Wales and Queensland (Table 7 and Figure 11). However, children in areas of Western Australia serviced by a NDMBS-funded organisation had substantially lesser improvements in all summary indicators, compared with children living in other parts of the State. The effects in other jurisdictions were undetectable due to small numbers of children in the analysis.

Table 7 Difference in the change in summary child development indicators, NDMBS-serviced areas versus non-NDMBS areas, 2009-2015, by State and Territory.

State/Territory	Percentage point difference in change			
	Highly developed strengths	Emerging strengths[#]	Vulnerable in ≥1 domains[#]	Vulnerable in ≥2 domains[#]
NSW	0.6%	-3.8%	1.1%	-1.0%
VIC*	3.8%	-8.3%	0.6%*	1.6%*
QLD	-0.2%	-3.2%	-1.0%	-2.2%
SA	-0.8%	0.2%	3.9%*	-1.5%*
WA	-1.7%	5.4%	5.5%*	11.1%
TAS	-15.6%	8.7%	0.3%*	1.9%
NT	-3.1%	6.6%	15.5%*	10.0%*
Australia	-0.1%	-0.9%	0.4%	0.9%

* The changes observed in these indicators were within the margin of error

[#] As these are indicators of deficit, a negative difference represents a greater improvement in the NDMBS-serviced areas.

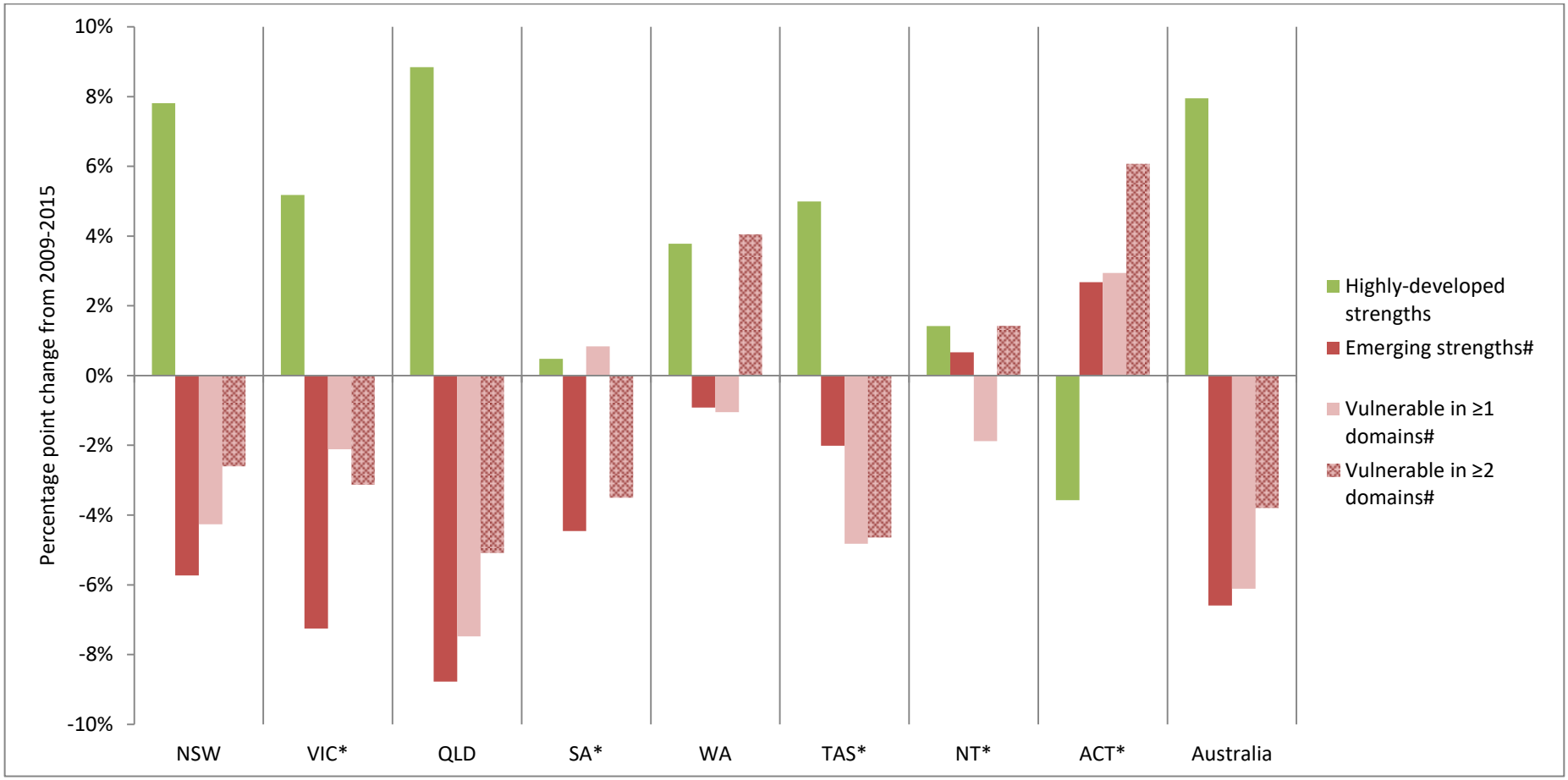

Figure 49 Change in summary indicators for child development indicators in NDMBS-serviced areas from 2009-2015, by State and Territory. *The changes observed in these jurisdictions were within the margin of error. # As these are indicators of deficit, a negative change represents an improvement.

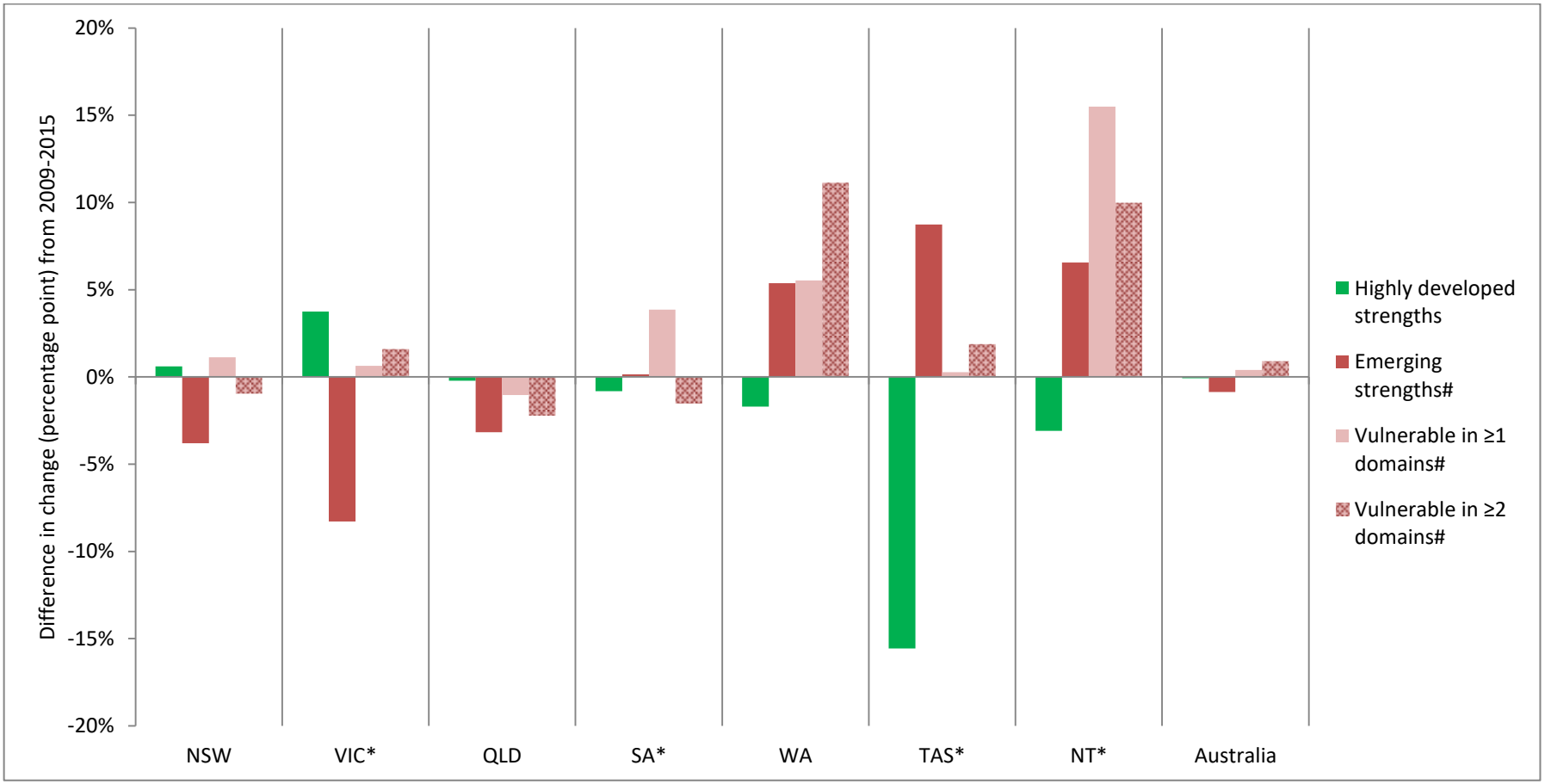

Figure 50 Difference in the change in summary early childhood indicators between NDMBS-serviced areas and non-NDMBS areas, 2009-2015, by State and Territory. *The changes observed in these jurisdictions were within the margin of error. # As these are indicators of deficit, a negative change represents a greater improvement in NDMBS-serviced areas.

Discussion

Overall, population measures of early child development indicate improvements in areas that were serviced by NDMBS-funded organisations. However, comparisons with non-NDMBS areas suggest that the contribution of the NDMBS program to these improvements have been modest on a national scale. In this first 'before and after' evaluation of the program, we have been unable to demonstrate a substantial effect on the school readiness of Aboriginal and Torres Strait Islander children resulting from NDMBS investment. However, as the program has targeted areas of highest need, it is possible that child development indicators in these areas may have worsened in the absence of investment.

The largest comparative improvements in early child development were in the 'emotional maturity' and 'physical health and wellbeing' domains. The AIHW assessment of the program, which lacked baseline data, found that there was a 13.8 percentage point greater improvement over 12 months in the proportion of NDMBS-funded organisations that completed health checks for more than half of all children aged four years, compared with non-NDMBS organisations (10). The quality of these health checks cannot be assessed, but they may have resulted in prevention of, or early intervention in, physical illness or problems with emotional development. Relative improvements observed in the proportion of organisations with more than half of children fully immunised at ages one, two and five years may also help explain the improvements in the 'physical health and wellbeing' domain found in the present evaluation. Hospitalisation for infection in the first five years of life has been found to marginally increase the likelihood of a child being developmentally vulnerable in all AEDC domains (11).

While greater gains have been made in NDMBS areas in Queensland and NSW, this is not the case in Western Australia and the Northern Territory. In 2015, 57% of Western Australian and 98% of NT children living in NDMBS areas were also in remote or very remote areas, in contrast to under 1% of children in NSW and under 12% in Queensland. It is plausible that remoteness has led to less favourable outcomes in WA and NT. In the 2013 Descriptive Analysis, NDMBS-funded organisations indicated that the recruitment and retention of qualified staff was their greatest challenge, and that this

problem was "amplified in rural and remote areas" (12). In particular, services had difficulty in recruiting suitably qualified Aboriginal and Torres Strait Islander staff. A systematic review conducted in 2010 identified the following three evidence-based strategies for developing and maintaining a skilled and qualified rural and remote health workforce to improve Aboriginal and Torres Strait Islander health outcomes:

- promote rural and remote Aboriginal and Torres Strait Islander health practice to health students;
- provide additional support, such as training, improved cultural competence, and peer mentoring to the existing health workforce; and
- develop and support the Aboriginal and Torres Strait Islander health workforce at a local level (13).

In spite of the differences in language backgrounds between the two groups, the large improvements observed in NDMBS areas in the 'communication skills and general knowledge' domain were exceeded by improvements in non-NDMBS areas. Preschool attendance has been implicated in improved English proficiency at the time of starting school in children from linguistically diverse backgrounds (14). However, while a slightly larger proportion of children in the non-NDMBS group had attended a preschool program in 2009 (72% versus 69% in NDMBS-areas, Table 1), this gap had closed by 2015 (83% versus 84%).

Substantially fewer 2009 AEDC assessments of Aboriginal and Torres Strait Islander children who had a non-Indigenous teacher were completed with the assistance of a cultural consultant in NDMBS areas (Table 1). However, this disparity was essentially reversed by 2015 (34% of children in NDMBS areas versus 31% in non-NDMBS areas). Assuming that a non-Indigenous teacher would assess a child more favourably with consultation, the small observed improvements relative to non-NDMBS areas may have been inflated.

LIMITATIONS OF THE STUDY DESIGN AND ANALYSIS

The AEDC is just one measure of school readiness related to characteristics of the child. It does not measure the ability of schools to engage children in high quality teaching and learning (9). It is also influenced by factors outside the scope of the NDMBS, such

as access to appropriate preschool programs, and the availability of Aboriginal and Torres Strait Islander school staff who can facilitate transition to school.

We followed up the same IAREs over time, not the same children. Therefore, we were unable to measure or control for child-related factors that may have confounded the results. We cannot be certain that any maternal and child health services received by the children in the NDMBS group in the 2015 Census were funded by the NDMBS program. Aboriginal and Torres Strait Islander families may seek health care outside NDMBS-funded services, where these are available. Many may also have moved in or out of the NDMBS-serviced areas.

The accuracy of this evaluation has been significantly hindered by the low resolution of available geographical data. Funding is provided for NDMBS for an organisation, not for a geographical area, and organisations are not required to report on the resident locations of the children and families they service. These areas are unlikely to match the IARE boundaries. Funded organisations may have changed the locations of service delivery between 2007 and 2015 and were not required to report such changes.

The 2011-12 Audit Report concluded that:

> *…the emphasis on minimising performance reporting requirements has had a significant impact on the quality of performance data available to assist managers and external stakeholders. As a consequence, very few performance indicators and targets were developed and there was no agreement to any baseline information against which to measure change. This has limited [the Department's] ability to understand the program's effectiveness and, in particular, the impact and contribution it is making to the outcomes of the [National Partnership Agreement on Indigenous Early Childhood Development]. This will also constrain the ability of the Department to conduct an evaluation of the program...*

The nKPI data provides mostly information about processes-of-care rather than outcomes, and is not reported by every organisation that offers maternal and child health services. Therefore, we support the conclusion of the AIHW assessment that nKPI data cannot be used to evaluate the effectiveness of the NDMBS. One option that may assist future evaluations would be to require NDMBS-funded organisations to report the usual resident postcodes of the children and families who have received services funded by the program. This high-resolution data would allow a more accurate evaluation using AEDC and NAPLAN data, and allow evaluation using other population-level health

indicators. For example, analysis of data from the National Perinatal Data Collection could allow evaluation of NDMBS outcomes such as maternal smoking, antenatal visits and neonatal deaths (15); and data from the Australian Immunisation Register would allow evaluation of immunisation coverage (16).

Recommendations

1. Enhance support for NDMBS-funded organisations that deliver services in remote and very remote areas. Focus should be on strategies that develop the remote maternal and child health workforce, particularly Aboriginal and/or Torres Strait Islander Workers/Health Practitioners and Aboriginal and Torres Strait Islander midwives and nurses.

2. Require organisations that receive NDMBS funding to regularly report the postcodes of children and families who receive services to allow future evaluations of effectiveness.

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CHAPTER 6 –TEACHING EXPERIENCE

No one learns as much about a subject as one who is forced to teach it.

Peter F. Drucker

ABBREVIATIONS

LFF	Lesson from the field
LSIC	Longitudinal Study of Indigenous Children
MAE	Master of Philosophy (Applied Epidemiology)
NCEPH	National Centre for Epidemiology and Population Health
PCA	Principal component analysis

My role and lessons learned

MAE scholars are required to complete two teaching exercises: participating in teaching the first year scholars; and presenting a Lesson from the Field (LFF) to our own MAE cohort.

I worked in a team of four on a session to teach the first year students about confounding. The team was motivated and teleconferenced early on to ensure we would be ready in time. We remembered how tired of lectures we had been by the time the second-year students taught us, so we aimed to develop a session that would be interactive and get people out of the classroom. I came up with the idea of a murder skit to illustrate the relationship between an exposure, a confounder and an outcome, and we developed this idea together. We then divided up the more formal part of the session between us and came together to review the sections. A few weeks before the course block, we received some criticism of our skit and presentation slides from the NCEPH lecturer. I think we all felt a little deflated, and I realised with some embarrassment (as an experienced trainer) that we had not written a lesson plan. Developing a plan (Appendix 6.1) did focus our efforts and led to a simpler and clearer session. The presentation slides are shown in Appendix 6.2.

Due to illness in the family, I was unable to participate in the delivery of the confounding teaching session. However, I did assist in the delivery of the "Outbreak Investigation" subject, leading a small group case study discussion. With such depth and breadth of knowledge and experience among scholars, I was a bit daunted by this. I found it easier to take on a facilitator role and draw out the group participants in discussion, rather than trying to appear as an expert.

I developed my LFF on Principal Component Analysis (PCA). I chose this topic as I had spent much time and energy trying to understand the technique in order to use it in my epidemiological project (Chapter 3), and I thought other scholars might find it useful for their own MAE projects or future work. I also wanted to share the Stata command I had learned for adding metadata to datasets and variables.

In developing the self-directed learning package (Appendices 6.4 and 6.5), I wanted to describe PCA simply and avoid getting bogged down in technicalities. I know from my experience in training Aboriginal Health Workers that it helps to 'layer on' different ways of explaining the same concept, so I provided a written explanation, an audio-visual explanation, as well as storytelling and a case study exercise. The most time consuming part was making a dummy dataset for which PCA would actually work. An important lesson I learnt was to check my work carefully: there was an error in the exercise and I had to send out an amended version.

My MAE colleagues found the exercise challenging, but nonetheless enjoyable and useful. I had several thought-provoking discussions. I was asked how to interpret the results of the Wilcoxon rank-sum test. This led me to revisit my understanding of what is actually tested. While I had thought it was a test of equality of medians, the Wilcoxon rank-sum test actually provides a measure of effect size. After further research, I found a user-written Stata command that calculates the estimate and confidence interval for the effect size, and I was able to use this in the analysis for my epidemiological project.

I also took the opportunity to co-supervise a medical school student for their research project. The student chose to analyse factors associated with ear disease in children in the Longitudinal Study of Indigenous Children (LSIC). I was able to share the lessons I had learned about using the LSIC data, but also general research skills such as refining the research question, choosing the correct method for the question and data, and writing for publication. Working with the student was a challenging but rewarding experience.