Economic Analysis of Maternal Health Behaviours

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Statement of Originality

I hereby certify that the work embodied in the thesis is my own work, conducted under normal supervision. The thesis contains no material which has been accepted, or is being examined, for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made. I give consent to the final version of my thesis being made available worldwide when deposited in the University's Digital Repository, subject to the provisions of the Copyright Act 1968 and any approved embargo.

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- Kaylee Slater, Megan Rollo, Zoe Szewczyk, Lee Ashton, Tracy Schumacher, Clare Collins. Do the Dietary Intakes of Pregnant Women Attending Public Hospital Antenatal Clinics Align with Australian Guide to Healthy Eating Recommendations? *Nutrients*, 2020. 12(8): p. 2438. DOI: 10.3390/nu12082438

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Contents

List of Abbreviations

Abbreviation	Description
ADG	Australian Dietary Guidelines
AES	Australian Eating Survey
AIHW	Australian Institute of Health and Welfare
ALSWH	Australian Longitudinal Study on Women's Health
AR-DRGs	Australian Refined Diagnosis Related Groups
ARFS	Australian Recommended Food Score
AUD	Australian Dollars
BIA	Budget Impact Assessment
BMI	Body Mass Index
CBA	Cost-Benefit Analysis
CCA	Cost-Consequence Analyses
CE	Cost-Effective
CEA	Cost-Effectiveness Analyses
CHEERS	Consolidated Health Economic Evaluation Reporting Standard
CI	Confidence Interval
CReDITTS	Clinical Research Design and Statistical Services
CUA	Cost Utility Analyses
DAG	Directed Acyclic Graph
DALY	Disability Adjusted Life Year
EGWG	Excessive Gestational Weight Gain
FASD	Fetal Alcohol Spectrum Disorder
GDM	Gestational Diabetes Mellitus
HMRI	Hunter Medical Research Institute
HNEH	Hunter New England Health
HNELHD	Hunter New England Local Health District
HTA	Health Technology Assessment
ICER	Incremental Cost Effectiveness Ratio
IQR	Interquartile Range
JHH	John Hunter Hospital
MSAC	Medical Services Advisory Committee
NCD	Non-Communicable Diseases
NHMRC	National Health and Medical Research Council
NRV	Nutrient Reference Values
NSW	New South Wales
OR	Odds Ratio
PBAC	Pharmaceutical Benefits Advisory Committee
QALY	Quality Adjusted Life Year
RCT	Randomised Controlled Trial
RECap	Research Electronic Data Capture

RR	Rate Ratio
SD	Standard Deviation
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
WHO	World Health Organisation

Thesis Abstract

Background and aims: Identifying, measuring, and valuing the economic impact of antenatal guidelines and their implementation has been identified as a key strategy for informing investment in health promotion and improving efficiency in healthcare. The research question of this thesis was: what is the economic impact of improving the modifiable maternal health risk behaviours, alcohol and dietary intake, on health care resource use during the antenatal period? To address this question, the thesis aims were:

1. Identify and synthesize evidence regarding the costs and impacts of antenatal nutrition and alcohol interventions and their associated implementation strategies.

2. Assess the cost, cost-consequence, and cost-effectiveness of a multi-strategy practice change intervention in increasing antenatal care addressing the consumption of alcohol by pregnant women.

3. Assess the economic impact of maternal diet quality and weight status of pregnant women and their impact on resource use in the delivery period.

Methods: To address the first objective, a systematic review of economic evaluations of antenatal nutrition and alcohol interventions and their associated implementation strategies was conducted. For the second objective, an economic evaluation was undertaken alongside a randomised controlled trial (RCT) of a multi-strategy practice change intervention designed to support antenatal care staff in providing a model of care consistent with clinical guideline recommendations for alcohol consumption in pregnancy. For the third objective, an observational study was conducted to gather self-report data and inpatient medical records for N=670 pregnant women in Newcastle, Australia, to examine the economic impact of maternal diet quality on resource use in the antenatal period.

Results: The systematic review identified a paucity of economic evidence regarding antenatal nutrition and alcohol interventions and no economic evaluations of assocaited investment in implementation. The trial-based economic analysis determined the practice change intervention to be both more effective and more costly than usual care. The average incremental cost per eligible clinician was $993 (range: $640-$1928) and $591 (range: $329 - $940) per woman who received all guideline elements. The observational study found higher body mass index (BMI) was associated with increased odds of caesarean delivery; women in obese class II (35.0–39.9 kg/m2) had significantly higher odds of caesarean delivery compared to women of normal weight (OR = 2.13, 95% CI 1.03 to 4.39; p = 0.04). The average cost per patient was $7962, $9309, and $9914 for women in

the normal weight category, obese class II, and obese class III, respectively. Higher diet quality was associated with a small statistically significant reduction in maternal length of stay.

Conclusion: The research included in this thesis addressed a small and significant gap in the evidence base necessary to inform greater understanding of the cost and cost-effectiveness of current nutrition and alcohol recommendations in pregnancy. The thesis provides new evidence regarding the economic impact of maternal health behaviours and antenatal health promotion interventions. Specifically, the economic evidence available to inform investment in future maternal alcohol and nutrition interventions was mapped, synthesized, and the gaps in the literature identified. The trial-based economic evaluation was the first to identify, measure, and value investment in antenatal guideline implementation efforts. Whilst healthcare funders' willingness to pay for the incremental effect of this intervention is unknown, the strategic investment in systems change is expected to improve the efficiency of the practice change intervention over time. The observational study identified that poor dietary patterns are common during pregnancy; thus, interventions to improve maternal BMI and diet quality could deliver substantive economic benefits to the healthcare system and community. The evidence presented in this thesis addresses the need for decision makers to be cognisant of the resource use implications of policy implementation.

Chapter 1

Introduction

1.1 Chapter Overview

Pregnancy is a unique period in which health promotion interventions have the potential to improve both maternal and infant outcomes in the antenatal period as well as reduce the burden of disease across the lifespan [1, 2, 3]. While the body of evidence for improving antenatal care in relation to maternal nutrition and reducing alcohol consumption continues to expand, there remain significant gaps in knowledge. The purpose of this chapter is to describe the current state of economic evidence and objectives of this thesis.

The Chapter begins by summarising the role of health promotion guidelines within Australia's health policy framework. *"The Australian Dietary Guidelines"* (ADG) provide recommendations about the amount and types of foods Australians need to eat for health and wellbeing. Australia's escalating burden of non-communicable diseases (NCD) is evidence of poor implementation and adoption of the ADG, and of the need to identify effective and efficient guideline implementation methods. Australia's national *"Clinical Practice Guidelines: Pregnancy Care"* (2019) are the standard reference for health professionals providing antenatal care [4]. These guidelines include recommendations based on the ADG regarding nutrition and alcohol intake in pregnancy that are to be provided by antenatal health care practitioners. The evidence informing the nutrition and alcohol intake recommendations in these guidelines is described, and significant gaps in the economic evidence informing the cost, and cost-effectiveness the nutrition and alcohol recommendations, and their implementation, are identified.

Finally, the need for economic evidence informing clinical guideline development and implementation is considered within the context of Australia's health care system. In summary, investment in evidence-based health promotion, providing evidence to inform clinical practice guidelines, and developing strategies to improve guideline implementation has been identified by the Australian Government as a feasible approach to reduce the economic and social burden of disease, and derive greater value from health care expenditure [5]. The chapter concludes with the aims and objectives of this thesis, together with an outline and summary of its structure.

1.2 Evidence-based nutrition and alcohol consumption guidelines in Australia

1.2.1 Determinants of health, origins of chronic non-communicable disease and the role of guidelines for informing health promotion activities

Health promotion is a broad term, defined as "activities that help communities and individuals to increase control over their health behaviours" [6]. Health promotion emphasises "preventing the root causes of ill health, rather than on treatment and cure and incorporates elements of governance (e.g. legislation and taxation), health literacy and population health programs (e.g. public awareness campaigns) and urban planning" [7]. Strategies for promoting health and mitigating health risk factors are best described on a continuum from proximal ('bottom up') through intermediate to distal ('top down') determinants [6]. This continuum assists in identifying how decision makers and health care providers can best respond to, or manage, health determinants. Distal determinants of health include national, institutional, legal, and cultural factors that influence health by acting on intermediate and proximal factors [6]. Collectively, health determinants are factors which influence an individual's health. These factors include an individual's social and economic environment, their physical environment, their genetic characteristics, and their modifiable health behaviours [8]. Health determinants can influence an individual's health status in a positive or negative way. Determinants that affect health in a negative way are referred to as 'risk factors' as they can increase the likelihood of developing a chronic disease, or impact the management and outcomes of other conditions [9].

Based on their proximity to the individual, health determinants can be classified as distal, intermediate or proximal. Distal factors are less readily modified than proximal or intermediate determinants [6]. Evidence-based guidelines are an example of a distal health promotion strategy which influences intermediate and proximal factors to improve the health of a population. In comparison, proximal health determinants have a more direct effect on health, with intermediate and distal determinants having decreasingly discernible effects [6]. Proximal determinants can act on a micro or macro level, acting on units as small as individuals, or as large as society as a whole. Proximal determinants include lifestyle and behavioural factors such as alcohol consumption, nutrition or chronic disease management to prevent premature death. Intermediate determinants of health are material factors such as an individual's wealth and socio-economic status, the built and natural environment, the health care system and access to and delivery of health

care service [10].

In Australia's health system, health promotion policies and their associated guidelines are used to provide an overarching framework to identify, prioritise and monitor initiatives within the context of the governments' preventive health agendas [11]. A policy outlines a department's or organization's intent to achieve a particular outcome and guidelines are a subset of supporting documents that provide guidance and non-mandatory advice on best practice [12]. Of relevance to this thesis, Australia's National Nutrition Policy [11] is supported by the ADG [13]. Australia's current National Nutrition Policy was last updated in 1992 and may be considered outdated [14]. National health promotion agencies Nutrition Australia, the Dietitians Association of Australia, the Public Health Association of Australia and The Heart Foundation have released a joint policy statement calling for the National Nutrition policy to be updated [14]. Reviewing the existing guidelines and providing evidence to inform future policies and guidelines is a distal health promotion strategy for reducing the burden of chronic disease [4].

The social and economic burden of chronic diseases is significant. In 2016 nearly 87% of deaths in Australia were associated with eight chronic diseases: arthritis; asthma; back-pain; cancer; cardio-vascular disease; chronic-obstructive pulmonary disease; diabetes; and mental health conditions [15]). In addition, 37% of hospitalisations were attributable to chronic disease and 35% of health problems managed in general practice (primary care) were chronic conditions [9]. in 2018, the five risk factors contributing the most to Australia's burden of disease were largely preventable, and include tobacco use (8.6%), overweight and obesity (8.4%), dietary risks (5.4%), high blood pressure (5.1%), and alcohol use (4.5%) [16]. It has been estimated that 38% of Australia's burden of disease could be prevented by reducing individual exposure to modifiable risk factors via health promotion strategies [16]. Improving adherence to national health promotion guidelines has been identified as a proximal health promotion strategy to improve individual health behaviours and reduce the social and economic burden of chronic disease [6].

At present, Australians show poor adherence to national dietary and alcohol guidelines, meaning the potential of these guidelines to improve health outcomes and reduce the economic and social burden of chronic disease is not realised [5]. Implementation strategies are required to ensure the barriers to adoption and adherence are addressed and return on investment, in the form of improved health and decreased burden of disease, is realised [17]. Implementation science has been defined as "the scientific study of methods to promote the systematic uptake of research findings and other evidence-based practices into routine practice, and, hence, to improve the quality and effectiveness of

health services" [17]. The scope of implementation science research is broader than traditional clinical research, focusing not only at the patient level but also at the provider, organisation, and policy levels of healthcare [17]. As a discipline, implementation science is akin to quality improvement in that these disciplines share the objective of improving the quality of healthcare, and many methods in these two fields overlap. Whilst quality improvement research begins with a specific problem in a specific health care system, implementation science typically begins with an evidence-based practice that is underutilised and systematically identifies and addresses associated gaps in quality at the provider, clinic or healthcare system level [17]. Implementation science in nutrition and alcohol research builds upon concepts developed in implementation science to provide guidance on how best to implement evidence-based cost-effective nutrition and alcohol programs into practice [18]. The application of implementation science in the field of nutrition is in its infancy [19], and applied health economic evaluation of nutrition and alcohol interventions and their associated implementation strategies is completely novel; the latter is the focus of this thesis.

1.2.2 The Australian Dietary Guidelines: recommendations for diet, alcohol and health promotion

1.2.2.1 The Australian Dietary Guidelines: the implementation and adoption of dietary recommendations

The ADG provide information about the types and amounts of foods, food groups, and dietary patterns that promote health and well-being, reduce the risk of diet-related conditions such as high cholesterol, high blood pressure, and obesity, and reduce the risk of chronic disease such as type two diabetes, cardiovascular disease, and some types of cancer [13]. The guidelines were first published in 1982, and the most recent were published in 2013 [13].

There are five overarching ADG, with further specifications for specific sub-populations. The five overarching guidelines are [13],

- Guideline 1: To achieve and maintain a healthy weight, be physically active and choose amounts of nutritious food and drinks to meet your energy needs.
- Guideline 2: Enjoy a wide variety of nutritious foods from these five core groups every day; vegetables, fruit, grain (cereal) products, lean meat and poultry, dairy (or dairy alternatives).
- Guideline 3: Limit intake of foods containing saturated fat, added salt, added

sugars and alcohol.

- Guideline 4: Encourage, support and promote breastfeeding.
- Guideline 5: Care for your food; prepare and store it safely.

The ADG are intended for use by health professionals, policy makers, educators, food manufacturers, food retailers, and researchers, so they can help Australians to eat healthy diets [20]. However, there are no routine national or state-based implementation strategies to ensure these guidelines are translated into practice by their intended users and the everyday health behaviours of Australians [20]. At present, the eating habits of many Australian's do not meet these recommended dietary guidelines. The Australian Institute of Health and Welfare (AIHW) reports almost 99% of children, 97% of men, and 95% of women do not consume the recommended serves of vegetables, and more than two-thirds (69%) of children and almost half (47%) of adults exceed the recommended intake of free sugars, which should account for less than 10% of energy [7]. The majority of Australians also fail to meet the recommended number of food serves in any of the five core food groups [21]. Of relevance to this thesis, many women fail to meet nationally recommended nutrition targets and do not appear to improve their diet quality when planning to become pregnant, or during pregnancy [22, 23].

1.2.2.2 The Australian Dietary Guidelines: the implementation and adoption of alcohol recommendations

With respect to diet-related health behaviours, alcohol use is unique, as it is the only substance which is both a macro-nutrient and a drug affecting brain function [13]. As such, evidence-based guideline recommendations for alcohol consumption are included in the ADG [13]. The relevant excerpt from the guidelines is presented below:

- Guideline 3d: If you choose to drink alcohol, limit intake. For women who are pregnant, planning a pregnancy or breastfeeding, not drinking alcohol is the safest option [13].

This recommendation is in addition to the separate, alcohol specific guidelines published by the National Health and Medical Research Council (NHMRC) which provide guidance for Australians to reduce their risk of harm from drinking alcohol [24]. The 2020 NHMRC Alcohol Guidelines are:

- Guideline 1 (Adults): To reduce the risk of harm from alcohol-related disease or injury, healthy men and women should drink no more than 10 standard drinks a

week and no more than four standard drinks on any one day. The less you drink, the lower your risk of harm from alcohol.

- Guideline 2 (Children and people under 18 years of age): To reduce the risk of injury and other harms to health, children and people under 18 years of age should not drink alcohol.
- Guideline 3 (Women who are pregnant or breastfeeding):
  - To prevent harm from alcohol to their unborn child, women who are pregnant or planning a pregnancy should not drink alcohol.
  - For women who are breastfeeding, not drinking alcohol is safest for their baby.

Despite these evidence based-guideline recommendations, alcohol is the most common substance use disorder drug in Australia [25]. One in six Australian's consuming alcohol at levels placing them at lifetime risk of alcohol related injury and one in four consuming alcohol at levels placing them at risk of single occasion harm, at least monthly [25]. According to Australia's *"National Drug and Strategy Household Survey"*, the number of women abstaining from drinking during pregnancy has increased from 40% in 2007 to 56% in 2016 [7]. However, one in four women (25%) continue to drink alcohol after finding out they were pregnant [7]. Similarly, national surveys and prospective cohort studies in Australia report the prevalence of maternal alcohol consumption at any time during pregnancy to be between 35% and 72% [26].

1.2.2.3 Why Australia's nutrition and alcohol guidelines include pregnancy-specific recommendations

Pregnancy is a unique period, during which maternal health improvements have the potential to influence maternal and infant outcomes in the short term, and reduce the burden of disease across the infants lifespan [1, 2, 3]. If a woman has less than adequate nutritional intake in the antenatal period, the "Developmental Origins of Health and Disease" hypothesis suggests the foetus may be programmed for a greater lifetime risk of chronic disease [27, 28]. The antenatal period is defined as covering the time from conception until birth. The importance of adhering to healthy dietary behaviours and abstaining from alcohol in the antenatal period are well recognised, as evidenced by explicit pregnancy guidelines in both the ADG and the NHMRC alcohol guidelines [29, 13].

Sub-optimal antenatal nutrition is common in developed countries and contributes to excessive gestational weight gain, gestational hypertension, pre-eclampsia, gestational

diabetes mellitus, pre-term birth, low and high birth weight, birth defects, and stillbirth [30, 31, 32, 33, 34, 35]. The consumption of alcohol during pregnancy can result in birth defects, and behavioural and neurodevelopmental abnormalities known as Fetal Alcohol Spectrum Disorder (FASD). The symptoms of FASD vary between individuals, based on the level of alcohol consumed during pregnancy, and can persist into adulthood [36]. FASD is the most common preventable cause of neurodevelopmental abnormalities in the western world [37].

1.2.3 The evidence informing the Australian Dietary Guidelines antenatal nutrition and alcohol intake recommendations

The current ADG (2013) were developed by the NHMRC with advice from experts on the Dietary Guidelines Working Committee and funding from the Australian Government Department of Health and Ageing [38]. The analysis and recommendations from this review were used to update the 2003 version of the ADG. The amounts of various foods needed to meet the estimated nutrient requirements for groups of Australian individuals of different ages, genders, lifestyle, body size, and activity was informed by mathematical modelling designed to translate nutrient reference values (NRVs) into food consumption patterns [39]. The modelling was undertaken for the NHMRC by expert consultants under the auspices of the Dietitians Association of Australia. The work was informed by *"A Review of the Evidence to Address Targeted Questions"*, a systematic review to inform revision of the ADG which investigated the evidence regarding the complex inter-relationships between food, diet, and health and food and nutrition, social diversity and the food supply [39]. The report, *"Modelling System to Inform the Revision of the Australian Guide to Healthy Eating"* (2011) [39] states, "whilst health and well-being were the primary drivers of the dietary models, it was important that models were realistic, i.e. that the models were achievable and that the foods comprising the models were accessible, culturally acceptable, affordable and available to all Australians [39]". The systematic review to inform the revision of the ADG did not include evidence from economic evaluations [39] and the cost, efficiency, and affordability of their recommendations is unknown.

1.2.4 Australia's Clinical Practice Guidelines for Pregnancy Care: the implementation and adoption of recommendations for antenatal health promotion

The *"National Clinical Practice Guidelines for Pregnancy Care"* (2019) provide evidence-based guidance to maternity service providers and the consumers of their care [4]. First

published in 2008, the guidelines were developed to ensure that women in Australia are provided with consistent, high- quality, evidence-based maternity care [4]. Included in these guidelines is a series of health promotion recommendations specific to maternal nutrition, alcohol intake, smoking, and the advice clinicians should be offering pregnant women [40]. At present, these guidelines are not routinely translated into clinical practice by antenatal care providers [26]. Further, the investment required to ensure that these guidelines are routinely implemented into practice is unknown.

1.2.5 The evidence informing the Clinical Practice Guidelines for Pregnancy Care antenatal nutrition and alcohol intake recommendations

The current *"Clinical Practice Guidelines: Pregnancy Care"* (2019) were developed by NHMRC expert advisory committees, after and independent of the ADG. They are based on systematic reviews of the available evidence and include recommendations based on levels of available evidence [40]. The level of evidence informing a recommendation is ranked from Grade A (gold standard) to PP (practice points), based on the level of evidence available to support the recommendation. Table 1.1 is an excerpt from the NHMRC (2009) *"Levels of Evidence and Grades for Recommendations for Developers of Guidelines"* and NHMRC (2011) *"Procedures and Requirements for Meeting the 2011 NHMRC Standard for Clinical Practice Guidelines"*[41]. Table 1.2 provides a definition of the grades of recommendations (for 2016-17 and 2018-19 reviews) based on the NHMRC *"Levels of Evidence and Grades for Recommendations for Developers of Guidelines"*.

Table 1.1 NHMRC definition of grades of recommendations

Type	**Definition**
Grade A	Body of evidence can be trusted to guide practice
Grade B	Body of evidence can be trusted to guide practice in most situations
Grade C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
Grade D	Body of evidence is weak and recommendation must be applied with caution
CBR	Recommendation formulated in the absence of quality evidence (where a systematic review of the evidence was conducted as part of the search strategy)
PP	Area is beyond the scope of the systematic literature review and advice was developed by the EAC

Where sufficient evidence was available, it was graded according to NHMRC *"Lev-*

Table 1.2: NHMRC Definition of grades of recommendations	
Type	**Definition**
Evidence-based recommendation	Body of evidence can be trusted to guide practice
Qualified evidence-based recommendation (QEBR)	Body of evidence can be trusted to guide practice in most situations
CBR	Recommendation formulated in the absence of quality evidence (where a systematic review of the evidence was conducted as part of the search strategy)
PP	Area is beyond the scope of the systematic literature review and advice was developed by the EAC

els of Evidence and Grades for Recommendations for Developers of Guidelines" (2009) [41]. Where evidence was lacking, consensus-based recommendations (CBR) were developed. For areas beyond the scope of the systematic review, practice points were developed based on Expert Advisory Committees [4]. Of the 183 "recommendations/practice points" in the *"Clinical Practice Guidelines: Pregnancy Care"* (2019), only five (2.7%) were supported by economic evaluation. These included maternal smoking interventions, gestational age assessment, ultrasound assessment of foetal anatomy, maternal screening for group B streptococcus, and screening for maternal thyroid dysfunction [42].

1.2.5.1 Smoking cessation recommendations

Smoking cessation recommendations are beyond the scope of the ADG. However, feature prominently in the *"Clinical Practice Guidelines: Pregnancy Care"*, alongside nutrition and alcohol guidelines, as significant lifestyle factors contributing to the health and well-being of a woman and her baby during pregnancy [4]. Smoking is the most common modifiable risk factor for pregnancy complications, and has been associated with poor dietary intake [43] and adverse maternal and infant health outcomes [44].

Currently, there are nine Australian pregnancy care guideline recommendations for tobacco smoking. Refer to Table 1.3. Six guidelines are applicable to all pregnant women (guidelines 11, 12, and 13 and practice points m, n, and o), and three are specific to sub-populations (adolescents and Indigenous populations). Of the six applicable to all pregnant women, three (50%) were informed by Grade A or Grade B evidence, meaning that the evidence can be trusted to guide practice in most or all situations.

Table 1.3: NHMRC recommendations and practice points for tobacco smoking.

#	Recommendation/practice point	Grade
11	At the first antenatal visit assess the woman's smoking status and exposure to passive smoking	A
11	At the first antenatal visit give the woman and her partner information about the risks to the unborn baby associated with maternal and passive smoking.	A
11	At the first antenatal visit if the woman smokes, emphasise the benefits of quitting as early as possible in the pregnancy and discuss any concerns she or her family may have about stopping smoking.	A
12	Offer women who smoke referral for smoking cessation interventions such as cognitive behavioural therapy.	B
M	At each antenatal visit, offer women who smoke personalised advice on how to stop smoking and provide information about available services to support quitting, including details on when, where and how to access them.	PP
13	If, after other options have been explored, a woman expresses a clear wish to use nicotine replacement therapy, discuss the risks and benefits with her.	B
N	If nicotine replacement therapy is used during pregnancy, intermittent–use formulations (gum, lozenge, inhaler and tablet) are preferred to continuous-use formulations (nicotine patches).	PP
O	Smoking status should be monitored and smoking cessation advice, encouragement and support offered throughout pregnancy.	PP
P	Health care professionals involved in the care of Aboriginal and Torres Strait Islander women should be aware of the high prevalence of smoking in some communities, and take account of this social norm when discussing smoking and supporting women to quit.	PP
Q	Culturally appropriate smoking cessation services should be offered.	PP
R	In discussing smoking and supporting Aboriginal and Torres Strait Islander women to quit smoking, health professionals should draw on the expertise of anti-tobacco workers where available.	PP

Legend: The number in the first column is the recommendation/practice point number as per the order listed in the guidelines. The second column contains the recommendation. The third column contains the grade for the evidence as per Table 1.1 and Table 1.2 levels of evidence informing recommendations/practice points.

Australia has achieved notable success in implementing smoking cessation policies [45, 7]. The *"National Drug Strategy Household Survey"* showed that the daily smoking rates halved between 1991 and 2016 (from 24% to 12%)[7]. In 2014, 11% of women who gave birth in Australia had smoked at some point during their pregnancy, representing a decrease from 15% in 2009 [4]. More recently, the Cancer Council *"Tobacco in Australia"* report found only 9.9% of Australian women who gave birth in 2017 smoked at some point during their pregnancy, with higher rates in the first 20 weeks of pregnancy (9.5%)

than after 20 weeks of pregnancy (7.3%) [46].

The current *"Clinical Practice Guidelines: Pregnancy Care"* (2019) recommendations for smoking cessation were informed by an economic evaluation that assessed whether recommending specific smoking cessation interventions to pregnant women who smoke was cost-effective compared to minimum intervention alone or a "do nothing" scenario [42]. The minimum intervention was the intervention likely to be received by pregnant women even if the recommendation is not generally implemented. The minimum intervention was assumed to be the application of the "5A's" brief smoking cessation intervention framework by general practitioners and referral to Quitline [42]; the "5A's" framework recommends general practitioners (1) Ask, (2) Advise, (3) Assess, (4) Assist, and (5) Arrange care, as further described elsewhere [47]. The analyses found that cognitive behavioural therapy and nicotine replacement therapy were likely to be cost-effective interventions for smoking cessation in pregnancy [42]. In most scenarios, nicotine replacement therapy was the preferred option as it was less costly than cognitive behavioural therapy. If costs incurred by the patients are considered, such as cost of attending the doctor's appointment and for nicotine replacement therapy, cognitive behavioural therapy was the more cost-effective solution. All comparator scenarios were preferable to the counterfactual, "do nothing" [42].

1.2.5.2 Dietary intake recommendations

In the *"Clinical Practice Guidelines: Pregnancy Care"* (2019), nutrition and nutrition supplements were identified as having insufficient evidence to provide a basis for recommendations, and were prioritised for future review [4]. Of the five nutrition or nutritional supplement topics with sufficient evidence to inform evidence-based recommendations, one recommendation had a body of evidence that could be "trusted to guide clinical practice"; this was recommendation 6: "Inform women that dietary supplementation with folic acid, from 12 weeks before conception and throughout the first 12 weeks of pregnancy, reduces the risk of having a baby with a neural tube defect and recommend a dose of 500 micro grams per day" [4]. The remaining four were judged as supported by a body of evidence that "could be trusted to guide clinical practice in most or some situations with care in application being advised". Refer Table 1.4. The required investment and cost-effectiveness of interventions aiming to implement these guidelines into practice is currently unknown.

Table 1.4: NHMRC recommendations and practice points for nutrition.

#	Recommendation/practice point	Grade
6	Inform women that dietary supplementation with folic acid, from 12 weeks before conception and throughout the first 12 weeks of pregnancy, reduces the risk of having a baby with a neural tube defect and recommend a dose of 500 micrograms per day.	A
8	Do not routinely offer iron supplementation to women during pregnancy.	B
9	Advise women with low dietary iron intake that intermittent supplementation is as effective as daily supplementation in preventing iron-deficiency anaemia, with fewer side effects.	B
7	Advise women that taking vitamin A, C or E supplements is not of benefit in pregnancy and may cause harm.	B
5	Reassure women that small to moderate amounts of caffeine are unlikely to harm the pregnancy.	C
III	Advise women who are pregnant to take an iodine supplement of 150 micrograms each day. Women with pre-existing thyroid conditions should seek advice from their medical practitioner before taking a supplement.	CBR
l	Women at high risk of iron deficiency due to limited access to dietary iron may benefit from practical advice on increasing intake of iron-rich foods.	PP
H	Eating the recommended number of daily serves of the five food groups and drinking plenty of water is important during pregnancy and breastfeeding.	PP
I	For women who are underweight, additional serves of the five food groups may contribute to healthy weight gain.	PP
J	For women who are overweight or obese, limiting additional serves and avoiding energy-dense foods may limit excessive weight gain. Weight loss diets are not recommended during pregnancy.	PP
K	Specific attention needs to be given to promoting folic acid supplementation to Aboriginal and Torres Strait Islander women of childbearing age and providing information to individual women at the first antenatal visit.	PP

Legend: The number in the first column is the recommendation/practice point number as per the order listed in the guidelines. The second column contains the recommendation. The third column contains the grade for the evidence as per Table 1.1 and Table 1.2 levels of evidence informing recommendations/practice points.

1.2.5.3 Alcohol recommendations

In the *"Clinical Practice Guidelines: Pregnancy Care"* (2019), alcohol intake was identified as having insufficient evidence to provide evidence-based recommendations and was prioritised for future review [4]. There is no known safe limit of consumption during pregnancy and women are advised to abstain from alcohol consumption, refer to Table 1.5 [48]. The required investment and cost-effectiveness of interventions to implement these guidelines into practice is currently unknown.

Table 1.5: NHMRC recommendations and practice points for alcohol.

#	Recommendation/practice point	Grade
IV	Advise women who are pregnant or planning a pregnancy that not drinking is the safest option as maternal alcohol consumption may adversely affect the developing fetus.	CBR

Legend: The number in the first column is the recommendation/practice point number as per the order listed in the guidelines. The second column contains the recommendation. The third column contains the grade for the evidence as per Table 1.1 and Table 1.2 levels of evidence informing recommendations/practice points.

1.3 The need for applied health economic evaluation at the local level of health care provision

Weaknesses in Australia's Health Technology Assessment (HTA) system have resulted in many technologies and models of care being implemented, or subsidised without being formally assessed for clinical and cost-effectiveness [49]. In 2015, the Australian Productivity Commission report *"Efficiency in Health"* recommended investment in evidence-based health promotion, providing evidence to inform clinical practice guidelines, and developing strategies to improve guideline adherence as feasible approaches to reduce the economic and social burden of disease, and derive greater value from health care expenditure [5]. As evidenced by the ADG, the *"Clinical Practice Guidelines: Pregnancy Care"* (2019) and the recommendations in the Australian Productivity Commission report, economic evaluations of health promotion strategies are not routine, and this represents a substantial gap in the evidence base.

Economics is the science of studying how people use various, scarce resources to achieve a desired outcome [50]. Applied economics takes the conclusions drawn from economic theories and empirical studies and applies them to real-world situations with the aim of informing investment decisions and predicting possible costs, consequences and opportunity costs associated with those investments [51]. Health economics is the

application of economic concepts and methods to understand how people make decisions regarding their health behaviours and use of health care [52]. Applied health economic evaluation contributes to evidence based decision making in health care by identifying, measuring, and valuing health care interventions, programs, technologies, and models of care and assessing their effectiveness, efficiency, equity, impact, scalability, and sustainability to inform the range of vastly different but unavoidable decisions in health care [53].

Governments need to know whether tax payer funded health care is delivering value for money, and health care decision makers need to know whether the care delivered through a health care system is effective, efficient, and affordable [54]. Information on effectiveness and cost enables decision makers to select high value healthcare that provides patient outcomes that are affordable to the community [54]. Economic evaluations of health care interventions gained momentum in high income countries since the 1980s and 1990s [55], driven largely by western government regulatory agencies requiring evidence of cost-effectiveness before medical technologies would be reimbursed [50]. Over the past 30 years, two factors have promoted an increase in prominence of economic evaluation within health care decision making. First, increasing pressure on health care budgets has led to a shift in focusing from effectiveness alone, to cost-effectiveness [50]. Second, decision-making processes have emerged in several jurisdictions that enable the results of economic evaluations to be used as integral components of funding, reimbursement, or coverage decisions [50]. For example, in Australia the Pharmaceutical Benefits Advisory Committee (PBAC) and Medical Services Advisory Committee (MSAC) are national level evaluation bodies that have well established, centralised Health Technology Assessment (HTA) procedures to assess the effectiveness and cost-effectiveness of medicines and devices [49]. Australian states and territories have their own agencies designed to encourage and support clinical innovation and systems improvement [54].

At present, the same level of evaluation of technologies entering the health system is not routinely applied at the local level [54]. The Australian Productivity Commission identified inconsistent evaluation of health care as a major problem hindering improved efficiency in Australia's health care system [5]. A report published by the NSW Regional Health Partners as part of the Health Systems Improvement and Sustainability National Initiative titled "The Local Level Evaluation of Healthcare in Australia", stated health care evaluation at the local level is largely decentralised, decisions are frequently based on clinical findings alone, and if evidence is unavailable or not accessed, based on consensus clinician opinion [54]. The report also stated that information on effectiveness, cost, and efficiency enables decision makers to select high value healthcare that provides patient outcomes that are affordable for the community [54]. Further, health economic

evaluation of social and economic impacts has been identified as an integral component of local level health care evaluation [56]. Improved evaluation is a means of mitigating Australia's rising health care expenditure and deriving greater value from health care funding [54]. These gaps in the economic evidence base are substantial and beyond the scope of this thesis. This thesis aims to contribute a specific set of applied economic evaluations of health care at the local level. The findings of which are intended to contribute to informing local health care system decision making and future research.

1.4 Chapter summary

Given the rising demand for health care and resource constraints, identifying effective and cost-effective maternal diet and alcohol guideline implementation strategies is necessary to ensure antenatal health promotion strategies are implemented in routine practice and the economic and social benefits associated with promotion strategies are realised.

1.4.1 Thesis aims

Identifying, measuring and valuing the economic impact of antenatal guidelines and their implementation has been identified as a key strategy for informing investment in health promotion and improving efficiency in healthcare. The research question of this thesis was: what is the economic impact of improving the modifiable maternal health risk behaviours, alcohol and dietary intake, on health care resource use during the antenatal period? To address this question, the thesis aims were:

1. Identify and synthesize evidence regarding the costs and impacts of antenatal nutrition and alcohol interventions and their associated implementation strategies.

2. Assess the cost, cost-consequence and cost-effectiveness of a multi-strategy practice change intervention in increasing antenatal care addressing the consumption of alcohol by pregnant women.

3. Assess the economic impact of maternal diet quality and weight status of pregnant women and their impact on resource use in the delivery period.

1.4.2 Thesis structure

The following figure presents the structure of this thesis in a flow diagram.

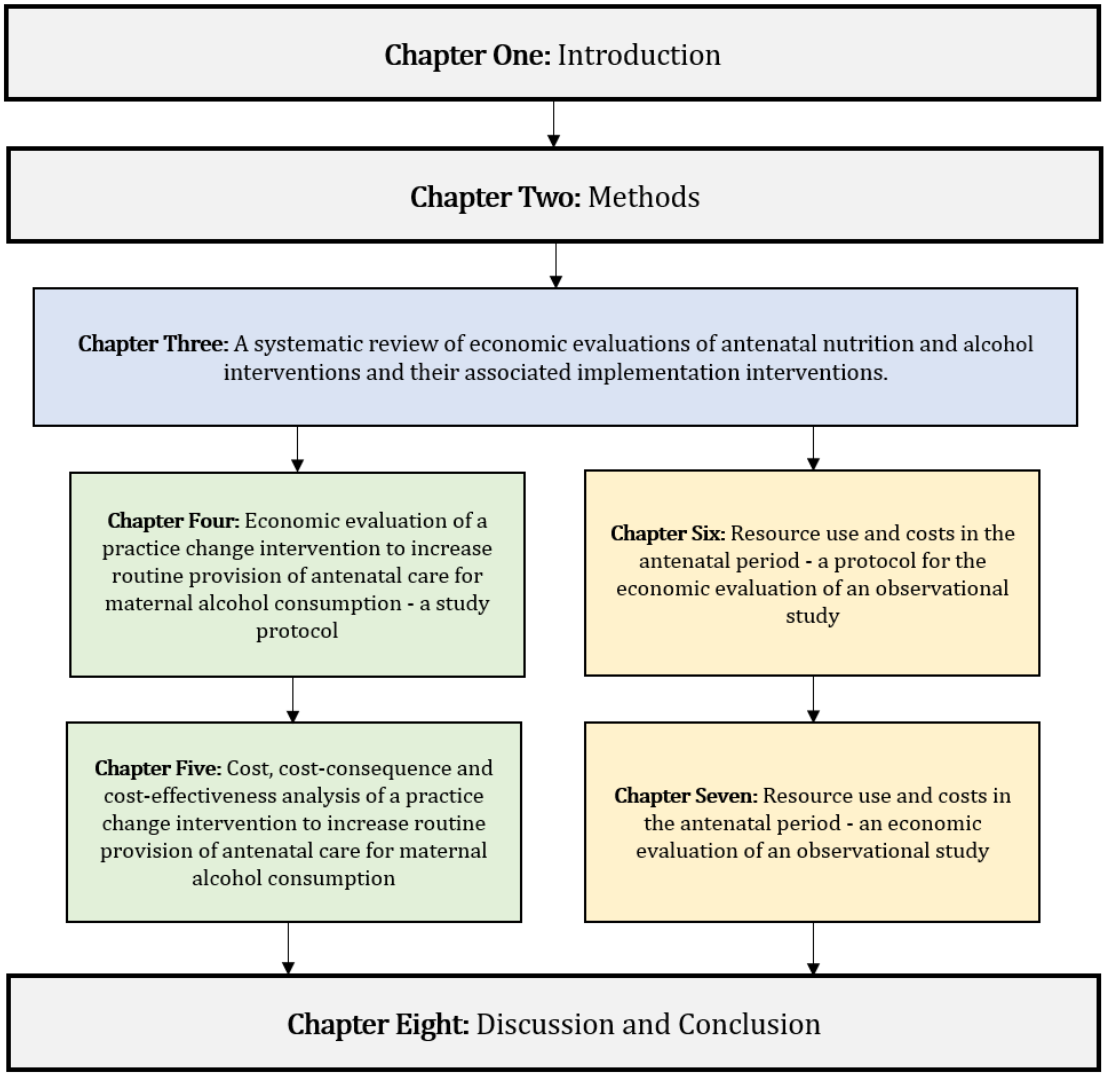

Figure 1.1: Flow diagram of thesis structure

1.4.3 Thesis overview

The research included in this thesis addressed a small, and significant gap in the evidence base necessary to inform greater understanding of the cost and cost-effectiveness of current antenatal nutrition and alcohol guideline recommendations, and their implementation.

Chapter One provides background and contextual information relevant to this thesis. This introductory chapter also includes the aims and objectives of this thesis, together with this outline. Chapter Two provides additional, unpublished details of the research methods, including economic data collection, used in this thesis.

The systematic literature review included in Chapter Three builds on the discussion in Chapter One. The existing economic evidence surrounding antenatal nutrition and alcohol interventions and their implementation is identified and appraised. The published manuscript includes a brief summary of the health and economic implications of sub-optimal antenatal nutrition and alcohol consumption, and advocates for the application of economic evaluation to health promotion interventions and their associated implementation strategies. The findings of this review highlight the paucity of economic evidence for nutrition and alcohol interventions in the antenatal period and discusses the implications of these gaps in the evidence base for informing future health promotion interventions. This review also highlights the dearth of evidence regarding the real-world implementation of cost-effective interventions and the limitations of this gap in the evidence. This work was published as a review article in *Nutrition Reviews*, a top ten ranking nutrition journal with an impact factor of 5.8 (2018). The findings of this literature review preface the subsequent economic evaluations.

Following the systematic literature review, this thesis includes into two distinct economic analyses of health promotion targets, first, maternal alcohol consumption, and second, maternal nutrition. These independent analyses build on the findings of the literature review, addressing the gaps in the evidence by providing original trial-based economic analyses. Each economic evaluation is prefaced with a protocol stipulating the economic study plan. Chapter Four includes the protocol and Chapter Five presents the outcomes of an economic evaluation of an implementation of an evidence-based model of antenatal care for alcohol consumption. The economic evaluation identifies, measures and values key resource and outcome impacts arising from the multi-strategy practice change intervention and will quantify the additional costs (savings) and effects of the implementation strategy compared with usual practice. The protocol in Chapter Four is published in *Implementation Science Communications* and the outcomes paper is currently under review in *Implementation Science* journal.

Unlike antenatal alcohol exposure, the range of potential antenatal nutrition targets are numerous and varied. Despite being a precursor to antenatal health care cost-drivers such as body mass index (BMI), diabetes, and hypertension [13], maternal diet quality, its relationships with antenatal health care utilisation and costs remain unexplored [52]. Chapter Six presents the protocol and Chapter Seven includes the published outcomes of an observational cross-sectional study investigating the relationship between antenatal

diet quality, health care resource use, and costs incurred during the delivery admission. The Chapter Seven appendix includes all resources developed to coordinate the successful recruitment of a large sample (N=1119) of pregnant women with detailed dietary data, for subsequent linkage with maternity medical records (N=670 had dietary data linked to medical records). The outcomes of Chapters Six and Seven provide insight into associations between antenatal diet quality and resource use in the delivery period, with a view to inform future health promotion interventions and their implementation strategies. The protocol in Chapter Six was submitted to various journals for publication but is included as a chapter in this thesis due to challenges with the relative timing of developing and publishing an economic evaluation protocol and the observational nature of the data. The outcomes manuscript presented in Chapter Seven was published in a 2020 *Nutrients* Special Issue titled *"The Guidelines for Balanced Diet and Healthy Lifestyles during Pregnancy: The Management of Health and Morbidity in Pregnancy"*. The findings of this study were presented in a 10-minute oral presentation at the *Health in Pre-conception, pregnancy and postpartum Early and Mid-Career Researcher Collective*, in December 2020.

Chapter Eight summarises the results of Chapters Three through Seven and discusses their implications for future research, limitations and future directions. The outcomes of these chapters are intended to inform the conduct of future interventions, their implementation and improve the conduct of future economic evaluations of health promotion interventions.

Chapter 2

Economic Data Collection and Other Research Methods Used in This Thesis

2.1 Chapter Introduction

The study designs and research methodologies used in this thesis include a systematic literature review, economic evaluation of data from a randomised controlled trial, and the collection, statistical analysis and economic analysis of observational data. These applied health economic analyses draw on economic, and to a lesser extent, statistical and epidemiological theory, to identify, measure, and value the costs and consequences associated with maternal health behaviours. The purpose of this chapter is to provide additional, unpublished details regarding the data collection and analysis methods used in this thesis.

Following the systematic literature review presented in Chapter Three this thesis reports two distinct economic evaluations of two different maternal health behaviours: alcohol intake and diet. Chapters Four and Five describe an economic evaluation of an implementation intervention which builds on existing evidence regarding the social and economic impact of maternal alcohol consumption [57, 58, 59], the effectiveness of screening and brief interventions for alcohol misuse [60, 61], and the need for greater understanding of the economic impact of changing clinical practice to ensure it adheres to evidence based guideline recommendations [62]. The review in Chapter Three also highlights a paucity of evidence regarding the economic impact of maternal dietary intake [10], the investment required to improve maternal diet quality [63], and suitable existing data available for secondary analyses of these topics. As such, Chapters Six describes the recruitment of participants to an observational study of maternal diet quality, the collection of self-report data and linked medical records, and measurement of dietary intake. Chapter Seven includes the published economic analyses of observational data to address this gap in the literature.

During the development of the observational study of diet quality, an opportunity arose for the candidate to take a lead role in the conduct of the study. As a Hunter Medical Research Institute (HMRI) employee and PhD student located at the HMRI (which is geographically nestled within the John Hunter Hospital (JHH) site), it was possible to leverage existing relationships between the HMRI and the health service. This facilitated a collaborative model of research including stakeholder engagement, development of a successful recruitment strategy, and the translation of findings back to the health service. The contents of the current chapter thus include unpublished details of the iterative approach to collecting, assessing, and improving methods for collecting and recording data for use in the applied health economic evaluations reported in this thesis.

2.2 Economic Data Collection and Research Methods Used in Chapters Four and Five

There is imperfect evidence to inform decisions regarding whether, and how to implement evidence-based guidelines into clinical practice [64]. In 2007, a systematic review of empiric studies was published which assessed the methodological quality of economic evaluations of guideline implementation interventions in clinical practice. The review found that a combination of poor reporting and methodologically flawed economic evaluations rendered the evidence base of limited use to decision making [64]. Of particular relevance to the current chapter, the review identified the need for increased methodological guidance, especially regarding the collection and synthesis of data used to evaluate the economic aspects of developing and implementing guidelines into clinical practice [64]. Over a decade later, in 2018 a published systematic review of empirical studies examining the costs and consequences, cost-effectiveness, and/or cost-benefit of strategies directed towards enhancing the implementation of public health interventions and policies in developed countries found the quality of the evidence base remained mixed [62]. At the time writing this thesis, guidelines for data collection and data synthesis for economic evaluations of implementation interventions have not yet been developed. In the absence of such guidelines, the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist were adhered to in each chapter of this thesis. The recommendations from the 2007 and 2018 reviews, among others, informed the identification, measurement, valuation, and reporting of economic evidence used in this thesis [64, 62, 65]. This section provides additional unpublished detail regarding why particular methods of identification and measurement of resource use were used.

2.2.1 The economic evaluation of a multi-strategy practice change implementation intervention to increase antenatal care addressing the consumption of alcohol by pregnant women

An implementation intervention has been defined as a "single method or technique to facilitate change" and an implementation strategy as "an integrated set, bundle or package of discreet implementation interventions ideally selected to address specific barriers to implementation success" [17]. Implementation interventions may include efforts to change behaviour at the patient, provider, system, and policy level [17]. In comparison to effectiveness studies, implementation studies typically focus on the rates and quality of use of evidence-based practices, instead of their effects [17]. For example, in studying the effects of a model of care to reduce maternal alcohol consumption, the

impact of increased screening, advice, and referral on maternal alcohol intake would be an evidence-based practice outcome. However, measuring the patient reported proportion of clinicians screening for maternal alcohol consumption, or providing appropriate advice and referral, is better described as an implementation study outcome.

Relevant to this thesis, in 2015, an National Health and Medical Research Council (NHMRC) Partnership Projects grant was awarded (APP1113032) to identify effective and cost-effective mechanisms for integrating evidence-based alcohol care into the routine practice of antenatal clinical services through a randomised controlled implementation trial (RCT). The study design and rationale for the study design is detailed in the trial protocol by Kingsland et al., titled *"A practice change intervention to improve antenatal care addressing alcohol consumption by women during pregnancy: research protocol for a randomised stepped-wedge cluster trial"* [61]. The primary outcome measures for this trial were the proportion of antenatal appointments at timepoints of 'booking in', 27–28 weeks gestation and 35–36 weeks gestation for which women reported whether they were:

1. Assessed for alcohol consumption;
2. Provided with brief advice related to alcohol consumption during pregnancy;
3. Received relevant care for addressing alcohol consumption during pregnancy; and
4. Assessed for alcohol consumption and receiving relevant care.

The implementation study primary outcomes are appropriate for implementation science but are challenging subjects for economic evaluations. Economic data was to be collected prospectively throughout the trial duration (from baseline to follow-up) and detail the resource use associated with the implementation intervention and direct research costs associated with the trial. The challenge with conducting an economic evaluation of an implementation intervention is that resource use data is recorded at the level of the implementation intervention location (sector), but the implementation study outcomes are collected at the level of the recipient (patient). There is thus a disconnect between implementation costing data collected at the level of the health service and implementation outcomes collected at the level of patients based on reported receipt of care. This was explored in a sensitivity analysis where the cost per woman in receipt of care was calculated by extrapolating the total number of women through each sector during the trial period, based on the sample proportion of women surveyed. The findings from the identification, measurement and valuation of prospective trial-based economic data are detailed in Chapters Four and Five.

2.2.2 The identification, measurement and valuation of resources required to deliver an implementation intervention

Failing to record the resources required to change clinician behaviour can lead to underestimation of costs, bias cost-effectiveness estimates, and result in misalignment between published evidence and actual health care delivery [66]. Alternatively, accounting for implementation costs when evaluating public health interventions generates a more realistic estimate of the cost-effectiveness of an intervention [66]. To prospectively collect economic data throughout the trial, a project management log (cost capture template) was developed in a single Microsoft Excel (2013) workbook and used to record the resources expended during the intervention, for later costing. Akin to a project budget with itemised reporting, the cost capture template categorised resources into the following categories:

1. **Labour**: all health service, non-health service, and research staff time invested in the trial was recorded in the labour-data worksheet. Staff time was recorded in minutes and an award wage or grade was attached to each item. The labour-data collection worksheet was also used to record the budget holder for each staff member e.g. NSW Government Department of Population Health, the University of Newcastle, or a specific hospital involved in the trial.

2. **Materials**: items such as stationary, education materials, electronic hardware, or software were recorded in the material-data worksheet. Where possible, receipt invoice numbers were recorded alongside individual items.

3. **Joint costs**: items incurred across multiple projects, for example the maintenance costs of a website portal supporting different interventions, capital costs including one-off investments such as the purchase of additional office buildings or motor vehicles, were recorded in the joint-cost worksheet. Items were then prorated based on NSW Health rates for shared resources.

4. **Miscellaneous costs**: items not easily classified into the other categories. For example, venue hire, travel, and overnight accommodation were recorded in the miscellaneous-cost worksheet. Each item was then valued using receipts, market rates, or NSW Health rates, including allowances for meals, travel and other allowances for the relevant year and region (NSW Health rates and allowances vary between capital cities, regional, and rural areas).

Where possible each item was dated, listed as a research, development, or implementation cost, and either associated with its specific intervention site or listed as a shared

resource. A version of this prospective cost-capture tool had been piloted in work conducted alongside but separate to this thesis and was used to inform the development of this tool. Refer to 'Additional Publications' on page xvii of this thesis for details of the projects that also involved this cost capture template.

2.3 Economic Data Collection and Research Methods Used in Chapters Six and Seven

2.3.1 The identification, collection, measurement and valuation of resource use for an economic evaluation of maternal health behaviours

As discussed in Chapter One, there is a documented paucity of evidence regarding the economic impact of health promoting behaviours, and an urgent need for improved understanding of how population health can be improved in a cost-effective way [5, 67, 52]. In comparison with maternal alcohol consumption, the economic impact of poor maternal diet quality and the implications for health service resource use are poorly documented [10]. To increase knowledge in this area, this thesis included the collection of observational, cross-sectional data for a sample of pregnant women, to measure maternal dietary intake and assess the economic impact of maternal diet on costs borne by the health service during delivery.

The observational study was approved by The University of Newcastle Human Research Ethics Committee, Australia in May 2016 (study reference number H-2017-0101), and the Hunter Area Research Ethics Committee in August 2016 (Reference number: HREC/16/HNE/189). Pregnant women aged 18 years or older at 28-36 weeks gestation (third trimester) and planning to deliver at the John Hunter Hospital, Newcastle, Australia were eligible to participate. A target sample size of 600 was estimated from the literature and supported by expert opinion.

2.3.2 Feasibility study to assess recruitment potential

The candidate had a lead role in managing the study, recruitment and applications for ethics approval and data linkage for the observational study of diet quality. Given the research team had limited experience recruiting participants directly from the JHH or accessing linked medical records data, an initial feasibility study was performed. The aims of this feasibility study were to: (1) assess recruitment rates attainable using the various methods proposed in the original study registration and ethics approval applica-

tions (see below); and (2) assess the labour time and resources required for recruitment. The results of the feasibility study were intended to inform and optimise the larger observational study recruitment approach and were not intended for publication. However, the methods and results of the feasibility study provide important context regarding the methods and outcomes reported in Chapters Six and Seven, and their contribution to the findings and recommendations described in Chapter Eight. They are therefore described here.

2.3.2.1 Recruitment feasibility study: Methods

In 2016 the observational study was registered, and approved with initial recruitment methods including poster advertisements, media articles, and social media posts. Poster advertisements were to be placed around the JHH antenatal outpatient clinic. Upon taking the project lead role in 2017, posters that included a summarised participant information statement, a uniform resource locator (URL) and quick response (QR) code to access the survey directly were developed. The following posters and flyers were placed around the antenatal outpatient clinic on information display boards and in bathroom stalls:

- A3 colour posters;
- A4 colour posters with pull-tabs;
- A5 black and white fliers were placed on the reception desk;
- A5 black and white fliers were placed in 'Antenatal Clinic and Birthing Information Packs' by administration staff; and
- A5 black and white fliers were placed on 'Outpatient Clinic Information Board'.

The JHH antenatal clinic is open five hours a day, five days a week. During this pilot recruitment period flyers were also provided directly to women attending the JHH antenatal outpatient clinic as they waited for their appointment. Each poster contained a customised, individual short URL using free link management platform, Bitly, a free URL shortner that provides data on URL access (https://bitly.com/). For this study individual Bitly links were used for each poster, flyer, or media article to provide statistics on the traffic associated with each recruitment method.

In mid-2017 an interview was conducted with HMRI media and communications team to develop a media brief for the 'HMRI News' webpage and provide expert advice on the development of social media content. The media brief was circulated via the 'HMRI

News' website, in the weekly HMRI 'affiliate news' email and on HMRI social media. The HMRI news article can be accessed here: https://hmri.org.au/news-article/counting-cost-diet-during-pregnancy. The social media content was posted across multiple social media outlets (e.g. Twitter, Facebook, and Instagram) throughout recruitment. Refer to Appendix 7.1: Prepared Media Content for the Study. During this time a local newspaper (The Newcastle Heald) reported an article promoting the study. The newspaper article was also disseminated across University of Newcastle and HMRI social media platforms. The Newcastle Herald news article regarding recruitment of the diet quality study can be found here: https://www.newcastleherald.com.au/story/5203152/carb-counting-made-easy-in-pregnancy/. Each article and social media platform had its own unique Bitly link to measure traffic associated with each media platform.

2.3.2.2 Recruitment feasibility study: Results

Recruitment was conducted from September 2017 through November 2017 (12 weeks), during which 16 participants were recruited. Based on Bitly links and survey response data, it was identified that the most successful method for recruiting participants was to directly approach women in the antenatal clinic before their appointment and ask them to complete the survey on their mobile phone. When asked, "How did you find out about the study?" 13 participants (82%) stated that they were "approached in the antenatal clinic waiting room by research staff", one (6%) stated 'flyer/poster', and two (12%) selected 'other' without providing further detail. Of these 16 participants, four (25%) completed the entire survey and the remaining 12 (75%) had insufficient time to complete the survey before being called to their appointment. The Bitly links indicated that the media articles, flyers in birthing packs and flyers place in the clinic resulted in zero recruited participants.

During this initial recruitment feasibility study the survey was hosted on Survey Monkey [68]: an online survey platform previously used by the Australian Eating Survey (AES) team to host the online version of the Australian Eating Survey. Prior to this study, Survey Monkey had been an effective tool for AES data collection in most circumstances. However, due to challenges specific to the JHH antenatal clinic setting, Survey Monkey could not be modified to the suit the needs of this project. There were several reasons for this. First, preliminary recruitment data indicated women were unable to complete their survey before being called to their appointment. At the time, Survey Monkey did not have the functionality to email participants the remainder of their survey for completion. Second, the antenatal clinic offers a wide range of services from pre-conception planning to antenatal, post-natal, and gynaecological care. Survey

Monkey did not have the functionality to allow women less than 28-weeks' gestation to provide their contact details and be electronically invited to complete the survey when they reached the eligible gestation period. Third, the antenatal clinic waiting room had limited-to-no internet connection, meaning participants did not have reliable internet connectivity on their mobile phones and were often unable to even access the survey whilst in the waiting room. Fourth, Survey Monkey did not have an 'offline' version allowing a survey to be completed without internet connection and later uploaded when a connection became available. Participants who could access the survey were thus unable to save their progress and later upload responses when a connection was available.

The feasibility study demonstrated that of all the piloted recruitment strategies, direct recruitment from the antenatal outpatient clinic was the only effective method. However, this method was inefficient, and a number of barriers required addressing in order to recruit the intended sample of 600 participants. The identified barriers were:

- Poor internet connectivity and mobile reception in the antenatal clinic prevented participants from commencing and/or completing the survey;
- High variation in appointment waiting times prevented many participants from completing the entire survey while in the clinic;
- There was no method to follow-up participants with incomplete surveys; and
- The clinic provided care to patients at all stages of the antenatal period and there was no method to follow-up women who were less than 28 weeks gestation when they were first approaches, but who would be eligible at a later period of gestation.

These barriers were unique to this study recruitment and were unknown prior to the feasibility study. To address these barriers, an optimised recruitment strategy was designed a corresponding ethics amendment submitted to the Hunter Area Research Ethics Committee and approved in November 2017 (Reference number HREC/16/HNE/314).

2.3.3 Observational study recruitment: main round

2.3.3.1 Recruitment optimisation: Methods

To design the recruitment strategy for the main recruitment stage advice from experts with experience in recruiting for large clinical trials, data collection, and database development was sought to overcome the barriers identified during the pilot stage. To address the lack of internet and mobile reception, it was advised to transfer the survey to a survey management platform with offline functionality. In consultation with the

HMRI Clinical Research Design and Statistical Services (CReDITTS) team, the research team decided to build and administer the survey using Research Electronic Data Capture (REDCap), a secure web application for building and managing online surveys and databases [69]. REDCap allowed for the survey to be completed offline and uploaded when an internet connection was available. The transfer from Survey Monkey to REDCap also allowed the development of methods for concurrently addressing several other barriers to recruitment, including:

- The development of automated emails to send incomplete surveys to participants for completion.
- For participants who had not completed their survey five days after commencing, the development of a series of automated reminder emails to prompt participants to complete their survey.
- The collection of contact information from women less-than 28-weeks' gestation, and the development of an automatic electronic survey invitation to send to these women when they reached 28 weeks gestation, inviting them to participate in the study.
- Sourcing of three University of Newcastle owned computer tablets to use for survey completion within the clinic waiting room.

During the recruitment development phase JHH Midwives, Nurses, Aboriginal Health Workers, and administration staff in the antenatal clinic were approached for advice on how to improve engagement with patients in the clinic waiting room. A key recommendation from these staff was to inform all antenatal clinic staff about the study, and its method of recruitment involving direct contact with patients in the clinic. As such, a series of four in-services were conducted to inform clinic staff of the study objectives, methods and recruitment procedures. (Refer to Appendix 7.2: "About Our Study": In-service for Antenatal Clinic Staff for a copy of the PowerPoint presentation that was used during the in-services for clinic staff).

Based on results from the feasibility study, the A3 colour posters and A4 posters with pull-tabs from the initial recruitment method remained in the clinic through the study duration. The A5 black and white fliers placed on the reception desk and within the 'Antenatal Clinic and Birthing Information Packs' and on the 'Outpatient Clinic Information Board' were discontinued. (Appendix 7.3: Study Recruitment Flyer placed in Antenatal Outpatient Clinic).

To maintain a full-time presence in the clinic, third and fourth-year undergraduate Nutrition and Dietetics students from the University of Newcastle were engaged as volunteer recruitment personnel. The volunteer position description was developed and circulated on the University of Newcastle Nutrition and Dietetics undergraduate student eLearning course website and students were invited to apply for the positions (Appendix 7.4 Volunteer Position Description). All student applicants were interviewed and answered a series of role specific questions (Appendix 7.5: Volunteer Recruitment Interview Questions).

Successful student applicants were required to attend a mandatory training and induction workshop prior to commencing their role in the clinic. The workshop commenced with a summary of the background to the project, the research hypothesis and aims, and a detailed description of the study design and ethical considerations (Appendix 7.6: Volunteer Training and Induction Workshop Presentation). The workshop included details of the study, the student's roles and responsibilities, together with safety and ethical considerations, scheduling and logistics, immunization requirements, and student parking options. The workshop included a script for students to use when recruiting new participants. Students were also invited to role play recruitment scenarios with other students; scenarios varied from "possible scenarios" to "highly unlikely scenarios" were included to allow students to practice brainstorming responses to questions they may be asked. Students were repeatedly advised not to offer dietary advice to people in the clinic. Finally, students were invited to complete the survey themselves so they were familiar with questions the participants would be asked. At the training workshop each student was also provided a training manual with all necessary information to complete their tasks in the clinic (Appendix 7.7: Volunteer Recruiter Manual). The training manual included any information that was presented in the induction workshop, contact information, and answers to frequently asked questions provided to assist students in their role. All students were required to have attended the introductory workshop and provide evidence of vaccination status required for clinical placement prior to commencing in the clinic. A total of three workshops were held.

In total, 12 student volunteers participated in recruitment for this study. Each student attended a training session in the clinic where they practiced recruiting participants and were provided feedback. After at least one, and no more than three training shifts in the clinic students were provided autonomy and worked as individuals or student pairs in the clinic. Students were provided the opportunity to debrief and report back to research staff at the end of each shift. One of the students who participated in the recruitment also went on to complete their Honours degree (Research) using data from this study, refer to page xvii: Additional publications co-authored during candidature.

2.3.3.2 Recruitment main round: results

The main recruitment phase using the optimised recruitment approach commenced in March 2018. After 12 weeks, a total 485 participants had commenced the survey. Of these, 235 (48.4%) had completed the entire survey. The anticipated timeline to completing recruitment was 10 months (December 2018). During recruitment a weekly report was circulated to study investigators providing an update and summary of the recruitment progress to date, refer to Table 2.1.

Table 2.1: Recruitment Progress for Stakeholder Update				
Date	**Surveys Started**	**Surveys Completed**	**Weekly Total Completed**	**% Total Completed (n=600)**
23/3/18	74	14	14	2%
30/3/18	131	49	35	8%
6/4/18	204	82	33	14%
13/4/18	254	103	21	17%
20/4/18	294	128	25	21%
27/4/18	310	139	11	23%
4/5/18	336	151	12	25%
11/5/18	372	173	14	29%
18/5/18	387	186	13	31%
25/5/18	430	200	14	33%
1/6/18	454	215	15	36%
8/6/18	485	235	20	39%
15/6/18	515	252	17	42%
22/6/18	542	261	9	44%
29/6/18	562	276	15	46%
6/7/18	594	295	19	49%
13/7/18	615	307	12	51%
20/7/18	637	320	13	53%
27/7/18	655	334	14	56%
3/8/18	663	342	8	57%
10/8/18	676	355	13	59%
17/8/18	699	365	10	61%
24/8/18	737	386	21	64%
31/8/18	776	412	26	69%
7/9/18	793	423	11	71%
14/9/18	843	458	35	76%
21/9/18	878	474	16	79%
28/9/18	914	500	26	83%
5/10/18	930	514	14	86%
12/10/18	954	527	13	88%
19/10/18	973	546	19	91%
26/10/18	998	553	7	92%
2/11/18	1042	580	27	97%
9/11/18	1072	597	17	100%
16/11/18	1115	616	19	103%

It was anticipated that all women would have given birth by March 2019, and the patient medical records data were to be retrieved after this date.

2.3.4 Economic data collection: accessing linked patient medical record data

Acquisition of admitted patient medical record data commenced in February 2019. Maternal and infant health and demographic data was sourced from Hunter New England Health (HNEH) databases eMaternity and iPM using patient medical records numbers. Where possible, medical records data were used to confirm self-report responses collected from study participants to reduce potential error or bias in reporting. During this process, it was discovered that once inpatient data was recorded, it could take up to six-months for the data to being processed by the Hunter New England Local Health District (HNELHD) Activity and Performance (Finance) Unit. That is, additional to the procedures in accessing inpatient data there was a further minimum 6-month delay in identified patient data being costed by the Activity and Performance Unit. Further to this, the Activity and Performance Unit are not a research unit equipped or required to process external data requests for research purposes. We were informed that retrieving identified patient cost data for this cohort would need to be processed by NSW Health Treasury, which would involve additional delays and likely incur a fee.

Between 2017-2020, alongside the conduct of this study, significant changes to HNEH data access policies occurred. The NSW *"Health Data & Information Custodianship Policy"* was published in 2013 and defines a set of principles for the management and maintenance of NSW core data and information assets [70]. These principles align with national and international best practice, industry standards and practices. In 2017, the HNELHD developed its own policy for compliance with state guidance. This policy was identified for revision in 2019 and was released in late 2020. Navigating the data access policies and changes in compliance requirements that occurred throughout the duration of this project required familiarisation with the NSW Health data policy, as well as local HNELHD policy.

2.4 The economic analysis of maternal diet quality, body mass index and resource use in the perinatal period using observational study data

2.4.1 The identification, measurement and valuation of resource use using linked medical records data

Accessing identified admitted patient cost data for the delivery period was not feasible for this study. As such, the study design was modified and resource use proxies for inpatient

cost were identified. A scoping literature review was conducted and expert stakeholders such as Midwives, Clinical Midwife Educations, Obstetricians, Nurses, Statisticians, and Epidemiologists, were consulted to identify resource use that is known to be associated with BMI and/or diet quality. After extensive discussion, review, and feedback, four specific outcomes were identified:

- Mode of delivery: caesarean versus vaginal (natural, instrumental, breech, compound)
- Maternal length of stay: in days
- Maternal admission to intensive care: yes or no
- Midwifery-in-the-home service utilisation: total number of follow-up care visits associated with maternal discharge post-delivery

It was intended that once an association between the exposure and the outcome was established, each resource use item would be costed. Mode of delivery was costed using and The *"Australian Refined Diagnosis Related Groups"* (AR-DRGs) classification system. The AR-DRG codes classify units of hospital output and group inpatient stays into clinically meaningful categories consisting of similar levels of complexity (outputs) consuming similar amounts of resources (inputs) [71]. Maternal length of stay is a parameter that informs an inpatients AR-DRG code, therefore could not be costed separately and was reported in natural units (days). Maternal admission to intensive care could be costed using AR-DRG codes. Similar to length of stay, number of midwifery-in-the-home service utilisation could not be costed based on individual patient AR-DRG codes and was also reported in natural units (number of visits).

2.4.2 Analysis of observational data using directed acyclic graphs (DAGs) for causal inference

We hypothesized that high Body Mass Index (BMI) and low diet quality would be associated with increased healthcare resource use, with diet quality potentially having a direct effect, independent of BMI. However, there exist complex preconception processes that influence maternal and infant health outcomes and resource use, that may also influence diet quality [72]. The limitations of traditional methods for assessing associations in observational studies and inferring causality is widely recognised [73]. Incorrect causal inferences are more likely to occur in observational studies than clinical trials due to confounding bias [73]. However, the use of experimental design in the antenatal

period is often restricted as there are issues with ethics and practicalities [73]. In order to investigate causality, observational data must be interrogated carefully with attention to the potential for known and unknown confounders and other biases [73].

Causal inference has an important role in public health research, as the determination that an association is causal indicates the possibility for an intervention [72]. Causal inference in epidemiology has been defined as "an exercise in measurement of an effect, rather than as a criterion-guided process for deciding whether an effect is present or not" [74]. The determination that an association is causal, and the strength of the effect, can have profound public health consequences indicating a need for reducing exposure to detrimental agents or increasing exposure to beneficial ones [72]. Similarly, false interpretation of the true relationship due to confounding or biases can have profound public health consequences, resulting in the dissemination of incorrect information and wrongly indicating a need for changes in exposure [75].

Causal diagrams such as directed acyclic graphs (DAGs) are increasingly used in modern epidemiology to identify confounding variables for inclusion in regression models to control confounding bias [76]. DAGs provide important advantages to traditional methods of confounder adjustment, which often simply involve adjusting for all suspected confounders [77, 74]. Advantages of DAGs include their ability to distinguish confounders from mediators and thus allow estimation of both total and direct effects [76]. By distinguishing confounders from mediators, the DAG can address separate hypotheses regarding total and direct effects[1]. When estimating total effects[2], the model is not adjusted for mediating variables, since the interest in in the sum of all exposure effects, including direct effects on the outcome, and any effects mediated by other variables [77]. Alternatively, when estimating direct effects, the model is adjusted for mediating variables, thereby partitioning direct and indirect effects. Importantly, traditional methods often inadvertently adjust for mediators, by considering these as confounders, and thereby do not distinguish between total and direct effects [77].

Another advantage of DAGs includes their ability to increase the efficiency of confounder adjustment by identifying minimum sufficient adjustment sets, and to identify variables for which adjustment is not indicated and can actually introduce bias[3] due to collider stratification [78]. The basis of confounder adjustment using DAGs is the

[1] An indirect effect of an exposure acts on the outcome through a third variable whereas a direct effect does not act through any other variables [77].

[2] A total effect is then the sum of the direct effect and any indirect effect(s) between a given exposure and outcome [77].

[3] In DAGs literature, bias is defined as a systematic, incorrect interpretation of the true relationship between the exposure and the outcome, and a confounder is defined as a common cause of the exposure and the outcome [76].

requirement to close any "open backdoor paths" which can be traced from the outcome back to the exposure via causal arrows (excluding the arrow linking exposure and outcome) [74]. Open paths can be closed by adjusting for one or more variables on the path. As such, if multiple confounding variables lie on the path, it may be necessary to simply adjust for one of these variables, in order to close the path and control confounding [78]. This approach differs from traditional statistical methods which would often include the entire set of variables in the model. Compared to the traditional approach, using adjustment sets based on backdoor paths has multiple advantages, including maximisation of statistical power and avoidance of collider stratification bias and collinearity [78, 76].

Whilst more common in statistics and epidemiology research, the use of DAGs in economic evaluation and nutrition research is relatively novel. For the purposes of informing the analysis in Chapters Six and Seven, a scoping literature review was conducted to identify a list of variables that could be included in the DAG. The manuscript in Chapter Seven includes a list of variables that was reviewed by expert dietitians, epidemiologists, obstetricians, midwives, and statisticians before the final set of variables was agreed upon. The scoping literature review also identified that maternal diet quality is stable pre- and post-conception [23]. As such, we hypothesised there would be a direct effect of diet quality on resource use in the delivery period and an indirect effect, acting through BMI. Given the available self-report and linked medical records data, two alternative measures for maternal weight status were identified. The first, was self-reported maternal weight and height recorded at the time of completing the survey (28-36 weeks gestation). The second was patient pre-pregnancy BMI reported during the 20-week booking-in visit, recorded by antenatal clinic clinicians and sourced from linked medical records. The second measure was deemed the more accurate measure of maternal weight status and used throughout the analyses.

DAGitty, a browser-based environment [79] was used to create three DAGs to visually depict the direct and total effect of interest for the study aims. The simplified diagrammatic form of aim (ii), the total effect of pre-pregnancy BMI on resource use is presented in Figure 2.1:

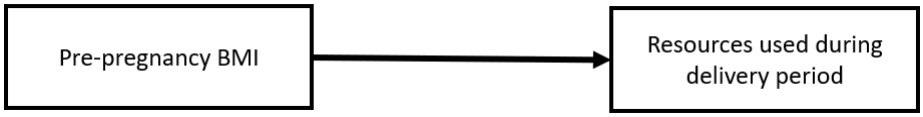

Figure 2.1: Simplified DAG for aim (ii), estimate of the total effect of pre-pregnancy BMI on resource use.

The simplified diagrammatic form of aim (iii), the total effect of diet quality on

resource use is presented in Figure 2.2:

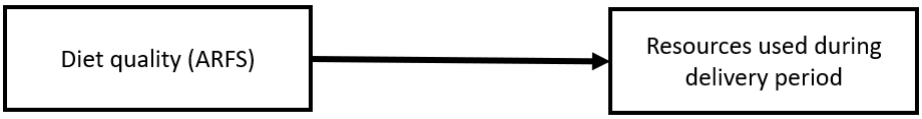

Figure 2.2: Simplified DAG for aim (iii), estimate of the total effect of diet quality on resource use.

The simplified diagrammatic form of aim (iv), the direct effect of maternal diet quality on resource use is presented in Figure 2.3:

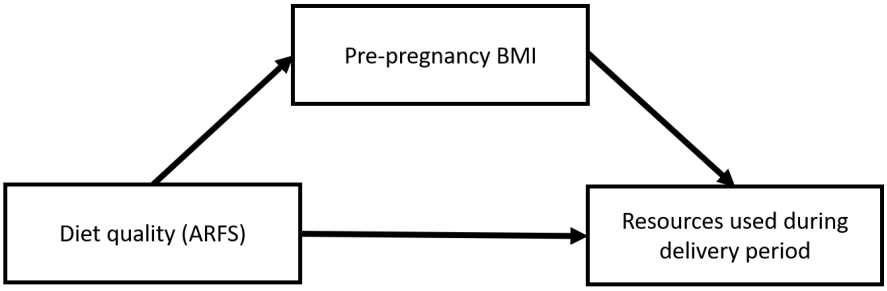

Figure 2.3: Simplified DAG for aim (iv), the hypothesized relationship between diet quality and resource use.

The complete DAGs are available as a supplementary file attached to the publication (Appendix 7.1 Manuscript Supplementary File).

The findings from the collection, identification, measurement and valuation of cross-sectional data is detailed in Chapters Six and Seven.

2.5 Chapter Summary

This chapter contains additional unpublished information regarding the trial-based economic analyses detailed in Chapters Four and Five, and the collection and analysis of observational data in Chapters Six and Seven. The methods used to collect economic data were unique to the trials included in this thesis. However, provide important lessons for informing future economic data collection methods for both randomised controlled trials and observational studies. The economic evaluations conducted in this thesis were subject to the available data, the limitations of which also inform future methods for analysing trial-based economic data and costing observational study data. The lessons learned throughout the conduct of this thesis directly informed the discussion and recommendations in Chapter Eight.

Chapter 3

A systematic review of economic evaluations of antenatal nutrition and alcohol interventions and their associated implementation interventions

3.1 Chapter Overview

Australia's pregnancy specific dietary guidelines and antenatal clinical guidelines for nutrition and alcohol consumption were summarised in Chapter One. Without consideration for how these guidelines will be implemented, return-on-investment in the form of health gains and reductions in the social and economic burden of disease can be stifled [52]. Chapter 3 reports the methods and results related to two systematic literature reviews. The purpose of these reviews was to assess the extent to which economic evaluations have been applied to (1) antenatal nutrition and alcohol interventions and (2) investment in activity to achieve uptake of relevant antenatal nutrition and alcohol policies and guidelines, that is implementation.

The increasing application of implementation science in healthcare is not accidental [62]. Implementation science has developed as a research discipline with the objective of converting evidence into routine practice, and is defined as the scientific study of methods to promote the uptake of research findings into routine healthcare practice or policy [80]. Proven implementation strategies and programs have evolved to influence the uptake of evidence-based, effective, and cost-effective interventions [81]. Whilst effective, these strategies come with additional resource requirements and opportunity costs which are often overlooked [62]. Implementation interventions compete for the same resources as other interventions. Identifying, measuring and valuing the resources directed towards implementation, in conjunction with an assessment of effectiveness, informs the value for money derived from implementation investment [62].

The contents of this chapter were published in *Nutrition Reviews* in July 2020, citation as follows:

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3.2 Published manuscript

Lead Article

A systematic review of economic evaluations of antenatal nutrition and alcohol interventions and their associated implementation interventions

Zoe Szewczyk , Elizabeth Holliday, Brittany Dean, Clare Collins, and Penny Reeves

Context: *Improving maternal nutrition and promoting alcohol abstinence during pregnancy are key to reducing subsequent economic and social impacts. However, antenatal nutrition and alcohol interventions are underused, partly because economic evidence to support investment is limited.* ***Objective:*** *The purpose of this systematic literature review was to assess the extent to which economic evaluations have been applied to antenatal public health interventions, and implementation strategies addressing maternal nutrition and alcohol intake.* ***Data Sources:*** *Two separate systematic reviews were conducted to address the 2 stated aims. Both reviews adhered to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The searches were conducted using the following databases: Medline, EMBASE, Cochrane, EconLit, CINAHL, and the National Health Service Economic Evaluation Database, accompanied by a handsearch of gray literature.* ***Data Extraction:*** *Review 1 returned 9599 records after duplicates were removed, from which 12 economic evaluations were included. Review 2 returned 136 records after duplicates were removed, with none eligible for inclusion. The articles included in review 1 comprised 10 economic evaluations of nutrition interventions and 2 evaluations of alcohol interventions.* ***Data Analysis:*** *Methodological quality was assessed using the Drummond 10-point quality checklist. Methodological quality was high, with variation in reporting practices and predominance of modeled evaluations.* ***Results:*** *Antenatal nutrition and alcohol interventions offer value for money and have potential to considerably reduce healthcare costs. No evidence regarding intervention implementation cost was identified.* ***Conclusion:*** *The current evidence base has important gaps that limit its value to decision makers. Incorporating health economic principles and methods into health promotion interventions will inform decisions about how to derive value from investment in healthcare.*

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INTRODUCTION

Health promotion interventions targeting pregnant women have the potential to improve maternal and infant outcomes in the short term and reduce the burden of disease across the life span.[1–3] Specifically, poor nutrition and alcohol consumption during pregnancy have been identified as risk factors for adverse health outcomes during the antenatal period and throughout an infant's life.[1] National dietary guidelines provide specific advice about healthy eating during pregnancy.[4–7] Despite these guidelines, suboptimal antenatal nutrition is common in developed countries and may contribute to excessive gestational weight gain, gestational hypertension, preeclampsia, gestational diabetes mellitus, preterm birth, low and high birth weight, birth defects, and stillbirth,[8,9] and may result in increased utilization of healthcare resources throughout the delivery period[10] and across the life span.[11–13] Similarly, alcohol consumption during pregnancy can increase the risk of various adverse health and developmental problems for infants and older children.[14–17] Clinical practice guidelines recommend that pregnant women abstain from alcohol use, since there is no safe level of alcohol consumption during pregnancy.[18,19] Despite these recommendations, alcohol use during pregnancy is common[20,21] and fetal alcohol spectrum disorder is the most common preventable cause of neurodevelopmental abnormalities in the western world.[17] Improving maternal nutrition and promoting alcohol abstinence during pregnancy are identified mechanisms for reducing subsequent economic and social impacts.[22–24] However, health promotion interventions during the antenatal period are underused, partly because economic evidence to support investment is limited.[25]

In healthcare, guideline adherence and evidence-based and cost-effective practice do not occur spontaneously.[26] Without processes for implementing cost-effective interventions into practice, return on investment in the form of health gains and improved health service efficiency may not be realized. Implementation strategies are distinct from public health interventions, which focus on health behaviors and health outcomes. Implementation strategies are explicitly designed to improve service delivery, intervention (or model-of-care) adoption, and service outcomes.[27] Successful implementation strategies and programs increase the uptake of effective and cost-effective public health interventions and programs.[28] However, these strategies require additional resources,[27] and the cost of implementation may be so substantial that the intervention itself is no longer cost-effective. In economics, the value of these resources is measured in terms of their opportunity cost – that is, the value forgone from an alternative use.[29] The process of identifying, measuring, and valuing the resources required for health promotion interventions and their implementation, in conjunction with their effectiveness, informs the value for money derived from investment in health promotion and is important for health service efficiency.[26] Economic evaluation is an important tool for determining which interventions offer value for money and is an integral part of the decision-making process for health technologies and interventions.[30]

The application of economic evaluation to health promotion interventions is increasing, but its application to implementation interventions remains uncommon.[26,27] A recent systematic review of economic evaluations of smoking cessation interventions during pregnancy identified limited high-quality economic evaluations of antenatal smoking cessation interventions and also that results from poor-quality evaluations are likely to lead to misinformed decisions being made, with unintended negative impacts on health and economic outcomes.[30] Greater understanding of the cost-effectiveness of antenatal nutrition and alcohol interventions and their implementation strategies is warranted to inform future healthcare policy, investment allocation, and research priorities.[31] The current systematic review appraised the published literature for evidence regarding the cost-effectiveness of public health promotion interventions and implementation strategies designed to improve their adoption.

The aims were to (1) identify empirical economic evaluations of antenatal public health interventions targeting nutrition and alcohol published between January 2000 and May 2019, (2) identify empirical economic evaluations of implementation strategies relating to antenatal public health interventions targeting antenatal nutrition and alcohol intake, and (3) synthesize the evidence to develop recommendations for the conduct of future economic evaluations.

METHODS

To address the research aims, 2 separate reviews were conducted: (1) economic evaluations of antenatal nutrition and alcohol interventions, and (2) economic evaluations of associated antenatal public health implementation interventions. The searches were limited to studies published in English between January 2000 and May 2019. This time frame was considered appropriate to ensure relevance to the current healthcare context and technologies used to deliver interventions.

Table 1 **PICOS criteria for inclusion of studies**

Parameter	Criterion
Population	Women in the antenatal period, defined as the time from conception until the time of birth[32]
Intervention	Any intervention or combination of interventions promoting abstinence from alcohol in pregnancy. In addition, any nutrition intervention or combination of interventions, as classified by the World Health Organization categories of nutrition interventions: Behavioral nutrition interventions focus on the adjustment of personal practices and habits; fortification interventions involve the addition of nutrients to staple foods; supplementation refers to the provision of individual or mixtures of nutrients separately from the diet; regulatory interventions are those aimed at regulating certain nutrition-related activities or actions which have an impact on nutrition health outcomes; situational nutrition interventions are those that take place in a specific setting[33]
Comparison	Any comparator intervention including no intervention, "usual care," or "treatment as usual"
Outcome	Any relevant economic outcomes including cost, cost-consequence, cost-utility and cost-benefit ratios, incremental cost-effectiveness ratios, and net monetary benefit statistics
Study design	Included studies were modeled or trial-based economic evaluations. Modeled economic evaluations are broadly defined as the reproduction of events and possible consequences due to alternative options at the cohort or individual level using mathematical and statistical frameworks and secondary data sourced from existing evidence and databases.[34] Studies were considered full economic evaluations if they reported information on both the costs and effects of interventions[29] Studies were excluded if the economic evaluation was incomplete or available in abstract form only. Studies of multidisciplinary interventions (eg, lifestyle programs) that included a dietary component but did not report the nutrition intervention outcomes separately were not included. Studies of "substance use" interventions that combined treatment for alcohol and illicit drugs but did not report the alcohol intervention outcomes separately were not included

Review 1: evaluations of antenatal nutrition and alcohol interventions

Table 1 shows the PICOS (population, intervention, comparison, outcome, and study design) criteria used for the inclusion of studies in review 1.

Review 2: evaluations of antenatal nutrition and alcohol implementation interventions

In review 2, we also sought to assess whether the included studies reported on development costs, public health implementation execution costs, and subsequent changes in the cost of healthcare provision. The inclusion and exclusion criteria used in review 1 were replicated for review 2 with the addition of implementation terms. Implementation interventions were defined as any initiative designed to influence the uptake of public or population health interventions in community or clinical settings.[35]

Search strategy and selection

Review 1. Both reviews adhered to the 5-step approach for preparing systematic reviews of economic evaluations for informing evidence-based healthcare decisions, as recommended by van Mastrigt et al[36]. An initial scoping review of the Medline database was conducted with assistance from an accredited librarian, followed by analysis of the text words contained in the title, abstract, key words, and reference lists. For review 1, a preliminary scoping review identified 3 themes, with studies relating to (1) the antenatal period; (2) nutrition or alcohol interventions; and (3) economic evaluations. Specific search filters for each theme were developed iteratively in response to findings of the preliminary scoping review. Where possible, validated or expert recommended search filters were used – eg, the filter for identifying economic evaluations developed by the Canadian Agency for Drugs and Technologies in Health.[28,36,37] Search filters were developed for Medline specifically and replicated for the following databases: EMBASE, Cochrane, EconLit, CINAHL, and the National Health Service Economic Evaluation Database. The Medline search strategies disaggregated by PICOS criteria category are shown in Table S1 (*please see the Supporting Information online*).

Reference lists from all identified reports and articles were handsearched for additional studies. A gray literature search of the following information platforms was conducted to identify articles not located in electronic databases: the National Institute for Health and Care Excellence, Health Technology Assessment, World Health Organization, Google, and Google Scholar. Both reviews followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol[38,39] for the conduct and reporting of systematic reviews (Table S2; *please see the Supporting Information online*).

All titles and abstracts of the search results were independently screened by 2 reviewers (Z.S. and B.D.). Two reviewers (Z.S. and B.D.) independently assessed full-text articles for inclusion. Disagreements on included texts were resolved by consensus.

Review 2. The search strategy and selection for review 1 were repeated for review 2. The 3 themes identified in

review 1 were used along with the addition of a fourth theme: implementation interventions.

Data extraction and analysis

The quality appraisal evaluated the methodological quality of the economic evaluation adopted, using the Drummond 10-point quality checklist.[40] To determine any omissions or limitations in the included evaluations, the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist[41] was used as the data extraction template. The CHEERS checklist consolidation and elaboration article provides best-practice recommendations for reporting of health and economic outcomes, regardless of intervention type or evaluation methodology.[42] The CHEERS checklist was used to inform the reporting of review results.

Two reviewers (Z.S. and P.R.) performed data extraction of the first study and discussed the results, before Z.S. performed data extraction on the remaining studies. Discrepancies were discussed and resolved by consensus. All data was recorded in a Microsoft Excel (2016) database.

Evidence synthesis

There are currently no agreed-upon methods for pooling combined estimates of cost–effectiveness, extracted from multiple evaluations using meta-analyses, meta-regression, or other quantitative synthesis.[36,43] Pooling of economic evaluations is not recommended owing to likely sources of heterogeneity including different populations, jurisdictions, study settings, time horizons, measures of effect, and economic outcome measures.[36] The broad inclusion criteria and health economic content further excluded the possibility of quantitative synthesis. The results are summarized in the form of a narrative synthesis of qualitative studies.

RESULTS

Results of searches and screening

Review 1. The search produced 13 238 records, of which 3639 duplicates were removed. The title and abstract of 9599 texts were then screened. A total of 22 records met the eligibility criteria. After full-text assessment, 10 records were excluded. Reasons for exclusion included ineligible intervention (n = 3), wrong outcomes (n = 2), wrong study design (n = 1), wrong patient population (n = 3), and wrong setting (n = 1). A total of 12 texts were identified for inclusion; Figure 1 shows the literature search process for review 1.

Review 2. The search produced 172 records, with 36 duplicates were removed. The title and abstract of 136 texts were screened, of which 5 were identified for full-text assessment. After full-text assessment, all 5 records were excluded for the following reasons: unsuitable outcome measure (n = 3) and wrong study design (n = 2). Regarding the second aim, this review identified no empirical economic evaluations of antenatal public health implementation interventions; Figure 2 shows the literature search process for review 2.

Study characteristics

A summary of the data extracted using the CHEERS checklist template for review 1 is provided in Table 2. Three studies included evaluations in 2 countries[44–46]; for the purpose of this review each evaluation was treated as separate and included in both settings. Three studies presented full economic evaluations in 2 settings – Australia and New Zealand[44–46] – and 2 others were conducted in Australia only.[47,48] Three studies were conducted in the United States,[49–51] 2 in the Netherlands,[52,53] 1 in the United Kingdom,[54] and 1 in multiple sites across Europe.[55]

Two studies included a variety of interventions, ranging from those delivered at a population level (eg, interventions addressing underlying social, economic, and environmental conditions) to those delivered directly to individuals. Seven studies evaluated population-level interventions[44–47,49,51,52] and 5 studies specifically targeted pregnant women.[48,50,53–55] Of the 7 that targeted pregnant women as a subpopulation within a population-level intervention, 5 targeted those at risk of folic acid deficiency[44,47,49,51,52] and 2 specifically targeted pregnant alcohol consumers.[45,46] Of the interventions delivered directly to individuals, 1 study targeted women with mild iodine deficiency,[55] 1 targeted women at increased risk of preeclampsia,[50] 1 targeted women at increased risk of gestational diabetes mellitus,[55] and 1 targeted tobacco smokers.[50]

A variety of interventions targeting antenatal nutrition and alcohol consumption were identified. Several studies included a set of intervention options and compared the comparative cost-benefit and/or cost-effectiveness of alternate strategies. For the purpose of this review, each intervention-strategy was assessed independently; there were 5 voluntary supplementation interventions,[44,48,50,53,54] 5 mandatory fortification interventions,[44,47,49,51,52] 2 advertising campaigns,[45,55] 2 behavioral interventions,[44,55] 2 educational interventions,[45,55] 2 interventions that assessed (mandatory and/or voluntary) warning labels on alcohol packaging,[45,46]

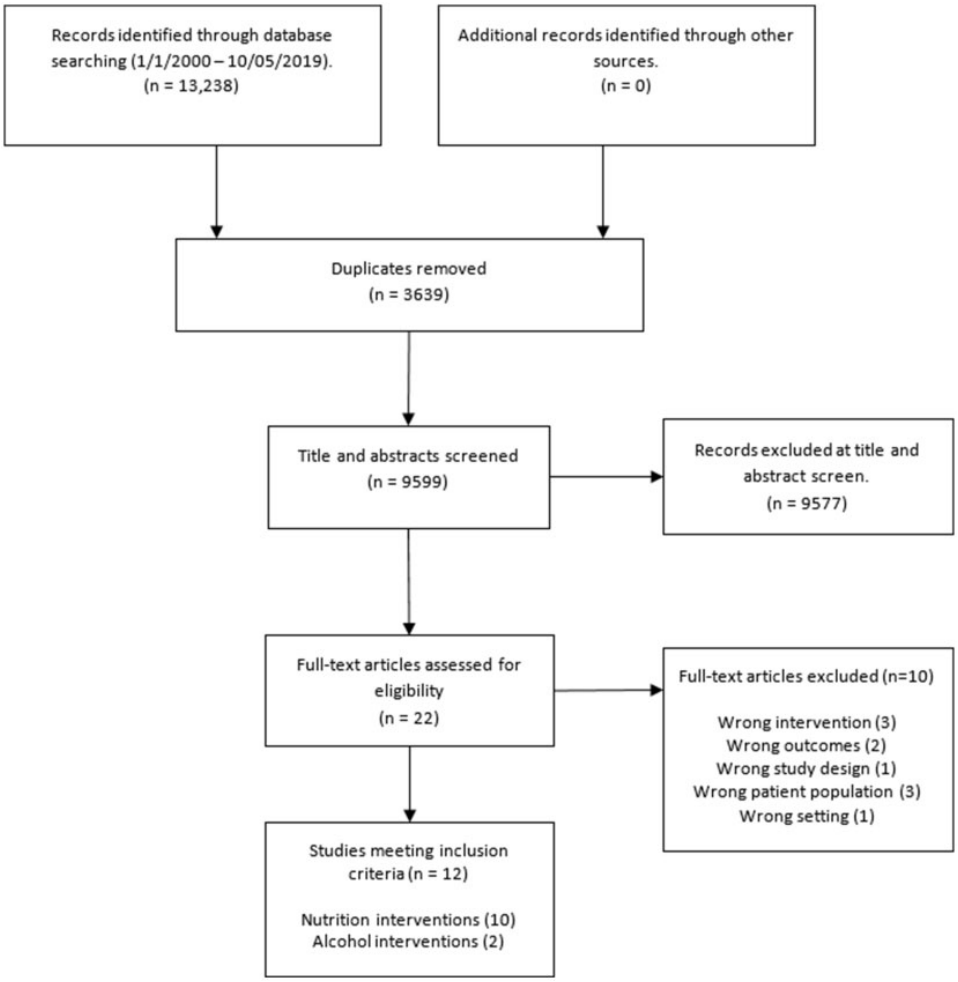

Figure 1 **Flow diagram of the literature search process for review 1.**

and 1 that assessed residential care for high-risk women.[45]

Of the included studies, 12 reported cost-effectiveness evaluations,[44,46–52,54,55] 4 reported cost-benefit evaluations,[45,46,51,56] 3 included cost-utility evaluations,[44,47,52] and 1 described a decision analytic model that estimated net financial benefit.[53] There were 2 health technology assessments of interventions targeting pregnant alcohol consumers.[45,46] Both included a cost-benefit evaluation[45,46] and one also included a cost-effectiveness evaluation.[45]

Within health economics, an evaluation time period is referred to as a "time horizon." Considering nutrition and alcohol interventions in pregnancy have the potential to improve infant health across the life span, only 4 studies had a "lifetime" time horizon.[47,49,52,54] Time horizons less than "lifetime" varied from 12 months or less[46,48,55,57] to 5 years,[45] 10 years,[44] and 18 years.[50] Two studies included a variation in time horizon as a sensitivity analysis parameter.[44,45] Eight studies reported discount rates between 0% and 7%, with 3% being the most commonly used discount rate. Five studies included either a justification or reference for the discount rate used.[47,50–52,54]

Data included in the evaluations

There were 10 modeled and 2 trial-based evaluations.[48,55] All 12 included studies reported the values, ranges, and, where necessary, references for study parameters and measures of effectiveness. Literature review was the most commonly used method for identifying and sourcing effectiveness data for modeled evaluations.

The perspective (or viewpoint) informing the selection, measurement, and valuation of resources and costs

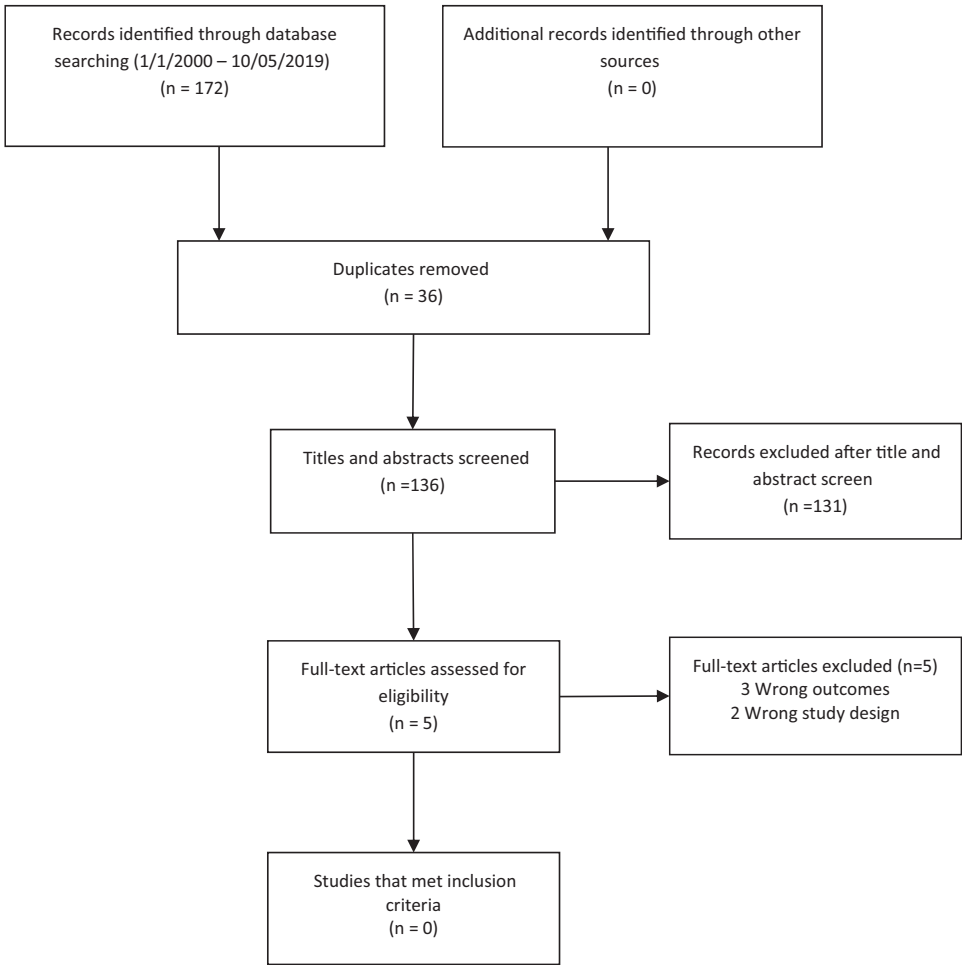

Figure 2 **Flow diagram of the literature search process for review 2.**

varied across the included studies. The identification and inclusion of economic outcomes was most comprehensive in the 2 health technology assessments of alcohol interventions,[45,46] as government-commissioned health technology assessments represent the most thorough form of economic evaluation. The range of economic outcomes included direct costs to the healthcare system and direct costs to the alcohol industry, as well as indirect costs such as productivity loss, and out-of-pocket expenses to individuals and their families. The inclusion of costs and outcomes was most varied across the 5 mandatory folic acid fortification interventions; for example, only 2 studies included the value of consumer choice where mandatory, population-level fortification had been actioned.[44,47] The costs to carers (such as carers' time and travel costs), opportunity costs, and loss of income for carers were not routinely assessed.[44,47,49,52] Of the interventions delivered in primary or tertiary care settings, 4 did not include the cost of implementing the intervention into practice in the economic evaluation.[48,50,54,57] No nutrition studies considered the cost of implementing the intervention. One briefly mentioned "optimising intervention uptake" by tailoring the intervention to participants' preferences, but did not make explicit reference to an implementation-intervention and its associated costs.[55] This review confirmed that the existing literature on economic evaluation generally adopts a restricted perspective.[58]

The measurement and valuation of preference-based outcomes was highly varied and included the following: quality-adjusted life years (QALYs) gained[49]; life years gained per QALY[44,47]; disability-adjusted life years avoided[44]; life years gained and QALYs gained[44,47,49]; intelligence quotient points gained[52]; cases avoided[47]; cost savings[51]; and expected net financial benefit.[44,52] Of the fortification interventions that included a utility value among the effectiveness

Table 2 **Summary of studies included in review 1**

Study	Country	Targeted public health issue	Participants	Setting	Type	Intervention strategy	Comparators	Measure of effect (outcome)	Perspective	Modeled or trial-based analysis	Time horizon	Economic findings
Grosse et al (2005)[51]	USA	NTD prevention	Total population; pregnant women	Community	CEA and CBA	Mandatory folic acid fortification in flour	No fortification	Number of NTDs prevented	Government	Modeled	Lifetime	Fortification resulted in annual benefit of $312 million to $425 million and cost savings were in the range of $88 million/y to $145 million/y
Jentink et al (2008)[52]	Netherlands	NTD prevention	Total population; pregnant women	Community	CUA and CEA	Mandatory folic acid fortification in flour	No fortification	Net cost per discounted LYG and net cost per discounted QALYs	Societal	Modeled	Lifetime	In the base case and most SA, enrichment was estimated to be cost-saving. Fortification remains cost-effective as long as enrichment costs do not exceed €5.5 million
Rabovskaja et al (2013)[47]	Australia	NTD prevention	Total population; pregnant women	Community	Decision-analytic model and CEA	Mandatory folic acid fortification in flour	No fortification	QALYs, LYG, and NTDs avoided	Societal	Modeled	Lifetime	Mandatory fortification was found to be cost-effective; however, inclusion of the loss of consumer choice can change this result. Even with mandatory fortification, mean folate intake will remain below the recommended NTD preventive level
Bentley et al (2009)[49]	USA	NTD prevention	Total population; pregnant women	Community	CEA	Mandatory folic acid fortification in flour	No fortification, or fortification with 140, 350, or 700 mg folic acid/100 g enriched grain	Annual burden of disease, QALYs, and total cost	Societal	Modeled	Lifetime	Fortification was predicted to be cost-saving and provide positive net QALY gains at all fortification levels. Predicted annual gains of >26 000 QALYs and savings of >$263 million from NTD prevention far outweighed the QALYs lost and costs incurred from B12 masking and fortification itself
Dalziel et al (2010)[44]	Australia and New Zealand	NTD prevention	Total population; pregnant women	Community, primary, and secondary	CUA and CEA	Promoting supplementation via (1) multifaceted population-level campaign, (2) targeted campaign, and (3) brief advice Extending/maintaining voluntary fortification Promoting dietary folate via (1) population-wide marketing, and (2) targeted delivery Mandatory fortification	Within-trial	CUA: cost per DALY averted. CEA: cost per NTD prevented per annum	Government	Modeled	(1) ICER: usual practice vs intervention >10 y (2) modeled cost-utility over full life expectancy	Population-wide campaigns to promote supplement use and mandatory fortification were the most effective at reducing NTDs. Population-wide and targeted approaches to increase supplement use were cost-effective, as was extending voluntary fortification. Mandatory fortification was not cost-effective for New Zealand, with results uncertain for Australia. Promoting a folate-rich diet was least cost-effective, with benefits restricted to impact on NTDs
Monahan et al (2015)[54]	England	Antenatal iodine deficiency prevention	Pregnant women with mild iodine deficiency	Primary care	Decision-analytic model: CCA	Voluntary iodine supplementation	TAU vs supplementation	Cost per IQ point gained in offspring	Health service and societal	Modeled	Lifetime	Iodine supplementation was cost-saving from both a health service and societal perspective, with a net gain of 1.22 IQ points
Ahmed et al (2015)[48]	Australia	Reduction in incidence of premature birth and low birth weight	Pregnant women with depressive symptoms and perinatal complications	Tertiary care providers	CEA	Voluntary fish-oil (DHA) supplementation	Treatment as usual	Mean cost per delivery admission	Provider	Trial based	<12 mo	Average cost saved by DHA supplementation ranged from A$93 to A$211 per singleton pregnancy. Probability of cost-effectiveness dependent on investment ceiling ratio of ≥A$5000, above which the probability that supplementation is preferred is not significant
Meerten (2018)[53]	Netherlands	Preeclampsia prevention	Pregnant women, women at risk of PE, and women with low dietary calcium	Primary care (inferred)	Decision-analytic model: CBA	Voluntary calcium supplementation to all pregnant women; women at high risk of preeclampsia; and	Treatment as usual	Expected net financial benefit	Public finance	Modeled	20-wk gestation to discharge post delivery	Indicated 763 cases of PE will be prevented per 100 000 (25%); estimated net financial benefit of €4 621 465. Calcium supplementation resulted in 367 cases (8%) prevented; estimated net benefit €2 059 165. Resulted in

(continued)

Table 2 **Continued**

Study	Country	Targeted public health issue	Participants	Setting	Type	Intervention strategy	Comparators	Measure of effect (outcome)	Perspective	Modeled or trial-based analysis	Time horizon	Economic findings
						women with low dietary calcium						254 cases (13%) prevented; estimated net benefit €2 822 115
Broekhuizen et al (2018)[55]	Europe	Complications associated with GDM	Pregnant women at increased risk of GDM	Antenatal clinic or hospital	CEA	Promotion of healthy eating and/or physical activity (behavioral counseling)	Usual care	Gestational weight gain, fasting glucose, insulin resistance, and health-related QoL	Societal	Trial based	<12 mo	CEAC indicated HE + PA intervention was preferred. Fasting glucose and QALY ICERs indicated HE intervention was more costly and less effective than usual care. For gestational weight gain, and insulin resistance, HE was more costly and more effective than usual care
Yieh et al (2017)[50]	USA	Pediatric asthma prevention	Pregnant smokers	Community	Decision-analytic model: CEA	Voluntary vitamin C supplementation	Prenatal vitamin without additional vitamin C	QALYs	Societal	Modeled	Antenatal period to 18 y of age	Additional vitamin C during pregnancy prevented 1637 cases of asthma at age 18 y per birth cohort of pregnant smokers. Vitamin C supplementationwould reduce asthma-related childhood deaths and save $31 420 800 in societal costs at age >18 y per birth cohort
Health Technology Analysts (2010)[45]	Australia and New Zealand	FASD prevention	Total population; pregnant women; high-risk pregnant alcohol consumers	Community, primary care, and tertiary residential care	CBA and CEA	Primary prevention strategies; warning labels; media campaign; secondary strategy; education sessions; tertiary strategy; residential care for high-risk individuals	Care as usual	Direct costs: to health system and government agencies. Indirect costs: productivity loss, out-of-pocket costs to carers	Societal	Modeled	5 y (with 10-y timeline in scenario analysis)	AUS: All 4 strategies were cost-saving, with strategies 2 and 3 being most cost-effective. NZ: Strategy 3 was most effective, followed by strategy 1. In both countries, strategy 4 was resource-intensive and high cost yet represented value for money for the small minority of pregnant women targeted by this strategy
Joint Food Regulation System (2010)[46]	Australia and New Zealand	FASD prevention	Community; pregnant alcohol consumers	Community	CCA	FASD warning labels on alcohol beverages: voluntary (1) status quo, (2) FSANZ-developed code of practice, and (3) government style guide. Mandated warning labels	Within-trial	Expected net financial benefit	Societal	Modeled	1 y	Mandatory option 2 recommended owing to significant social impacts of FASD. Based on the estimated incidence rate for FASD in Australia of 5%, this suggests 1.18% of FASD cases would need to be prevented annually to offset costs associated with adopting mandatory labeling. NZ: At an estimated incidence rate of 3%, 8.8% of new FASD cases would need to be prevented annually to recover costs of labeling changes in New Zealand (likely to be upper limit on cost)

Abbreviations: AUD, Australian dollars; AUS, Australia; CBA, cost-benefit analysis; CCA, cost-consequences analysis; CEA, cost-effectiveness analysis; CEAC, cost-effectiveness acceptability curves; CUA, cost-utility analysis; DALY, disability-adjusted life year; DHA, docosahexaenoic acid; FASD, fetal alcohol spectrum disorder; FSANZ, Food Standards Australia New Zealand; GDM, gestational diabetes mellitus; HE, healthy eating; ICER, incremental cost-effectiveness ratio; IQ, intelligence quotient; LYG, life years gained; NTD, neural tube defect; NZ, New Zealand; PA, physical activity; PE, preeclampsia; QALY, quality-adjusted life year; QoL, quality of life; SA, sensitivity analyses; TAU, treatment as usual.

outcomes, there was a range of QALY losses associated with neural tube defects (NTDs).[44,47,49,52] One study used QALY losses of 18.91 for women and 0 for men to calculate QALYs gained through different fortification strategies.[49] Another listed the quality-of-life utility weights associated with different NTD lesions (by location) and life expectancy but did not present disaggregated costs and QALYs gained – only cost per QALY.[52] Another study used a utility weight for patients with an NTD of 0.55 based on the Health Utilities Index 2 and used measures of life expectancy and life years gained from other sources.[47] One used disability-adjusted life years [44] to calculate a disability weight for live NTD births surviving past age 1 of 0.52, of 1 for those with full loss of life, and of 0.01 for terminations due to NTDs.[44] The use of disability-adjusted life years in this article was questioned in another article included in this review.[47]

Analysis and interpretation of evaluation results

Incremental analysis of intervention costs and outcomes was conducted in 7 studies.[44–47,50,52,55] Eight studies provided sufficient explanation for conducting both univariate deterministic and probabilistic sensitivity analyses,[44–47,50,52,54,55] and 3 used crude methods for halving or doubling existing parameters,[49,51,52] of which 2 provided little or no justification for the chosen parameters.[49,51]

Of the supplemental interventions, all were found to be cost-saving.[48,50,54,57] Of the behavioral nutrition interventions, one provided behavioral counseling for healthy eating and/or physical activity for pregnant women at risk of gestational diabetes mellitus.[55] Cost-effectiveness acceptability curves indicated that the combined healthy eating plus physical activity intervention was the preferred intervention strategy. One study modeled 12 proposed scenarios for increasing antenatal folic acid intake in Australia and 11 for New Zealand. It found that greatest reductions in NTDs were estimated for a population-wide health promotion campaign aimed at promoting folic acid supplement use in women who may become pregnant. While a number of these interventions were absolutely and comparatively cost-effective, none of the proposed interventions were estimated to achieve a 10% reduction in total NTD cases.[44] Another study regarding mandatory fortification in Australia further supported this, finding that even with mandatory fortification, mean folate intake remains below the recommended NTD preventative level.[47]

Both health technology assessments of alcohol interventions reported fetal alcohol spectrum disorder prevention efforts as cost-effective, regardless of intervention strategy.[45,46] This is due to the high economic and social cost of caring for those with fetal alcohol spectrum disorder significantly outweigh the societal cost of interventions to reduce alcohol consumption in pregnancy.

Quality of economic evaluations

Ten studies scored "high" on the Drummond 10-point quality checklist (Table 3). The lowest scoring items on the Drummond quality checklist included a justification of the discount rate, or provided an explanation when costs were not discounted, and provided details of the statistical tests and the approach to sensitivity analyses and reporting of an incremental analysis. The choice of discount rate was justified in 5 studies, and an explanation for discounting (or not discounting) was provided in 6. Seven studies documented the details of statistical tests and the approach to sensitivity analyses, and justified the parameters included. No studies biochemically validated the trial outcome to assess intervention fidelity.

DISCUSSION

The review of economic evaluations of antenatal nutrition and alcohol interventions (Review 1) contributes to the existing body of evidence by identifying 12 economic evaluations of antenatal health promotion interventions. The economic evaluations included were of high quality, were well described, used appropriate health outcomes, and reached appropriate conclusions based on the data and results. Compared with economic evaluations of clinical or pharmaceutical healthcare interventions, the range of possible costs and effects associated with public health interventions and their implementation strategies is significantly broader.[42] The review found no consideration of the cost of implementing nutrition interventions into practice, and therefore the true cost of realizing the associated health benefits remains unknown. It was not possible to identify the value for money offered by the various intervention modalities owing to the substantial variation in health outcomes, costs, and evaluation of time horizons. The review of evaluations of antenatal nutrition and alcohol implementation interventions (review 2) identified no economic evaluations of implementation strategies that sought to increase uptake of nutrition and alcohol interventions. To usefully inform public health policy, investment decisions, and research priorities, there needs to be greater application of economic evaluations relating to antenatal health promotion interventions and their associated implementation-strategies. The current evidence base has important

Table 3 **Drummond 10-point quality appraisal summary for review 1**

		Results of appraisal (n = 12 studies): parameter present/ not present/ unclear / not applicable							
Parameter		Y	%	U	%	N	%	NA	%
Study design	Research question is clearly stated	12	100						
	Economic importance of the question is raised	12	100						
	Perspective is stated	12	100						
Selection of alternatives	Rationale for choices is stated	11	92			1	8		
	Alternatives compared are clearly described	11	92			1	8		
Form of evaluation	Evaluation form is stated	12	100						
	Form is justified in relation to question	11	92	1	8				
	Justification is given	11	92			1	8		
Effectiveness data	Sources of effectiveness estimates are stated	12	100						
	Details of design and results of effectiveness are given	11	92	1	8				
	Details of synthesis or meta-analysis are given if applicable	8	67			1	8	3	25
Benefit measurement and valuation	Primary outcome is clearly stated		0						
	Methods to value health states are stated	11	92			1	8		
	Valuation subjects are described	10	83	2	1				
	Productivity impacts are reported separately	11	92			1	8		
	Relevance of productivity impacts is discussed	11	92			1	8		
Costing	Resources use is presented in natural units and unit costs are reported separately	11	92	1	8				
	Methods for estimation of quantities and costs are described	9	75	3	25				
	Currency and price base are stated	12	100						
	Details of currency conversions or price adjustments are stated	12	100						
Modeling	Details of model are given	11	92	1	8				
	Choice of model and key parameters are justified	10	83	1	8	1	8		
Adjustments for timing of costs and benefits	Time horizon is stated	10	83	1	8			1	8
	Discount rate is stated if applicable	10	83					2	17
	Choice of rate is justified	5	42			5	42	2	17
	Explanation given when costs are not discounted	6	50	1	8	3	25	2	17
Allowance for uncertainty	Details of statistical tests are given	7	58	2	17	3	25		
	Approach to sensitivity analysis is stated	7	58	2	17	3	25		
	Choice of variables included in sensitivity analysis is justified	7	58	1	8	4	33		
	Ranges for parameter value variation are justified	9	75	2	17	1	8		
	Relevant alternatives are compared	11	92	1	8		0		
Presentation of results	Incremental analysis is reported	6	50			5	42	1	8
	Both disaggregated and aggregated outcomes are presented	12	100						
	Answer to study question is given	12	100						
	Conclusions are consistent with the reported data	12	100						
	Conclusions are accompanied by appropriate caveats	9	75	1	8	2	17		

Abbreviations: N, no; NA, not applicable; U, unclear; Y, yes

gaps that render it of limited value to decision makers. These gaps can be addressed by incorporating health economic principles and methods when evaluating interventions designed to improve the health outcomes of mothers and infants.

The selection, measurement, and valuation of costs and outcomes are determined by the economic evaluation perspective and time horizon.[58] Perspective is largely dependent on who the evaluation is intended to inform and can range from that of society to hospital administrators and national health ministries – whoever is responsible for the care provision.[41] This review identified a predominance of modeled economic evaluations with restricted time horizons and perspectives that focus on the relevant costs for those who commissioned the study. However, individual-level nutrition and alcohol interventions entail an opportunity cost for participants that was not considered in all included studies. Restricted evaluation perspective has sometimes been justified on account of data limitations, measurement difficulties, or limits in budgetary responsibilities.[58] From the current review it was not possible to make broad conclusions of the value of nutrition and alcohol interventions in relation to individuals. There is need for trial-based data that measures the costs and consequences of antenatal health promotion interventions

beyond the healthcare provider, to that of society. Inclusion of a societal perspective in economic evaluations of nutrition and alcohol interventions may also result in substantial differences in the valuation of interventions.[59] Limiting the time horizon of a modeled health promotion intervention to the trial duration prevents consideration of the potential lifelong social and economic benefits of antenatal health promotion interventions. The use of broader perspectives and, where possible, time horizons, has been encouraged in an effort to think more broadly about the costs and benefits of healthcare and health promotion interventions,[58] particularly when addressing chronic conditions.[59]

During the review screening process, a number of studies were ineligible for inclusion because they combined diet and exercise in multicomponent "lifestyle interventions."[13,60] While pragmatic, multidisciplinary interventions preclude comparative analysis of intervention components. It is recommended that nutrition and alcohol researchers looking to address this gap in the evidence collect cost data alongside trial data. A minimum data collection tool for nutrition intervention studies would include a preference-based outcome instrument that measures generic health status (eg, the Assessment of Quality of Life instrument or the Quality of Life Index [EQ-5D]). A minimum data collection tool would also include a detailed trial-based costing and inventory log (cost-capture template). There is no standardized cost-capture template as they are study-specific, but a basic cost-capture template should include all costs associated with the study, itemized for both resources and cost, labor and staff time, material costs, and miscellaneous costs (ie, travel costs, venue hire, and overheads).

The current review has several strengths and limitations that should be noted. First, this review builds on the existing findings of economic evaluations relating to health promotion – in particular, a systematic review of economic evaluations of smoking cessation during pregnancy.[30] Second, there was no prespecified protocol published for this review. Instead, reviewers followed the PICOS criteria for inclusion and the search strategy was documented for transparency purposes. A comprehensive search strategy was developed with the assistance of an accredited librarian, to ensure a maximum sensitivity search was conducted and that all relevant literature had been identified. It is possible that some economic evaluations of implementation strategies will have been missed. Investment in implementation strategies is often the responsibility of local health authorities, which may or may not have the capacity or capability to publish economic evaluations. Implementation strategies may also fall into the category of "quality improvement," which may not be formally evaluated. Published implementation studies may also have been missed owing to inconsistent use of key words and terms describing them and medical subject heading labeling convention.

CONCLUSION

Health promotion interventions have the potential to reduce healthcare costs. Ensuring their effective and cost-effective implementation is essential if governments are to achieve improved population health and contain per-capita health expenditure. Assessment of the effectiveness and cost-effectiveness of nutrition and alcohol interventions and their implementation strategies is necessary given competing claims on health budgets. Despite this need, there is an absence of evidence of the total cost and cost-effectiveness of antenatal nutrition and alcohol interventions and their implementation strategies. Greater understanding of the cost-effectiveness of providing health promotion services to pregnant women will help inform decisions about how to derive value from investment in healthcare.

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Declaration of interest. The authors declare no relevant interest to declare.

SUPPORTING INFORMATION

The following Supporting Information is available through the online version of this article at the publisher's website.

Table S1 **Systematic review of search terms**

Table S2 **PRISMA checklist**

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Chapter 4

Protocol for an economic evaluation and budget impact assessment of a randomised stepped-wedge controlled trial for practice change support to increase routine provision of antenatal care for maternal alcohol consumption

4.1 Chapter Overview

Economic evaluations of health promotion interventions and their associated implementation strategies are not routine. As of May 2019, there were 12 economic evaluations of nutrition interventions in pregnancy, two of which were health technology assessments of alcohol interventions. The systematic reviews identified a complete absence of economic evaluations of implementation interventions associated with either nutrition or alcohol interventions. Another recent systematic review of economic evaluations of public health implementation-interventions identified a total of 14 economic evaluations, none of which were in the antenatal setting [62]. Both reviews concluded that to usefully inform public health policy and investment decisions, there needs to be greater application of economic evaluation to understand the cost-effectiveness of health promotion and implementation efforts. Both reviews also concluded that amongst the existing literature, the methodological rigor and compliance with reporting guidelines was highly varied [62]. This review was updated in September 2021 and found no additional published papers which would have been included in either review in Chapter Three.

To address this specific and significant gap in the literature, this thesis includes two concomitant economic analyses of health promotion targets, (1) maternal alcohol consumption and (2) maternal nutrition. These independent analyses build on the findings of the literature review, addressing small but significant gaps in the evidence by providing original research. The first economic evaluation included in Chapters Four and Five, describes the cost, cost-consequence, and cost-effectiveness analysis of a multi-strategy practice change intervention in increasing antenatal care addressing the consumption of alcohol by pregnant women. The second economic analyses, reported in Chapters Six and Seven, sought to identify future targets for antenatal health promotion interventions by assessing maternal dietary intake and their economic implications.

Each economic analyses is prefaced by an economic study protocol (Chapter Four and Chapter Six). The protocol included in this Chapter describes the cost, cost-consequence, cost-effectiveness analysis and budget impact assessment of the multi-strategy practice change intervention in increasing antenatal care addressing the consumption of alcohol by pregnant women. This protocol was led and written by the candidate. However, Dr Reeves, the senior health economist and a chief investigator listed on the grant was listed as the first author based on the wishes of the investigator team. This protocol was published in *Implementation Science Communications* journal in 2020, citation as follows:

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4.2 Published manuscript

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STUDY PROTOCOL Open Access

Protocol for an economic evaluation and budget impact assessment of a randomised, stepped-wedge controlled trial for practice change support to increase routine provision of antenatal care for maternal alcohol consumption

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Abstract

Background: Antenatal clinical practice guidelines recommend routine assessment of women's alcohol consumption during pregnancy. The delivery of advice and referral when necessary are also recommended. However, evidence suggests there are barriers to the uptake of best-care guidelines. Effective, cost-effective and affordable implementation strategies are needed to ensure the intended benefits of guidelines are realised through addressing identified barriers. This paper describes the protocol for evaluating the efficiency and affordability of a practice change intervention compared to the usual practice in an implementation trial.

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Methods: The effectiveness of the intervention will be evaluated in a stepped-wedge randomised controlled implementation trial, conducted in an Australian setting. An economic evaluation will be conducted alongside the trial to assess intervention efficiency. A budget impact assessment will be conducted to assess affordability. The prospective trial-based economic evaluation will identify, measure and value key resource and outcome impacts arising from the multi-strategy practice change intervention compared with usual practice. The evaluation will comprise (i) cost-consequence analyses, where a scorecard approach will be used to show the costs and benefits given the multiple primary outcomes included in the trial, and (ii) cost-effectiveness analyses, where the primary outcome will be incremental cost per percent increase in participants reporting receipt of antenatal care for maternal alcohol consumption consistent with the guideline recommendations. Intervention affordability will be evaluated using budget impact assessment and will estimate the financial implications of adoption and diffusion of this implementation strategy from the perspective of relevant fundholders. Results will be extrapolated to estimate the cost and cost-effectiveness of rolling out the model of care.

Discussion: Uptake of clinical guidelines requires practice change support. It is hypothesized that the implementation strategy, if found to be effective, will also be cost-effective, affordable and scalable. This protocol describes the economic evaluation that will address these hypotheses.

Trial registration: Australian and New Zealand Clinical Trials Registry, ACTRN12617000882325. Registered on 16 June 2017

Keywords: Cost-effectiveness analysis, Health economics, Antenatal care, Protocol, Budget impact assessment

Contributions to the literature

- Research has shown the development and dissemination of clinical guidelines alone are insufficient to change practice and deliver improved patient outcomes. Further investment in strategies to increase adoption of guideline recommendations is required.
- Given escalating healthcare costs and constrained budgets in public health systems, effective, cost-effective and affordable implementation strategies are needed to ensure the intended benefits of clinical guidelines are realised.
- This protocol details the research methods that will be used to answer the following question: From the Australian healthcare system perspective, what is the cost and cost-effectiveness of the practice change intervention to increase the routine provision of antenatal care for maternal alcohol consumption compared to usual practice, and is it an affordable model for local health services?

Background

To prevent the potential adverse obstetric and foetal outcomes associated with women's alcohol consumption during pregnancy [1], clinical practice guidelines recommend that clinicians routinely assess alcohol consumption and advise all pregnant women that it is safest not to consume alcohol during pregnancy and of the potential harms associated with consumption. Guidelines also recommend clinicians refer to specific services when required [2]. It is also recommended that follow-up care is provided during subsequent antenatal visits. Despite these clear recommendations, the provision of routine antenatal care addressing maternal alcohol consumption during pregnancy is limited [3]. For example, in Canada, approximately 50% of health professionals have reported providing advice to pregnant women regarding the consumption of alcohol [4], and in the UK, two thirds of women reported receiving such advice from a midwife [5]. A 2005 Australian study of 1143 health professionals who provide antenatal care found that fewer than half (45%) routinely asked about alcohol consumption during pregnancy, 25% provided information on the effects of alcohol consumption during pregnancy and only 13% provided advice consistent with national drinking guidelines that recommended no alcohol consumption during pregnancy [6, 7]. A more recent study involving 166 midwives in Western Australia found that while almost all midwives

(93%) asked pregnant women about their alcohol consumption, just over half (54%) used a recommended standardised assessment tool to do so (AUDIT or AUDIT-C) [7–9]. In a recent survey of women who had recently visited public antenatal services in the Hunter New England local health district, Australia, less than two thirds (64%) of pregnant women reported that they received an assessment of their alcohol consumption and just over one third (35%) received advice and referral appropriate to their self-reported level of alcohol consumption since pregnancy recognition at their initial antenatal visit [9]. Less than 10% of women received such care at subsequent antenatal visits [9].

The development and dissemination of clinical guidelines alone are insufficient to change the current practice and deliver improved patient outcomes [10]. Further investment in strategies to increase adoption of guideline recommendations is required [11]. However, decisions about implementation intervention investment should be guided by consideration of effectiveness as well as economic efficiency, equity and affordability [12, 13]. Economic evaluation combines evidence about the cost and benefits of alternative interventions in order to identify investment opportunities that demonstrate value for money [14–16]. Given escalating healthcare costs and constrained budgets in public health systems, economic evaluations contribute significantly to the evidence base informing decision-makers and healthcare funders. Effective, cost-effective and affordable implementation strategies are needed to ensure the intended benefits of clinical guidelines are realised [17]. Similarly, assessment of the budget impact of implementation strategies is warranted to assess the affordability and financial consequences of healthcare practice changes. At present, there is limited evidence regarding the economic cost of adverse foetal and maternal outcomes associated with alcohol consumption during pregnancy [18–21] and no evidence concerning the cost-effectiveness of practice change interventions aiming to improve recommended antenatal care for maternal alcohol consumption [22]. This paper presents a protocol for the economic evaluation of an antenatal practice change intervention to improve care addressing alcohol consumption in pregnancy. The paper aims to answer the following research question: From the Australian healthcare system perspective, what is the cost and cost-effectiveness of the practice change intervention to increase the routine provision of antenatal care for maternal alcohol consumption compared to usual practice, and is it an affordable model for local health services?

The trial

Study design

The multi-strategy practice change implementation trial will be a randomised, stepped-wedge controlled trial. The protocol has been previously published [3]. In brief, the trial will be conducted in all public antenatal services within three sectors across two health districts in New South Wales, Australia. The model of care for addressing alcohol consumption by pregnant women will be delivered to sectors in a random, stepped order. The main outcomes are described below in the "Identification and measurement of outcomes" section and described in detail in Kingsland et al. [3].

Repeated cross-sectional outcome data will be gathered on a weekly basis across the three sectors for a period of 34 months. Baseline data collection, representing usual practice (control), will be collected for the three sectors from 7 months prior to the commencement of the intervention in the first sector to the start of the intervention in each sector. Follow-up data will be collected for the three sectors 7 months following completion of the intervention in the third and last sectors. The outcome results will be determined by comparing practice change outcomes between the baseline and follow-up periods for the three sectors combined.

Usual practice

Usual practice comprises the antenatal care for addressing maternal alcohol consumption during pregnancy that is provided in the baseline period prior to the introduction of the intervention. It is anticipated that such care is likely to vary by antenatal service and clinician. This is due to variability in local practice across the 3 sectors covering metropolitan, regional and rural localities, as well as the lack of an existing health district-wide guideline or procedure specifying the provision of routine care for addressing alcohol consumption during pregnancy.

The development and dissemination of the clinical practice guidelines have already taken place in Australia with the result that their associated costs and effects are common to both intervention and control study periods.

The intervention

A multi-strategy practice change intervention has been developed to support antenatal care staff to implement a model of care consistent with clinical

guidelines. The multiple strategies included in the intervention are presented in Appendix 2: Table 1. The model of care is based on an evidence-informed behavioural counselling framework [23] and includes clinician assessment of patient alcohol risk status using the AUDIT-C tool at the first comprehensive ('booking in') visit and at follow-up antenatal appointments at 27–28 weeks and 35–36 weeks gestation. All pregnant women will be provided with brief advice that it is safest not to consume alcohol during their pregnancy and of the risks associated with alcohol consumption at this time. Women who are at 'medium risk' of harm according to their AUDIT-C score of 3–4 will be offered a referral to the New South Wales Get Healthy in Pregnancy Service, an evidence-based telephone coaching service provided free of charge. Women at 'high risk' of harm from alcohol (AUDIT C score, 5+) will be referred to the Hunter New England Drug and Alcohol Clinical Service.

Methods and analysis

This economic evaluation has been conducted and reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) publication guidelines and good reporting practices [24].

Economic evaluation overview

Cost, cost-consequence and cost-effectiveness analyses will be undertaken comparing the intervention against the usual practice from a public health service perspective. This perspective is justified because ongoing funding for this intervention, especially if it translates into routine practice, will fall on public health services. To further aid decision-makers, budget impact analysis, including scale-up cost scenarios, will be presented alongside the cost-effectiveness findings. Costs will be reported in 2019 Australian dollars ($AUD). The time horizon for the inclusion of relevant costs and consequences will be the course of the trial (34 months). Costs and benefits occurring after 12 months will be discounted using an annual discount rate of 3% in the base case. Annual discount rates of 0 and 5% will be applied in a sensitivity analysis. The conduct, analysis and reporting of the economic analyses will adhere to the cost and economic analysis guidelines [14, 15, 25] and Consolidated Health Economic Evaluation Reporting Standards guidelines [15].

Common to all forms of economic evaluation is the analysis of cost. In this study, costing and budget impact assessments will be conducted to quantify how much more it will cost to pursue implementation efforts to affect practice change. The budget impact assessment will translate the health economic findings into more meaningful and relevant results for healthcare decision-makers and funders. In its simplest form, economic evaluation involves a listing of all cost/benefit implications of the alternatives under consideration, as in cost-consequences analyses [26]. A cost-consequence analysis is employed in this analysis because it provides information for spending decisions when implementation strategies are complex and are expected to have outcomes that are too disparate to be combined meaningfully. In this trial, there are four primary outcomes (see the "Identification and measurement of outcomes" section). Cost-consequence analyses permit value judgements without having to fully specify a relation between all the different measures of outcomes [11]. Cost-effectiveness will depend on the effect of the intervention on care provider behaviour. The greater the difference in expected outcomes between usual practice and the new model of care, and the more widespread the implementation, the more likely a strategy is to be cost-effective. In this study, the likelihood of achieving an outcome difference will be maximised by using a staged process to both understand the barriers to guideline adoption and to develop the implementation strategies [3]. All public antenatal services in the three sectors will receive the practice change intervention, including midwifery group practices, midwifery clinics, specialist medical services, Aboriginal Maternal and Infant Health Services (AMIHS) and multi-disciplinary teams caring for women with complex pregnancies or identified vulnerabilities.

Trial-based economic evaluation and budget impact assessment

Identification and measurement of outcomes

It has been suggested that one of the ways to improve efficiency in conducting economic evaluations of implementation interventions is to confine studies to measures of the care process or intermediate outcomes [11], for example, change in professional guidance adherence or compliance [3]. This approach is based on the premise that the guideline recommendations are cost-effective in and of themselves. In this study, the outcome measures are confined to the care process for efficiency. The implementation trial has four primary outcomes. They are the proportion of all antenatal clinic appointments (at 'booking in', 27–28 weeks gestation and 35–36 weeks gestation) for which women report the following:

1. Being assessed for alcohol consumption and level of risk using the AUDIT-C
2. Being provided with brief advice related to alcohol consumption during pregnancy
3. Receiving, relative to their level of risk, the relevant elements of antenatal care for addressing alcohol consumption during pregnancy (advise and refer)
4. Being assessed for alcohol consumption and level of risk using the AUDIT-C and receiving, relative to their level of risk, the relevant elements of antenatal care for addressing alcohol consumption during pregnancy (advise and refer)

Receipt of care will be measured by participant report during a computer-assisted telephone survey conducted after an antenatal consultation, at each of the three time points [3].

A secondary outcome will also be included. For women attending antenatal appointments at 'booking in', 27–28 weeks gestation and 35–36 weeks gestation, alcohol consumption since pregnancy recognition will be collected. Outcome measurement will be based on self-report of women using the total AUDIT-C score. AUDIT-C is a validated tool for assessing the risk of harm due to alcohol consumption [27].

Identification, measurement and valuation of costs

Cost data pertaining to the development and implementation of the practice change intervention will be collected prospectively using a resource use capture tool in tangent with trial administrative records. The intervention programme logic will be used to identify all the relevant costs directly and indirectly associated with the intervention. The cost capture tool, developed in Microsoft Excel (2013), allows researchers to prospectively document the activity and materials consumed at different phases of the intervention (development, immediate execution and maintenance) from all relevant stakeholders. The cost capture tool includes the following categories: (1) labour (health service and non-health service staff, including overheads to allow for additional costs of employment), (2) materials (non-labour cost items such as stationary, education materials, electronic hardware or software), (3) joint costs (incurred in connection with multiple projects, for example, the maintenance costs of a website portal supporting different interventions; capital costs such as one-off investments such as the purchase of additional office buildings or motor vehicles), and (4) miscellaneous costs (which include costs not easily classified into the other categories, for example, venue hire, travel and overnight accommodation). To maintain a conservative approach to cost estimation, the non-capital implementation costs will not be amortised.

Resource use valuation will be based on the concept of opportunity cost, that is, the value of the benefit forgone in not employing a resource for a different use. Market prices will be used as a proxy for the 'value of benefit' forgone [28].

Costing study

Appendix 3: Table 2 summarises the costs expected to be included in the study. The cost analysis will use measures of arithmetic means, between-group differences and variability of differences [29, 30]. Costs will be calculated individually for each sector in the trial, as well as aggregated across all sites. Intervention component costs will be disaggregated to provide insight into the cost of individual practice change intervention strategies.

Cost-consequence, cost-effectiveness and equity

As outlined above, the range of outcomes measured in the implementation trial is diverse, which lends well to a cost-consequence analysis. The analysis will adopt a scorecard approach to show a comparison of the costs and benefits associated with the intervention and usual practice. An economic summary measure is not calculated. A programme logic model will be developed to describe all possible inputs (costs) and impacts (consequences) associated with the intervention and usual care (Appendix 1: Fig. 1).

The cost-effectiveness analysis will be conducted subject to the assessment of intervention efficacy. The economic summary measure will be an incremental cost-effectiveness ratio (ICER). The ICER represents the additional cost required to achieve an additional unit of benefit [14, 29]. For this study, the ICER will be calculated as the incremental cost per percent change in the proportion of participants reporting that receipt of 'antenatal care for maternal alcohol consumption consistent with guideline recommendations' was provided to them during their antenatal consultation.

Distributional cost-effectiveness analysis (DCEA) is a framework for incorporating health inequality concerns into the economic evaluation of health sector interventions. Full DCEA requires the distribution of direct health benefits to be estimated from a decision-analytic model or trial-based analysis using parameter estimates specific to socio-economic groups. However, a simplified version

providing healthcare decision-makers and stakeholders with an evidence-based technique for evaluating whether new interventions can help to achieve the objective of health inequality reduction can be used when conducting a full DCEA is not practical or feasible [31]. To assess the equity implications of the intervention, the use of distributional cost-effectiveness will be explored in the scenario examining scale-up subject to the availability of requisite data [31, 32].

Budget impact assessment

Economic evaluations and budget impact analyses share many of the same data elements and methodological requirements and should be viewed as complementary. However, there are important differences in their methods and use cases [13]. The budget impact assessment will translate the results of the economic costing study into financial consequences relevant to decision-makers and fundholders within the health districts.

A model will be developed to describe the financial resources associated with the usual practice over the course of health districts' budgeting cycles. This will represent the base case or 'reference case'. The comparative scenario will model the required changes in health service resourcing that are expected to result from the adoption of this alternate model of care, including indirect and downstream impacts on other parts of the health service. Resource use data will be sourced from the implementation trial and costing analysis. All model assumptions and data inputs will be described in full. Justification for the inclusion or exclusion of relevant model parameters will be provided.

The budget impact assessment will adhere to the relevant local and international guidelines, as well as recommended formats for presenting the results so they are most useful to decision-makers [13, 33].

Sensitivity and uncertainty analyses

All analyses will be subject to one-way and probabilistic sensitivity analyses. These analyses test the impacts of plausible variation in data parameters on the cost outcomes and economic summary measure and provide an understanding of which values are associated with the greatest amount of uncertainty. Differences in costs or outcomes that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variabilities in effects that are not reducible by more information will be reported.

In addition, scenario analyses will be undertaken to explore the efficiency and budget impact of the state-wide implementation of the practice change model of care in maternity services across the whole state of NSW.

Discussion

This protocol sets out the plan to assess the cost, efficiency and affordability of a multi-strategy practice change implementation intervention compared to usual practice. The purpose of publishing this protocol is twofold; first, setting an a priori plan for the proposed analyses can reduce potential biases made from ad hoc analytic decisions. Deviations from this protocol will require description and justification in the final analyses. Second, there are benefits to the research and broader community in a greater understanding of economic evaluation, especially with respect to their conduct alongside implementation trials. There is a clear absence of research evidence of the effectiveness, cost, cost-effectiveness and budget impact of implementation strategies to improve antenatal care that addresses maternal alcohol consumption during pregnancy [34]. The application of economic evaluation to health-promoting, implementation interventions is limited [12] while the application of budget impact assessment at the local health service level is completely novel. This will be the first economic evaluation and budget impact assessment of an implementation strategy in this field [22]. It is expected that the practice change intervention will increase the extent to which women are assessed for alcohol consumption during pregnancy and given evidence-based advice and, where appropriate, referral to ongoing support services to avoid the consumption of alcohol for the remainder of their pregnancy. The outcomes of these analyses will then inform the state-wide scale-up of this implementation intervention and the next step in the research translation pathway.

Conclusion

This protocol outlines the assessment of cost, efficiency and affordability of a multi-strategy practice change implementation intervention compared to the usual practice. The outcomes of this economic evaluation will provide insight into the cost, cost-consequence and cost-effectiveness of implementation strategies designed to improve antenatal care addressing the recognised risk of alcohol consumption to the health and wellbeing of both the mother and child [34], and inform future healthcare policy, investment allocation and research.

Appendix 1

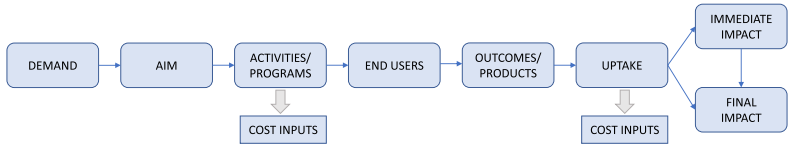

Fig. 1 Example intervention programme logic

Appendix 2

Table 1 Implementation strategy summary

Intervention component	Component details: *A full description of component details has been published elsewhere* [3].
Leadership and management	• Monthly meetings will be held with management from antenatal services to elicit support. • Service managers will be asked to distribute resources to staff and attend training sessions. • Monitoring and reporting of performance measures related to the intervention.
Local clinical practice guidelines	• A service-level guideline and procedure document will detail the model of care, including assessment, brief advice and referral pathways. • This document will be uploaded onto the health service's policy directory, disseminated by managers to all staff via email, and hard copies will be placed in staff common areas.
Electronic prompt and reminder system	• Existing point-of-care and medical record systems used by maternity clinicians will be modified to electronically prompt the use of the AUDIT-C alcohol screening tool. • Brief advice scripts will be displayed on the point-of-care system based on the woman's AUDIT-C risk score, and prompts and tools for referral to appropriate services.
Local opinion leaders/ champions	• Project-specific clinical midwife educators appointed to support staff to uptake the model of care and provide support at a one-on-one, team and service level. • Additional local antenatal clinical leaders will be engaged to provide encouragement and demonstrate required behaviours as required.
Educational meetings and materials	• Training will be provided to all antenatal service clinicians via a 30-min online training module and face-to-face sessions. Clinical midwife educators will facilitate clinicians in completing the online training and coordinate face-to-face training sessions. This will include lecture-style sessions, interactive sessions, case study-based sessions and one-on-one sessions. • Clinicians will be provided with written resources (hardcopy and electronic) to support the model of care, including standard drink measure charts and point-of care written prompts/reminders (e.g. stickers in charts).
Academic detailing	• Data from both medical records and telephone surveys conducted with women who attended the antenatal services will be used to provide feedback on adherence to the agreed model of care. • The clinical midwife educators will visit service teams in their antenatal clinics to provide feedback data and develop action plans to improve adherence.
Monitoring and accountability	• Antenatal service managers will report, interpret and monitor performance measures for the model of care. • These results will be disseminated to antenatal service staff through team meetings, emails and other usual communication mechanisms. • Performance measures will be built into the existing monitoring and accountability frameworks for antenatal services.

Appendix 3

Table 2 Description of resource use data for inclusion in the economic evaluation

Intervention component	Resource use details	Data collection method
Intervention strategy development	• Labour time: health district project/implementation support officer time. • Materials.	• Resource use capture template
Leadership and management	• Labour time: health district project/implementation support officer time, health service clinical staff (management from antenatal services).	• Resource use capture template
Local clinical practice guidelines	• Materials: guideline and procedure document development and provision. • Electronic dissemination.	• Resource use capture template
Electronic prompt and reminder system	• Materials: online/computer-based intervention component. • Electronic dissemination.	• Resource use capture template
Local opinion leaders/ champions	• Labour time: change champion, clinicians and trainers.	• Resource use capture template
Educational meetings and materials	• Labour time: health district project/implementation support officer time, health service clinical staff. • Materials: educational tools and resources.	• Resource use capture template
Academic detailing	• Labour time: project support officer, clinical service staff time.	• Project administrative records • Resource use capture template • REDCap self-report survey
Monitoring and accountability	• Antenatal service managers will report, interpret and monitor performance measures for the model of care. • These results will be disseminated to antenatal service staff through team meetings, emails and other usual communication mechanisms. • Performance measures will be built into the existing monitoring and accountability frameworks for antenatal services.	• Resource use capture template

Abbreviations
AUD: Australian dollars; AUDIT-C: Alcohol Use Disorders Identification Test; BIA: Budget impact assessment; CEA: Cost-effectiveness evaluation; DCEA: Distributional cost-effectiveness analysis; ICER: Incremental cost-effectiveness ratio

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Authors' contributions
JW, AS, MK, EE and AD developed the original research idea. MK and ED managed the trial. AS, PR and ZS provided expert statistical and economic advice and content. MK, JW and ED provided content expertise regarding implementation science. EE and AD provided content expertise regarding maternity care. ZS and PR wrote the manuscript with the support and guidance of all other authors. All authors reviewed and approved the final manuscript and provided feedback.

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Availability of data and materials
There are no datasets associated with this protocol.

Ethics approval and consent to participate
The trial was approved by the Hunter New England Human Research Ethics Committee (16/11/16/4.07; 16/10/19/5.15), the Aboriginal Health and Medical Research Council (1236/16) and the University of Newcastle Human Research Ethics Committee (H-2017-0032; H-2016-0422).

Consent for publication
Not applicable.

Competing interests
MK, ED, KC, LW and JW receive salary support from the Hunter New England Clinical Services Nursing and Midwifery, which contributes funding to the project outlined in this protocol. MK receives salary support from a NHMRC Translating Research Into Practice (TRIP) Research Fellowship (APP1150476). EJE is supported by a NHMRC Medical Research Futures Fund Practitioner Fellowship (APP1135959) and NHMRC CRE (APP1110341). All other authors declare that they have no competing interests.

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Publisher's Note

Chapter 5

Cost, cost-consequence, and cost-effectiveness analyses of a randomised stepped-wedge controlled trial for practice change support to increase routine provision of antenatal care for maternal alcohol consumption

5.1 Chapter Overview

Chapter Four presented the economic evaluation protocol for assessing the cost, cost consequence, cost-effectiveness and budget impact assessment of a practice change intervention to increase routine provision of antenatal care for maternal alcohol consumption compared to usual practice. This Chapter contains the outcomes of that cost, cost-consequence, and cost-effectiveness evaluation, submitted for publication in Implementation Science in July 2021.

National regulatory agencies such as the Pharmaceutical Benefits Advisory Committee (PBAC) and the Medical Services Advisory Committee (MSAC) in Australia, the National Institute for Health and Clinical Excellence in England and Wales, and managed care organizations in the United States require estimates of both the cost-effectiveness and the likely impact of new medicines and medical devices on national, regional, or local health plan budgets [82]. Recent research conducted as part of Australia's Health Systems Improvement and Sustainability national initiative identified a need for comprehensive economic evaluation at the local health service level [54]. This report also identified that health services staff do not always know how to translate the information in evaluation reports, particularly economic assessments, into practical information they can use in decision making. Specifically, whether a cost-effective technology is affordable, given the available health budget. A recommendation stemming from the research was to encourage the routine inclusion of BIA in any economic evaluation of health technology or model of care [49]. Whilst methods for conducting and reporting CEAs have been established and there are guidelines for reporting the budget impact of health technologies submitted to national decision making agencies, methods for reporting, conducting, and interpreting comprehensive economic evaluation, specific to a local context, do not exist [54, 83].

To address this gap, the Health Research Economics team at the Hunter Medical Research Institute partnered with NSW Regional Health Partners, a federally funded Centre for Innovation in Regional Health, to develop guidelines for BIA at the local level of health care. This guideline development project commenced in May 2020 and forms part of a body of work related to but not included in the research comprising this thesis. The BIA guideline project included a scoping literature review that identified and summarised national and international best practice in BIA and provided recommendations for guideline development. The guideline development project also included interviews with key executive and management staff from local health services and an audit of financial data included in submissions to a local health district committee with a remit for governing the introduction of new health technologies into the healthcare system.

These guidelines are expected to be published in 2022. Following the development of these guidelines and the publication of the economic evaluation in Chapter Four, a BIA of the introduction of a practice change intervention in a local health service will be conducted.

5.2 Published manuscript

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Implementation Science

RESEARCH Open Access

Cost, cost-consequence and cost-effectiveness evaluation of a practice change intervention to increase routine provision of antenatal care addressing maternal alcohol consumption

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Abstract

Background: Implementation of antenatal clinical guideline recommendations for addressing maternal alcohol consumption is sub-optimal. There is a complete absence of evidence of the cost and cost-effectiveness of delivering practice change interventions addressing maternal alcohol consumption amongst women accessing maternity services. The study sought to determine the cost, cost-consequence and cost-effectiveness of developing and delivering a multi-strategy practice change intervention in three sectors of a health district in New South Wales, Australia.

Methods: The trial-based economic analyses compared the costs and outcomes of the intervention to usual care over the 35-month period of the stepped-wedge trial. A health service provider perspective was selected to focus on the cost of delivering the practice change intervention, rather than the cost of delivering antenatal care itself. All costs are reported in Australian dollars ($AUD, 2019). Univariate and probabilistic sensitivity analyses assessed the effect of variation in intervention effect and costs.

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Contributions to the literature

- This is the first trial-based economic evaluation that identified, measured and valued the resources associated with the development and implementation of a practice change intervention to improve delivery of guideline recommended antenatal care addressing alcohol consumption by pregnant women.
- The findings inform decision makers of the cost, cost-consequence and cost-effectiveness of delivering a practice change intervention.
- Resource requirements were highest during the intervention period, however the average cost per woman is expected to decrease over time. Evidence of the cost profile is intended to inform decision makers of when, during the practice change process, different costs and benefits are expected.

Results: The total cost of delivering the practice change intervention across all three sectors was $367,646, of which $40,871 (11%) were development costs and $326,774 (89%) were delivery costs. Labour costs comprised 70% of the total intervention delivery cost. A single practice change strategy, 'educational meetings and educational materials' contributed 65% of the delivery cost. Based on the trial's primary efficacy outcome, the incremental cost effectiveness ratio was calculated to be $32,570 (95% CI: $32,566–$36,340) per percent increase in receipt of guideline recommended care. Based on the number of women attending the maternity services during the trial period, the average incremental cost per woman who received all guideline elements was $591 (Range: $329 - $940) . The average cost of the intervention per eligible clinician was $993 (Range: $640-$1928).

Conclusion: The intervention was more effective than usual care, at an increased cost. Healthcare funders' willingness to pay for this incremental effect is unknown. However, the strategic investment in systems change is expected to improve the efficiency of the practice change intervention over time. Given the positive trial findings, further research and monitoring is required to assess the sustainability of intervention effectiveness and whether economies of scale, or reduced costs of intervention delivery can be achieved without impact on outcomes.

Trial registration: The trial was prospectively registered with the Australian and New Zealand Clinical Trials Registry, No. ACTRN12617000882325 (date registered: 16/06/2017).

Keywords: economic evaluation, maternal and child, health service, alcohol drinking, implementation, cost

Background

Alcohol consumption during pregnancy is associated with adverse obstetric and infant outcomes that can have lifelong social and economic consequences [1, 2]. Specifically, alcohol consumption during pregnancy increases the risk of miscarriage, still birth and Fetal Alcohol Spectrum Disorder (FASD) which is the most common preventable cause of intellectual impairment in the western world [2]. Despite this, the 2019 Australian National Drug Strategy Household survey reports that 55% of Australian women consumed any alcohol during pregnancy, and 14.5% continued to drink once they knew they were pregnant [3]. No safe level of alcohol exposure has been established and Australian national alcohol guidelines recommend women abstain from drinking alcohol whilst pregnant, trying to become pregnant, or breastfeeding [4].

Public maternity services are important settings for the provision of antenatal care to a large proportion of pregnant women [5, 6]. International [7] and Australian [8, 9] antenatal clinical practice guidelines recommend that during initial and subsequent antenatal appointments all pregnant women: have their alcohol consumption assessed; be advised that it is safest not to consume alcohol during pregnancy and of the potential risks of consumption; and be offered referral for additional alcohol treatment services if required [3]. Despite such guideline recommendations, assessment and care for antenatal alcohol consumption in public maternity services is suboptimal [10, 11]. For example, in Canada approximately only half of surveyed health professionals reported providing advice to pregnant women regarding the consumption of alcohol [12]. In the United Kingdom two thirds of women reported receiving such advice from a midwife [13]. In a recent Australian survey less than two thirds of pregnant women reported that they received an assessment of their alcohol consumption and just over one third received advice and referral appropriate to their level of alcohol consumption at their initial antenatal visit [11]. Less than 10% of women received recommended care at subsequent antenatal visits [11]. Practice change strategies have been demonstrated to be effective in increasing the provision of evidence-based care in various clinical settings. Such strategies include educational meetings, local opinion leaders providing expert opinion, audit and feedback and electronic prompt and reminder systems [14–17]. No studies have reported the effectiveness of such strategies in improving the provision of care addressing maternal alcohol consumption by maternity services. Whilst effective, the delivery of these practice change strategies should be considered against their resource requirements [18].

Despite the increasing use of economic evaluation in health services research, its application to the assessment of the cost and cost effectiveness of practice change intervention strategies is limited [18] [19, 20]. A 2019 systematic review by Roberts et al. identified 30 studies that included implementation or improvement as part of an economic evaluation [20]. Of those, 14 were implementation studies and the most common focus was on implementation strategies of new care pathways or novel services [20]. Of these,

seven included a cost-effectiveness analysis (CEA), of which two were conducted in the Australian setting, one was a web-based intervention [21] implementation designed to improve the management of minor head injury in emergency departments [22]. Of the 14 implementation studies identified in this review, only six included specific implementation costs, such as those associated with staff training and education, the impacts of new processes on patient and carer costs and the cost of developing new processes [20]. Another recent systematic review of economic evaluations and cost analyses of guideline implementation strategies identified 235 implementation studies, of which only 10% provided information about implementation costs, with none providing detailed cost information [23]. Furthermore, this review identified 63 studies (27%) that reported an economic evaluation, however, overall the methodological quality was poor and very few included conclusions on the effectiveness or efficiency of implementing the guideline into practice [23]. Similarly, a systematic review of economic evaluations of antenatal nutrition and alcohol interventions and their implementation identified 12 studies, ten addressing nutrition intervention effectiveness and two addressing alcohol interventions [24]. The review found that although the alcohol interventions were cost-effective or cost saving, the cost and cost-effectiveness of the intervention and its associated practice change interventions were not reported, and have not been reported previously [24]. Failure to identify, measure and value explicit costs associated with implementation risks underestimation of the investment required to change practice. This has been identified as a missed opportunity to develop evidence about the importance of fixed and recurring costs associated with practice change interventions [20].

The importance of economic evaluation in the context of implementation science and how these analyses can be most efficiently incorporated into decision-making process has been recognised [19]. To address this evidence gap, a trial-based economic evaluation was conducted of a practice change implementation intervention that aimed to improve delivery of guideline recommended antenatal care addressing alcohol consumption by women during pregnancy. The aims of the economic evaluation were to:

1) Identify, measure and value the cost of developing and delivering a multi-strategy practice change intervention;
2) Report the costs and consequences of a multi-strategy practice change intervention; and
3) Determine the cost-effectiveness of a multi-strategy practice change intervention in improving antenatal care provider adherence to antenatal care guidelines compared to usual care.

The secondary aims for the economic evaluation were to report each of the aims by sector.

Methods

The trial

The practice change intervention trial has been reported by Kingsland et al. [25]. In summary, a randomised stepped-wedge controlled trial of a maternal alcohol practice change intervention was conducted in maternity services in three sectors in the Hunter New England Local Health District (HNELHD), New South Wales, Australia. Combined, the sectors provide antenatal care for approximately 6,100 women annually, accounting for 70% of public hospital births in the district [25]. The sectors provided antenatal care to women in a major city (Sector One: 4300 births per annum) and two regional/rural areas (Sectors Two and Three: 1200 and 600 births per annum respectively). The participating maternity services provided antenatal care for women through hospital and community-based midwifery clinics; hospital medical clinics; midwifery continuity of care group practices; Aboriginal Maternal and Infant Health Services (AMIHS); and specialist services caring for women with complex pregnancies or social vulnerabilities. All antenatal care providers in these services were eligible to receive the implementation strategies, including midwifery and medical staff and Aboriginal Health Workers (AHWs).

Outcome data were collected over a 35 month period from seven-months prior to commencement of the practice change intervention in the first sector to seven-months following completion of the intervention in the third sector [11]. Stepped delivery of the seven-month intervention period in each of the three sectors occurred in a random order at seven-month intervals [25]. All antenatal care providers who worked in the participating maternity services were eligible to receive the practice change intervention. The trial primary outcome measures were the proportion of antenatal appointments at 'booking in' (initial antenatal , 27–28 weeks gestation and 35–36 weeks gestation for which women report [1] being assessed for alcohol consumption, [2] being provided with brief advice related to alcohol consumption during pregnancy, [3] receiving relevant care for addressing alcohol consumption during pregnancy, and [4] being assessed for alcohol consumption and receiving relevant care [25].

Guideline recommended model of antenatal care

An evidence- and guideline-based model of antenatal care was developed to address alcohol consumption by pregnant women [25]. The model of care involved health care provider assessment of a woman's alcohol risk status using the AUDIT-C tool at the initial antenatal visit, and at follow up antenatal appointments at 27-29 weeks and 35-37 weeks gestation. The model of care also required all pregnant women were to be provided with brief advice indicating it is safest not to consume alcohol during pregnancy and of the risks associated with alcohol consumption. Women who were assessed as being at 'medium risk' of harm (AUDIT-C score: 3-4) were to be offered a referral to the NSW Get Healthy in Pregnancy Service, a free government provided evidence-based telephone coaching service for Aboriginal women, or to a face-to-face counselling service where available. Women who were assessed as being at 'high risk' of harm (AUDIT C score: 5+) were referred to Hunter New England Drug and Alcohol Clinical Services for further assessment and follow-up.

Practice change intervention

A multi-strategy practice change intervention to support the provision of the antenatal model of antenatal care was co-designed with input from health service stakeholders (e.g. senior maternity service staff, drug and alcohol service staff) and Aboriginal health organisations and women, and was guided by an implementation framework [26–29]. The intervention involved seven evidence-based practice change strategies: leadership and management; local clinical practice guidelines; electronic prompt and reminder system; local clinical/academic opinion leaders (change champions); educational meetings and educational materials; academic detailing (including audit and feedback); and monitoring and accountability for the performance of the delivery of health care [25]. Refer to Table 1.

Usual care

Prior to delivery of the practice change intervention in each of the three sectors, usual antenatal care addressing maternal alcohol consumption during pregnancy was provided [11]. An observational study was conducted in 2017-2018 to examine pregnant women's reported receipt of guideline recommended care addressing alcohol consumption during pregnancy [11]. The study found that although assessment and care for maternal alcohol consumption is highly acceptable to pregnant women, receipt of such care in public antenatal services is suboptimal and inconsistent [11].

Economic evaluation

Details of the approach to conducting the economic evaluation have been reported in the economic evaluation protocol [30]. A trial-based economic evaluation was conducted to assess cost, cost-consequence and cost-effectiveness of the development and delivery of the intervention. The analysis was conducted from a health-care provider perspective and was based on opportunity cost. The perspective was chosen as ongoing investment in the intervention, if translated into routine practice, would fall on public health services [30]. Costs incurred in 2017 and 2018 were adjusted for inflation using annual consumer price index [31]. All costs are reported in 2019 Australian dollars ($AUD).

The economic evaluation was conducted and reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) publication guidelines and good reporting practices [32]. Adherence to the CHEERS checklist is available in Supplementary Table 1.

Identification and measurement of outcomes

The economic evaluation was based on the trial primary outcome: the proportion of women at the initial, 27-28 weeks gestation and 35–36 weeks gestation antenatal visits who reported being assessed for alcohol consumption using the Alcohol Use Disorders Identification Test (AUDIT-C) tool, and who received the recommended elements of care (advice and referral) appropriate to their level of risk, as determined by AUDIT-C risk categories for pregnancy [30]. The trial primary outcome and the economic cost data were combined in an incremental cost-effectiveness ratio (ICER) calculated as the incremental cost per percentage increase in self-reported receipt of all guideline elements. ICERS by sector were reported as secondary outcomes.

Identification, measurement and valuation of practice change costs

At present, there are no guidelines for costing practice change interventions that aim to improve the implementation of guideline recommendations in health care settings [33, 34]. A recent pragmatic method for costing implementation strategies using time-driven activity based costing has been proposed by Cidav et al [33]. Time-driven activity-based costing is a micro-costing method widely used in business settings, which delivers

detailed, accurate and transparent information on activity costs designed to inform quality assurance processes and decision making [33, 35, 36]. The costing method involves three parameters; (i) frequency of the activity, (ii) time required to perform one single event of the activity, and (iii) per-hour price of the resources used to perform the activity [33]. The detailed information collected using this approach provides a direct link between the implementation inputs (resources utilized) and implementation outcomes [33]. Cidav's methods were used to inform the identification, measurement and valuation of implementation intervention data in the economic evaluation [33].

Intervention costs were prospectively identified and measured using a time-driven activity based cost-capture tool [30]. The cost-capture tool was developed in Microsoft Excel (2013) and allowed researchers to document the activity and materials consumed at different phases of the trial (development and delivery) and for all relevant stakeholders [30]. The cost-capture tool included the following resource use categories: [1] Labour [2]; Materials; and [3] Miscellaneous costs. Table 2 presents the approach to the valuation of unit costs for each item. Researcher officers involved in the trial delivery completed the cost-capture tool at the time of the cost being incurred throughout the trial duration. Labour, materials, and other implementation costs were captured, with the cost-capture tool built to allow expenses to be allocated to pre-coded cost categories and to one or more pre-coded implementation strategies. Following the reporting convention established in the CHEERs checklist, development and research costs are deemed 'start-up' costs [1]. We excluded development costs in this analysis as they represent the investment made by the research team to formulate the intervention components, and are not representative of the resource use required in 'steady state' operations. However, we separately reported the calculated value of the development costs to inform the upfront investment required to develop this intervention, where no similar model of care exists. Research related costs together with intervention development costs were excluded from the cost-consequence and cost-effectiveness analysis to achieve a focus on the costs and efficiency of the practice change intervention alone.

Cost data were treated as counts of resource use, weighted by unit costs. The cost for each sector was determined by summing the intervention delivery costs relevant to and coded for that sector. A cost per practice change strategy is reported to demonstrate the investment required for each of the seven strategies and to inform future intervention scale up and sustainability. The intervention was wholly additional to usual care, that is, no usual practice activity was displaced as a result of the intervention. Costs to providers, patients and private care providers (including opportunity costs) were not assessed.

Cost-consequence (CCA) and cost-effective analyses (CEA)

The results of the CCA are presented as the total cost of delivering the intervention alongside the range of outcomes reflected in the primary and secondary trial outcomes (consequences). The cost per eligible clinical provider is presented to demonstrate the cost and consequence of the intervention for those intended to provide the evidence-based model of care. Eligible clinical providers were all clinicians within the participating maternity services who provided antenatal care during the intervention period. Eligible clinical providers included midwifery and medical staff as well as Aboriginal Health Workers. It excluded clinicians who were not the primary providers of antenatal care (e.g. dietitians, diabetes educators and drug and alcohol clinicians). Eligible clinical providers were identified through rostering and payroll systems obtained from the participating maternity services. Modelled extrapolation of the self-report survey data was conducted to estimate the proportion of all women attending the participating maternity services who received all guideline elements during the intervention follow-up period. This extrapolation enabled estimation of the incremental cost per woman who received all guideline elements, in each sector. The average cost per woman was calculated as the cost of the practice change intervention, divided by the total number of women who are anticipated to have received all guideline elements based on the sample of women surveyed.

The trial-based CEA aligned the cost of the intervention against self-reported receipt of all guideline elements of antenatal care. The trial outcomes, reported as odds ratios, were converted to risk differences for inclusion in the CEA, e.g. the risk difference for the primary outcome refers to the percentage point (proportion) increase in the self-reported receipt of all guideline elements of antenatal care. This information was used to generate an ICER.

Uncertainty, sensitivity and sub-group analyses of ICERs

ICERs were calculated by sector to enable reporting of the variation in costs and effect sizes between the three sectors. One-way probabilistic sensitivity analyses

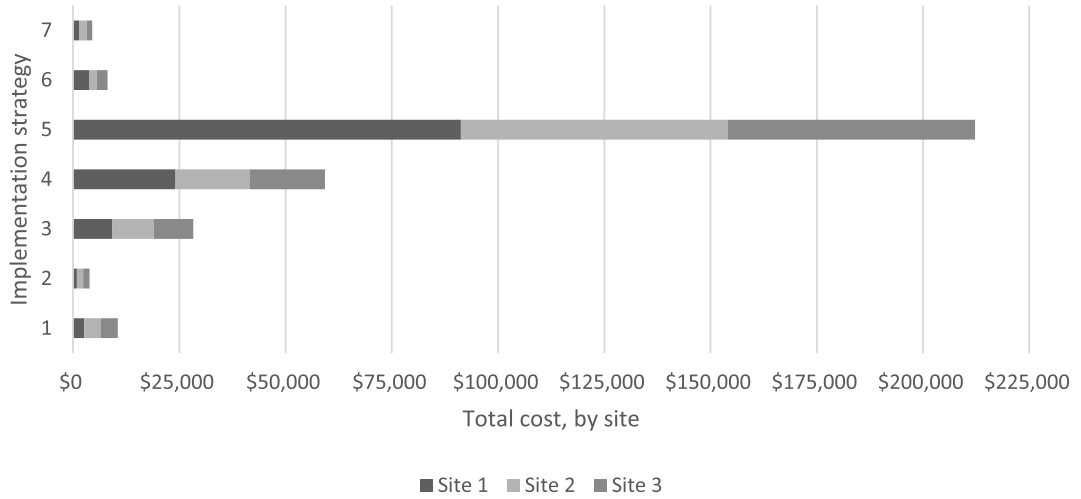

Fig. 1 Cost ($AUD, 2019) per practice change strategy, by sector. Practice change strategies: 1) Leadership/managerial supervision; 2) Local clinical practice guidelines; 3) Electronic prompt and reminder system; 4) Local opinion leaders/champions; 5) Educational meetings and educational materials; 6) Academic detailing, including audit and feedback; 7) Monitoring and accountability for the performance of the delivery of healthcare

assessed the effect of variation in the magnitude of treatment effect using the lower and upper confidence interval limits and variation in costs of intervention components using the lower and upper bounds of staff salaries. Non-parametric bootstrapping was undertaken to derive uncertainty intervals around the estimates for total cost and cost-effectiveness. Results from the sensitivity analyses were visually presented on a cost-effectiveness plane where the joint distribution of incremental costs were plotted against the incremental change in effect size between baseline and follow-up. Refer to Figs. 2 and 3.

Results

Cost

The resources invested to increase compliance with the guideline-based model of care were calculated as being wholly incremental to usual practice. The total cost of the practice change intervention across all three sectors was $367,646 of which $40,871 (11%) were development costs and $326,774 (89%) ($AUD, 2019) were intervention delivery costs. Of the intervention delivery costs, Sector one cost $133,188 (41%) of the practice change intervention costs. Sectors two and three incurred similar proportions of the practice change intervention cost, 30% and 29% respectively. The cost of labour was the main cost driver for the intervention, comprising 70% of the total intervention costs. Refer to Table 3.

Of the seven practice change intervention strategies 'educational meetings and educational materials' comprised 65% of the total intervention cost, followed by 'local opinion leaders/champions' with 18% of the intervention costs. The salary of the clinician midwife educator (CME) was the main cost driver for the 'educational meetings and educational materials' strategy. A CME was employed in each sector for the duration of the 7-month intervention. The CME for Sector one was employed at 1.0 full-time equivalent (FTE), the CME for Sector two at 0.6 FTE and Sector three at 0.4 FTE, relative to the number of births in each Sector. The remaining five intervention strategies each incurred between 1% and 8% of the total intervention costs. Refer to Fig. 1.

Cost-consequence and cost-effectiveness analyses

Significant intervention effects were found for receipt of all guideline elements (risk difference 9.33; 95% CI 7.67–10.98; $p = <0.001$). The increase in receipt of all guideline elements was seen across all three

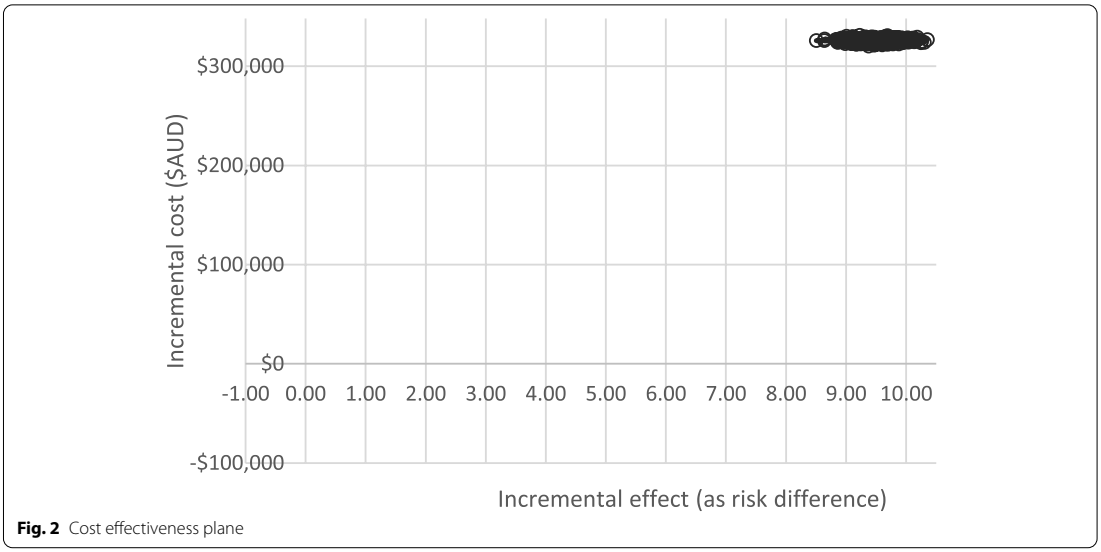

Fig. 2 Cost effectiveness plane

sectors. The average cost of delivering the practice change intervention per eligible clinician was $993 (Range: $640-$1928). Based on the average number of women in the service per month over the trial follow-up period, the extrapolated average cost per woman who received all guideline elements was calculated to be $591 (Range: $329 - $940). Variation in the average cost per woman was associated with variation in the average number of women through each service, per month between sectors. Sector one had a total of 6862 women through the antenatal service during the 21-month follow-up period, an average of 58 women per month reporting receipt of all guideline elements for the duration of the intervention. In comparison, Sector two had an average of 29 women per month reporting receipt of all guideline elements for

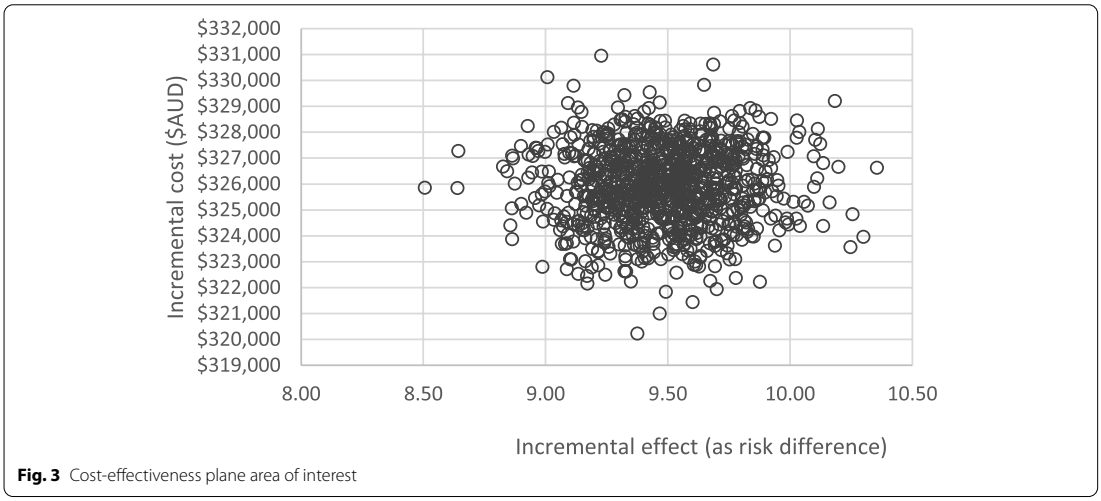

Fig. 3 Cost-effectiveness plane area of interest

a 14-month time period and Sector three had an average of 14 women per month for the seven-month time period. Refer to Table 4.

The calculated ICER per percentage point increase in self-reported receipt of all guideline elements was $32,570 (95% CI: $32,566–$36,340). The incremental cost per percent increase in women receiving all guideline elements ranged from $15,951 (95% CI: $13,109–$20,365) in Sector one and $5,618 (95% CI: $4,261–$8,25) in Sector two. Refer to Table 5.

Sensitivity analysis

The ICER in the sensitivity analysis was $35,024 (95% CI; $29,761 - $42,604), indicating that the ICER was sensitive to variation in labour costs Table 5.

Figures 2 and 3 present the joint distribution of incremental intervention cost and incremental effectiveness. All replications show a positive incremental benefit of the intervention over usual care, at increased cost. Figure 2 is a focussed view demonstrating limited variation of ICER pairs.

Discussion

This economic evaluation outlined the costs, consequences, and cost-effectiveness associated with the first published randomised controlled trial to examine the effectiveness and efficiency of delivering a practice change intervention to improve the implementation of guideline recommended care for maternal alcohol consumption. The intervention was effective at improving reported receipt of all guideline elements of care. The incremental cost of intervention delivery was calculated to be $326,774. Labour (staff time) was the main cost driver and variation in delivery costs across sectors was associated with design differences in labour time and travel costs for each sector.

The average cost over the trial period of delivering the practice change intervention per eligible clinician was $993, and $591 per woman who received all guideline elements. The cost of delivering clinician training was upfront and is not expected to require additional investment beyond the trial horizon. Clinician training modules were developed during the intervention and made permanently available online for staff to access as part of their ongoing clinician training. Further, in an effort to sustain the intervention effect size, implementation strategies were deliberately designed to affect permanent and scalable change within the health system, e.g. the inclusion of specific modules into the state-based e-maternity patient record management system, and performance measures were embedded into the health system. Therefore, these implementation strategies are expected to sustain the effect size post-intervention. As such, the average cost per woman is expected to reduce markedly with continued delivery of this new model of care over time (e.g. beyond the trial time horizon), with increased women receiving antenatal care and with scaling up to involve other maternity services/clinicians. Similarly, with respect to potential ongoing costs (beyond the trial time horizon) associated with this intervention and maintaining the intervention effect size beyond the trial time horizon.

Direct comparison between the results of this and previously reported studies of the cost and cost effectiveness of practice change interventions is not possible given the significant differences in the design and methods of the various studies. Broad comparisons with studies included in previous systematic reviews were also limited as the costs associated with the implementation of the practice change strategies is not often considered [20, 24, 37]. The review by Roberts et al. [20] identified one modelled CEA of a universal alcohol screening and brief intervention program in primary care in England [38]. This analysis compared the health and social care costs verses health benefits and found screening patients for alcohol consumption upon registration with a family doctor would steadily capture up to 96% of the population over a 10-year programme [38]. This study showed that alcohol screening and the provision of brief advice, led by practice nurses, provided cost savings to the health care system of £120m over 30 years [38]. Similar to the methods and findings of the present study, the cost of the intervention was estimated using activity costs and identified that resourcing needs for this intervention would be highest in the early years of the program due to the volume of new patients being screened, and would decrease over time [38]. This study did not include the cost of implementing this model of care into routine practice or addressing barriers to care delivery by relevant health service providers. In comparison, the practice change strategies used in the current study were designed to be embedded into the health care system to maintain the new model of care beyond the intervention delivery and follow-up period. As such, it is plausible that the demonstrated change in practice could be sustained beyond the trial time horizon and the average cost per woman screened would decrease as more women attend the antenatal service. Future studies could include longer

intervention follow-up periods to capture the number of women receiving care over a longer time period, as well as the health and societal benefits for mothers and their infants. Further research is also required to determine the cost of delivering the intervention at scale and whether economies of scale can be achieved in its delivery.

Implementation costs are recognised as an understudied aspect of implementation science [39, 40]. Saldana et al. proposed that one of the reasons implementation costs are not routinely examined is the lack of standard measurement [39]. More recently, Cidav et al. proposed a pragmatic approach to systematically estimating detailed resource use and costs of implementation strategies that combine time-driven activity-based costing with a leading implementation science framework [41] to guide specification and reporting of implementation strategies [33]. One of the key strengths of this study was the use of this time-driven activity based micro-costing to map implementation processes with actions, actors and strategies. This method provides transparent, granular cost estimation and allowed for a cost comparison of the different implementation strategies. It has been proposed that there could be value to using standardised methods for estimating implementation costs as it could allow decision makers responsible for determining the viability and feasibility of adopting new practices to benefit from the ability to generalise across settings [39, 42]. The transparent reporting of activity costs using a published time-driven activity-based costing method is intended to inform researchers and decision makers how specific components of an implementation intervention influence the total cost.

Another strength of this economic evaluation is the identification, measurement and valuation of development costs. That is, once the practice change intervention has been delivered, there are non-recoverable intervention components that remain within each sector. For example, the cost of developing and producing local clinical guidelines, the cost of developing educational materials and the cost of developing site-specific systems level monitoring and accountability measures. Saldana et al. argue development costs are an important consideration in decision making as policy makers must decide ex ante whether to invest in a new model of care and unrecoverable costs must be considered amongst the future benefits [39]. Transparent reporting of costs associated with the practice change intervention is intended to inform decision makers of when, during the practice change process, different costs and benefits can be expected [19].

It was not possible to calculate an ICER for the cost per additional service user (pregnant woman) who received all guideline elements of care. The study was designed and powered to measure effectiveness at the health sector level, thus precluding this ICER calculation. Given this limitation, the average cost per additional service user (pregnant woman) exposed to the recommended treatment was calculated. Another, limitation of the study was that the ICER was calculated on the assumption that the intervention was wholly additional to usual care, that is, no usual practice activity was displaced as a result of the intervention. Identifying, measuring and valuing the cost of usual care was beyond the scope of the trial and hence a limitation of the analysis. The trial time horizon was 35-months, and as such only upfront and short-term costs to health service providers were included. Similarly, the potential impact of increased referrals to drug and alcohol services and the longer-term benefits of alcohol-harm reduction to society at large, was not captured in this trial and is a noted limitation. Future economic evaluations should endeavour to include these components. The range of costs associated with sustaining changes in provider behaviour and maternal alcohol consumption is complex [2], and beyond the scope of the analyses.

Conclusion

The practice change intervention was effective at improving women's reported receipt of all guideline elements of care. The incremental cost of delivering the intervention was calculated to be $326,774. To our knowledge, no similar studies have been published in the literature. The economic evaluation provides information for decision and policy makers regarding the cost, cost-consequence and cost-effectiveness of delivering a practice change intervention to support the introduction of a model of care for addressing alcohol consumption by pregnant women. Given the positive trial findings, further research is required to assess sustainability and determine the cost of delivering the intervention at scale and whether economies of scale can be achieved.

Appendices

Table 1 Implementation Strategy Summary

Intervention component	Component details	Resource use details	Data collection method for costing
Leadership and management	• Monthly meetings were held with management from antenatal services to elicit support. • Service managers distributed resources to staff and attended training sessions. • Performance measures related to the provision of the model of care were monitored and reported on.	**Labour time:** • Health district implementation support officer and manager. • Health service antenatal clinical staff and management.	• Resource use capture template
Local clinical practice guidelines	• A service level guideline and procedure document detailed the model of care, including assessment, brief advice and referral pathways. • The document was uploaded onto the health service's policy directory, disseminated by managers to all staff via email and hard copies were placed in staff common areas.	**Materials:** • Guideline and procedure document development and provision. **Miscellaneous:** • Electronic dissemination. **Labour time:** • Health district implementation support officer and manager. • Health service antenatal clinical staff and management.	• Resource use capture template
Electronic prompt and reminder system	• Existing point-of-care and medical record systems used by maternity clinicians were modified to electronically prompt use of the AUDIT-C alcohol screening tool. • Brief advice scripts were displayed on the point-of-care system based on the woman's AUDIT-C risk score and prompts and tools for referral to appropriate services.	**Materials:** • Computer-based intervention component. **Labour time:** • Health district implementation support officer and manager. • Health service antenatal clinical staff and management.	• Resource use capture template
Local opinion leaders/champions	• Project-specific Clinical Midwife Educators were appointed to support staff to uptake the model of care and provide support at a one-on-one, team and service level. • Additional local antenatal clinical leaders were engaged to provide encouragement and demonstrate required behaviours as required.	**Labour time:** • Health district implementation support officer. • Clinical midwife educator (CME) change champion.	• Resource use capture template
Educational meetings and materials	• Training was provided to all antenatal service clinicians via a 30-minute online training module and face-to-face sessions. Clinical Midwife Educators facilitated clinicians completing the online training and coordinate face-to-face training sessions. This included lecture style sessions, interactive, case-study based sessions and one-on-one sessions. • Clinicians were provided with written resources (hardcopy and electronic) to support the model of care, including standard drink measure charts and point-of care written prompts/reminders (e.g. stickers in charts).	**Labour time:** • Health district implementation support officer. • CME change champion. • Health service clinical staff. • Expert clinicians. **Materials:** • Educational tools and resources	• Resource use capture template • REDCap database
Academic detailing	• Data from both medical records and telephone surveys conducted with women who attended the antenatal services were used to provide feedback on adherence to the agreed model of care. • The Clinical Midwife Educators visited service teams in their antenatal clinics to provide feedback data and developed action plans to improve adherence.	**Labour time:** • Project support officer. • CME change champion. • Clinical service staff time.	• Resource use capture template • REDCap database

Table 1 (continued)

Intervention component	Component details	Resource use details	Data collection method for costing
Monitoring and accountability	• Antenatal service managers reported, interpreted and monitored performance measures for the model of care. • These results were disseminated to antenatal service staff through team meetings, emails and other usual communication mechanisms. • Performance measures were built into the existing monitoring and accountability frameworks for antenatal services.	**Labour time:** • Health district implementation support officer. • Health service antenatal clinical staff and management. **Miscellaneous:** • Electronic dissemination.	• Resource use capture template

Table 2 Approach to valuation of resources, by cost category

Item	Description	Approach to valuation
Labour time	Health service labour time incurred during intervention development and implementation	Staff time was recorded in minutes and NSW Health staff grade was recorded in trial management logs and cost-capture templates. Labour time was valued using NSW Health Award 2019*
	Non-health service labour time incurred during intervention development and implementation	Staff time was recorded in minutes and job title was recorded in trial management logs and cost-capture templates. Labour time was valued using Fair Work Australia Award Wages or University of Newcastle Academic Staff and Teachers or Professional Staff enterprise agreement*
Materials	Material items used during intervention development and implementation. For example, changes to electronic medical records system, printed resources, and stickers	Purchase receipts and trial management logs were used to value material items.
Miscellaneous	Included catering for training sessions and staff travel allowance or use of fleet vehicle	Purchase receipts and trial management logs were used to value all miscellaneous items.

*Labour time was costed at 1.3 to account for additional overhead costs (on-costs) associated with employment

Table 3 Total intervention cost disaggregated by sector, resource use category and practice change strategy

	Total	Sector 1	Sector 2	Sector 3
Total intervention costs				
Total intervention development and practice change cost	$367,646	$154,927	$112,985	$99,733
Practice change intervention development cost	$40,871	$21,739	$13,883	$5,250
Practice change intervention delivery cost	$326,774	$133,188	$99,103	$94,483
Costs: by resource use category				
Labour cost	$229,566	$102,468	$64,692	$62,406
Material cost	$75,424	$25,338	$25,043	$25,043
Miscellaneous cost	$21,785	$5,383	$9,368	$7,034
Cost by strategy				
Leadership/managerial supervision	$10,528	$2,599	$3,940	$3,990
Local clinical practice guidelines	$3,875	$876	$1,484	$1,515
Electronic prompt and reminder system	$28,286	$9,171	$9,830	$9,285
Local opinion leaders/champions	$59,255	$24,126	$17,366	$17,763
Educational meetings and educational materials	$212,260	$91,224	$62,888	$58,148
Academic detailing, including audit and feedback	$8,100	$3,834	$1,715	$2,551
Monitoring and accountability for the performance of the delivery of healthcare	$4,471	$1,358	$1,881	$1,232

Table 4 Cost-consequence results (baseline to follow-up)

	Total	Sector 1	Sector 2	Sector 3
Cost				
Practice change intervention cost	$326,774	$133,188	$99,103	$94,483
Consequences				
Women reporting receipt of all guideline elements at baseline				
Mean (%) across all sites	13%	-	-	-
Women reporting receipt of all guideline elements				
Risk difference, post vs baseline (95% CI)*	9.33	8.35	17.64	12. 21
	(p <0.001)	(p <0.001)	(p <0.001)	(p <0.001)
	7.67–10.98	6.54–10.16	12.01–23.26	4.47–19.95
Eligible antenatal providers who received the intervention				
Total	329	208	72	49
Proportion	100%	63%	22%	15%
Average cost per eligible provider	$993	$640	$1,376	$1,928
Women reporting receipt of all guideline elements of care				
Time period (follow-up data collection)	Sept 2018 – May 2019	Sept 2018 – May 2020	Apr 2019 – May 2020	Nov 2019 – May 2020
Number of months	21	21	14	7
Proportion women who reported receiving all guideline elements	19%	18%	31%	27%
Total number of women who received antenatal care	8539	6862	1302	375
Total number of women who received all guideline elements	1658	1215	402	101
Average cost per woman	$591	$329	$493	$940
Average number of women who received all guideline elements, per month	79	58	29	14

* The primary outcome was reported as an odds ratio in the primary outcome's manuscript. For the purpose of economic evaluation, it was converted to risk difference for inclusion in an ICER

Table 5 Incremental cost-effectiveness ratios for the primary and secondary outcomes

	ICER	95% CI	
ICER for women reporting receipt of all guideline elements			
Total	$32,570	$32,566 - $36,340	
ICER per sector			
Sector 1	$15,951	$13,109	$20,365
Sector 2	$5,618	$4,261	$8,252
Sector 3	$7,738	$4,736	$21,137

Abbreviations
AUD: Australian dollars; AUDIT-C: Alcohol Use Disorders Identification Test; BIA: Budget impact assessment; CEA: Cost-effectiveness evaluation; DCEA: Distributional cost-effectiveness analysis; ICER: Incremental cost-effectiveness ratio.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13012-021-01180-6.

Additional file 1.

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Authors' contributions
MK, EE, JW, AS, AD, LW, TS and PR developed the original research concept and developed the study design. MK, EE, ED are responsible for overseeing data collection. ZS conducted the analysis. PR oversaw the analysis and provided feedback. ZS and PR developed the draft manuscript. All authors made substantial contributions to the manuscript development, read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The trial was approved by the Hunter New England Human Research Ethics Committee (16/11/16/4.07; 16/10/19/5.15), the Aboriginal Health and Medical Research Council (1236/16) and the University of Newcastle Human Research Ethics Committee (H-2017-0032; H-2016-0422).

Consent for publication
Not applicable

Competing interests
The authors declare that they have no competing interests.

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Publisher's Note

A full description of component details has been published elsewhere [43].

Chapter 6

Diet quality and resource use in the antenatal period: a protocol for the economic evaluation of an observational study

6.1 Chapter Introduction

The systematic review in Chapter Three found single micronutrient supplement interventions in the antenatal period may be a cost-effective health promotion intervention from the health service provider perspective [84]. The review also identified a paucity of economic evaluations of any other nutrition intervention modality or target (e.g. micronutrient, macronutrient, total diet). To identify future targets for antenatal health promotion interventions, maternal compliance with the *"Australian Dietary Guidelines"* (ADG) recommendations must be assessed, and potential targets for future health promotion interventions identified.

At present, Australian data for maternal nutrition intake during pregnancy is limited. A 2016 national study investigated maternal adherence to the ADG [85]. The cross-sectional web-based survey assessed the dietary intake of pregnant women against the ADG with respect to the Five Food Group recommendations and determine predictors of adherence to the recommendations. The study found that whilst most pregnant women in Australia perceive their diets to be healthy, their daily intake does not comply to national guideline recommendations. This national survey was conducted in 2013, had a total of 857 respondents, 402 of whom were from a South Australian cohort. The economic implications of maternal diet quality were not considered [85]. Similarly, a 2015 compared women's diets with recommended intakes from the new *"Australian Dietary Guidelines"* (2003) using data from the Australian Longitudinal Study on Women's Health (ALSWH) [86]. This study found that most women reported intakes below the recommended daily servings for all food groups, with the single exception of fruit. The study also found the reported intake diverged widely from guideline recommendations, for example less than 2% of women met the recommended daily intake of five servings of vegetables, with 75% of women needing to increase their daily consumption by more than two servings [86]. Median daily consumption of 'extra foods' was 4.1 (IQR: 2.9-5.5), higher than the recommended daily upper limit of 2.5 serves. The economic implications of failure to adhere to antenatal nutrition guideline recommendations is unknown. This aforemetioned ALSWH data on sociodemographic and behavioural characteristics including the dietary intakes of the young women (including pregnant women) was collected in 2001 and again in 2009. The most recent data collected regarding maternal dietary intake and compliance with ADG was 2013 [85], and is not specific to the local HNELHD context. Further, neither study collected economic data nor discussed the economic implications of failure to adhere to national dietary guidelines.

As discussed in Chapter One, this thesis separates into two separate economic analyses of maternal health behaviours. The first, in Chapters Four and Five included the comprehensive economic evaluation of a known health promotion target, maternal alcohol consumption. The second, included in Chapters Six and Seven, describes the collection of cross-sectional observational data to assess maternal dietary intake and its associated economic implications. Unpublished details regarding study research methods are described in Chapter Two. Maternal compliance with antenatal guideline recommendations was reported in by Slater et al. in the

following published manuscript:

Kaylee Slater, Megan Rollo, Zoe Szewczyk, Lee Ashton, Tracy Schumacher, Clare Collins. Do the Dietary Intakes of Pregnant Women Attending Public Hospital Antenatal Clinics Align with Australian Guide to Healthy Eating Recommendations? Nutrients, 2020. 12(8): p. 2438. DOI: 10.3390/nu12082438

The study found that of 534 women participating, none met guideline recommendations for all food groups. Highest adherence was for fruit serves (38%), and lowest for breads and cereals (0.6%). Only four women met the pregnancy nutrient reference values for folate, iron, calcium, zinc, and fibre from food alone [87].

Chapter Six presents the unpublished protocol describing the planned economic evaluation and statistical analyses to explore the association between maternal diet quality, weight status and health care resource use during the delivery period.

Diet quality and resource use in the perinatal period: an economic evaluation protocol

Authorship team

Ms Zoe Szewczyk, Dr Megan Rollo, Dr Natasha Weaver, Mr Simon Deeming, Associate Professor Elizabeth Holliday, Dr Penny Reeves, Professor Clare Collins.

6.2 Abstract

Background: Clinical practice guidelines recommend managing obesity in pregnancy using increased multidisciplinary monitoring to mitigate risk of adverse health outcomes for mothers and infants. The impact of pre-pregnancy obesity on resource use during pregnancy remains under explored. It is also unknown how diet quality contributes to maternal obesity and its economic implications.

Objective: 1) Quantify the relationship between pre-pregnancy body mass index (BMI) and health care resource use incurred during the delivery admission; and 2) evaluate the contribution of dietary quality on the relationship between BMI and healthcare resource use. This protocol describes the planned economic and statistical analyses.

Aim: (i) Assess the diet quality of pregnant Australian women attending a public hospital antenatal outpatient clinic; (ii) report associations between pre-pregnancy body mass index (BMI) and use of specific health care resources during the delivery admission. This includes mode of delivery, length of stay, admission to intensive care and midwifery in the home service use; (iii) report the contribution of dietary quality to associations between BMI and resource use; and (iv) value the independent effect of maternal dietary quality on resource use during the delivery admission.

Methods: Analyses will be conducted using cross-sectional data from pregnant women attending the antenatal outpatient clinics at the John Hunter Hospital, Newcastle, Australia. Maternal pre-pregnancy BMI, health and demographic data will be collected via patient medical records. Mode of delivery, maternal length of stay and midwifery in the home follow-up care data weill be obtained from patient medical records for the mother during the delivery admission. Dietary intake will be measured self-reported using the Australian Eating Survey (AES) food frequency questionnaire and diet quality quantified using the Australian Recommended Food Score (ARFS) AES sub-scale. The proposed economic analyses will take a health service perspective in identifying, measuring, and valuing resource use provided during the delivery admission.

Conclusion: Australia's health care spending is increasing, as is the prevalence of obesity. This study will investigate the relationship between obesity and dietary quality on health care system resource use in the delivery period. Findings will inform future research into health

promotion strategies aiming to mitigate the economic burden of maternal health behaviours during the antenatal period and provide evidence to inform clinical practice guidelines.

6.3 Introduction

Optimal maternal dietary patterns and weight gain during pregnancy are associated with reduced risk of adverse maternal and infant outcomes [88, 89]. However, many Australian women fail to meet nationally recommended nutrition targets and do not appear to improve their diet quality when planning to become pregnant, or during pregnancy [22, 23]. Sub-optimal maternal dietary patterns can contribute to high body mass index (BMI), excessive gestational weight gain (EGWG), gestational hypertension, pre-eclampsia, gestational diabetes mellitus (GDM), pre-term birth, low or high birth weight [90, 91], increased risk of miscarriage [92], birth defects, and stillbirth [93, 31]. In particular, obesity in pregnancy is now one of the most important challenges in obstetric care [94]. Approximately 50% of women who become pregnant have overweight (BMI >25kg/m^2 – 30kg/m^2) or obesity (BMI >30kg/m^2) [94] and the prevalence of obesity is rising [95]. High BMI during pregnancy has been strongly associated with EGWG [33], increased risk of GDM, pre-eclampsia, prematurity [33], large-for-gestational-age infants, caesarean delivery [96], miscarriage, antepartum stillbirth, complications at delivery, and increased postpartum weight retention [97, 33, 94]. Adverse maternal and infant outcomes in the perinatal period result in increased health care resource utilisation both in the perinatal period and across the mother's and infant's life span [98, 35]. Antenatal nutrition and weight status have been identified as targets for health promotion interventions aiming to improve maternal and infant health outcomes and reduce demand on the health care system [7].

Given the elevated risk to the mother and infant, obstetric and midwifery clinical practice guidelines recommend that health care facilities have well-defined pathways for the care of women with obesity, with increased management relative to the antenatal care pathways of non-obese women [4, 99]. Current clinical practice guidelines include summary data and consensus recommendations, but are not routinely informed by effectiveness or cost-effectiveness data that has quantified the impact of dietary intake and obesity on clinical outcomes and resource use [94]. This has resource use implications for the health care system. A recent study of infants born to mothers with overweight or obesity in the UK found the usage rate for all healthcare services was significantly greater in infants born to mothers with obesity than infants born to mothers with healthy weight [100]. Infants born to mothers with obesity experienced a 39% higher rate of inpatient admissions and a 55% longer duration of inpatient stays, utilising on average 72% more resource costs [100]. Similarly, a cross-sectional comparative study of the short and long-term effects of GDM on health care costs found GDM was independently associated with an average additional cost of €817.60 (2012) during pregnancy due to additional delivery and neonatal care costs, and an additional €680.50 in annual infant healthcare costs 2-5 years post pregnancy [101]. There is a sound economic argument for improving maternal nutrition

and obesity as a mechanism to improve maternal and infant outcomes and reduce health care resource use across the lifespan [52]. However, there is little high-level evidence quantifying the economic impact of maternal nutrition and obesity on health care system resources in the perinatal period. Evidence of maternal dietary intake, obesity, and their relationship with resource use is needed to better inform researchers, clinicians, guidelines, and decision makers of the economic impacts of current antenatal health promotion and clinical practice [5].

To address these evidence gaps, a cross-sectional population-based study was designed to quantify specific perinatal healthcare resource use associated with maternal weight status and diet quality in a sample of pregnant women attending a public hospital in NSW, Australia. We hypothesise that high BMI will be associated with increased healthcare resource use, and that low diet quality will be associated. Therefore, the aims of this study are as follows:

1. Assess the diet quality of pregnant Australian women attending a public hospital antenatal clinic;
2. Estimate the total effect of BMI, adjusted for diet quality, on health care resource use during the delivery admission, including mode of delivery, length of stay, admission to intensive care, and midwifery-in-the-home service;
3. Estimate the total effect of maternal diet quality on resource use during the delivery admission;
4. Estimate the direct effect of maternal diet quality on resource use during the delivery admission.

The Reporting will adhere to the *"Strengthening the Reporting of Observational Studies in Epidemiology"* (STROBE) guidelines. The protocol will document the study design, analysis plan, and economic analyses to ensure complete reporting, mitigate publication bias and avoid potential duplication [102].

6.4 Methods

6.4.1 Study Design

The study will be an observational cross-sectional study in which patients attended antenatal clinics for routine antenatal care and will be managed according to current clinical practice. The target sample size was 600 women with complete diet quality scores, which was informed by investigator experience and feasibility. Patients will be provided informed consent to participate. Self-reported demographic, health, and diet quality data will be collected at baseline (recruitment), and medical records data for the delivery admission will be collected after discharge of mother and infant.

The study has been approved by The University of Newcastle Human Research Ethics Committee, Australia (reference number: H-2017-0101) and Hunter Area Research Ethics Committee in August 2016 (reference number: HREC/16/HNE/189).

6.4.2 Study Population and Setting

Pregnant women aged 18 years or older at 28-36 weeks gestation and planning to deliver at the John Hunter Hospital will be eligible to participate in the study. The time period of 28-36 weeks gestation (third trimester) was selected since the AES assesses dietary intake over the previous three to six months [26], and should thus reasonably reflect typical dietary patterns in pregnancy. The John Hunter Hospital, located in the Hunter New England Local Health District, New South Wales, Australia is a large (550 bed) tertiary referral hospital delivering around 4000 babies each year [27]. Participants will not be excluded based on illnesses or known medical conditions.

6.4.3 Data Collection

Survey Tool

The survey includes four components: 1) Participant Screening 2) Participant Consent 3) Patient Demographics and Identification 4) The Australian Eating Survey (AES), adult version [103]. The entire survey comprised 225 questions that can be completed in about 25-35 minutes. Component one screens patients for eligibility. Component two includes the participant information statement. Component three collects measures of demographic characteristics, health behaviours and psychosocial measures including area of residence, country of birth, marital status, height, weight, smoking, listeria risk, highest educational qualification, ability to manage on income, self-reported health, and doctor-diagnosed medical conditions. Component four contains the AES questions. Patients will be screened for eligibility and provided with the patient information statement before providing informed, opt-in consent (see Figure 6.1). Study data will be collected and managed using Research Electronic Data Capture (REDCap) tools hosted at The University of Newcastle [104, 105]. REDCap is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources [105].

Study Recruitment

Volunteer research personnel (University students enrolled in the final years of a Bachelor of Nutrition and Dietetics) will recruit study participants from the clinic between March 2018 and November 2018. All personnel will be required to participate in mandatory workshop and

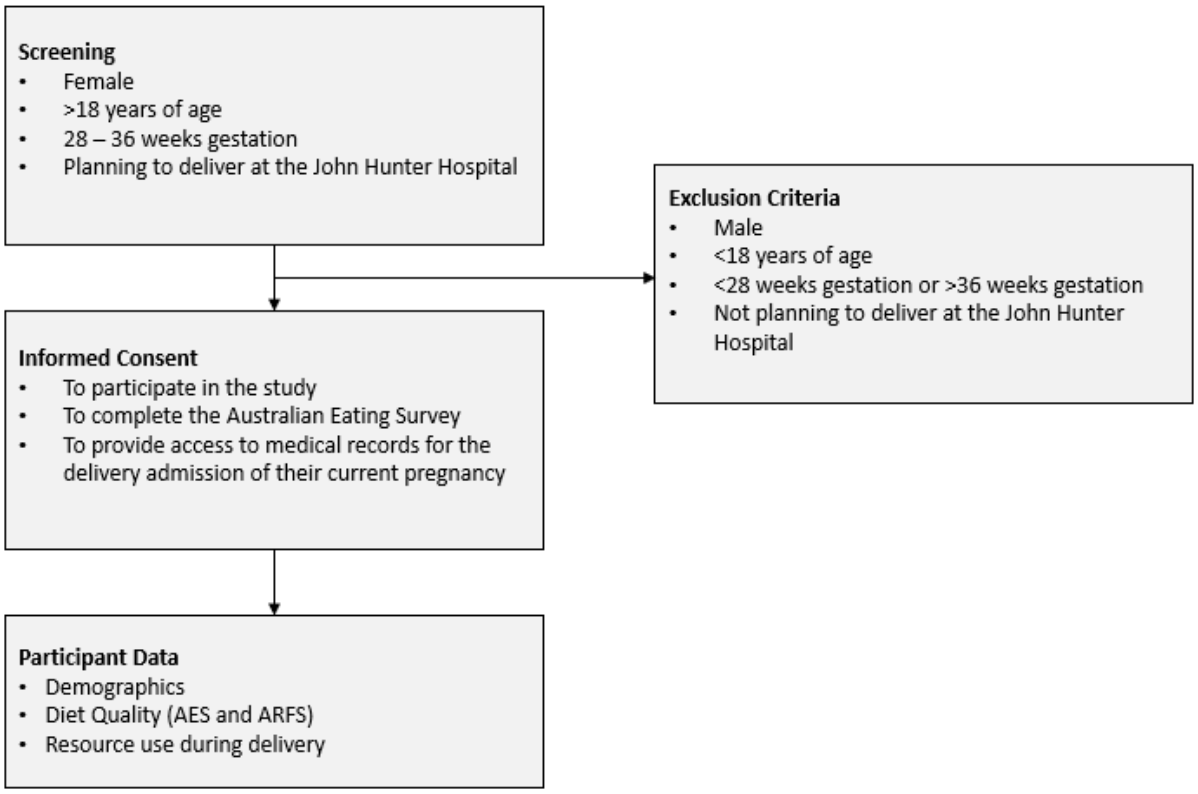

Figure 6.1: Participant inclusion critera

further in-clinic training alongside a project officer. A brief and informative script will be used by research personnel to verbally screen women for eligibility, inform women of the survey content and purpose, and invite women to participate. Consenting participants will complete the survey on a tablet via the REDCap offline mobile application. Women at less than 28 weeks gestation will be invited to complete 'Instrument 1: Participant Screening'; participants will be automatically invited to participate once they reach 28 weeks' gestation. Women unable to finish the entire survey in the clinic due to fatigue, distractions (e.g., other children or feeling unwell), or being called to their appointment will be emailed the remainder of their survey for later completion. An automated reminder email will be sent seven days later to all participants who have not finished the survey. All study participants are anticipated to have given birth by January 2019.

During recruitment, participant data will be stored in the password-protected REDCap application on password-protected tablets. At the end of each shift participant responses will be uploaded to the REDCap web-based survey management program and tablets will be cleared of all patient data. Data will be stored on a password-protected computer and access to the project data in REDCap requires a second password.

6.4.4 Economic Evaluation

The proposed economic analysis will take a health care provider perspective to identify, measure and value outcomes associated with the provision of healthcare in the delivery period. Hospital resource use data will be valued using the *"Australian Refined Diagnosis Related Group"* (AR-DRG) classification system. The analysis will exclude costs to patients and society.

Since the time horizon for inclusion of relevant resource use is set at less than 12–months, conversion or discounting of costs is not required [106].

Identification and Measurement of Outcomes

Diet quality will be quantified using the ARFS [107] which is derived from a sub-set of questions from the AES food frequency questionnaire for adults [107]. The AES is a 120-item semi-quantitative food frequency questionnaire designed to assess usual dietary intake of individuals aged 18 years or older based on a list of foods most commonly eaten by Australians. The AES has undergone comprehensive evaluation for validity and reliability and has been reported elsewhere [107]. The total ARFS score is calculated by summing the points for foods that are aligned with the core foods in the *"Australian Guide to Healthy Eating"* consumed at least weekly with a total score ranging from 0 to 73 [107]. A higher score reflects greater adherence to the *"Australian Dietary Guidelines"*, and therefore, better diet quality and variety.

Maternal clinical outcomes and resource use from the delivery admission and associated Maternity Home Services was collected from hospital databases using individual patient medical record numbers (MRN). Resource use required for the management of maternal obesity were identified from the literature and reviewed by content experts. For the purpose of this analyses resource use is defined as:

1. Mode of delivery: natural, surgical intervention, caesarean (coded as x, y, z).
2. Maternal length of stay: (count in days).
3. Maternal admission to intensive care: (yes or no).
4. Midwifery in the home service utilisation: total number of follow-up care visits associated with maternal discharge post-delivery (count).

Resource use will be valued using the *"Australian Refined Diagnosis Related Group"* (AR-DRG) classification system for admitted acute episodes of care in Australian public and private hospitals. The AR-DRG codes classify units of hospital output and group inpatient stays into clinically meaningful categories consisting of similar levels of complexity (outputs) consuming similar amounts of resources (inputs) [71]. Resource use will be reported in clinically relevant natural units alongside its associated mean and median cost.

A cost analysis will value the additional resource use associated with maternal diet quality using measures of arithmetic means, between-group differences, and variability of differences. Additional resource use will be calculated for each model and valued in natural units (e.g. days, number of events of care).

6.4.5 Statistical Analyses

Incorrect casual inferences are more likely to occur in observational studies than randomized controlled trials due to confounding bias, that is, some subjects may be more likely to be exposed to a 'treatment' due to uncontrolled factors that influence the outcome [108]. For the current study, there exist complex preconception processes influencing maternal and infant health outcomes and resource use, and these may also influence diet quality and discretionary food intake (see Table 1). To depict the assumed causal relationships between the exposure, outcome, and additional variables related to the exposure and/or outcome, directed acyclic graphs (DAGs) will be developed using existing evidence and expert opinion. The developed DAGs will be used to identify the minimum set of adjustment variables, which will be included in multivariable regression models to reduce confounding bias. DAGs will be developed using the web-based software tool DAGitty [79]. For aim (i) the diet quality of pregnant Australian women attending a public hospital antenatal outpatient clinic will be measured using the AES and reported as total ARFS. Intake of discretionary items will be reported along with the range, and proportion of women not meeting guideline recommendations.

For aim (ii) the contribution of BMI to mode of delivery, length of stay, admission to intensive care, and midwifery in the home service use will be assessed using multivariable generalized linear models (GLMs). For aim (iii) the contribution of ARFS to associations between BMI and resource use will be assessed using multivariable regression to estimate the unconfounded association of ARFS with each resource use outcome. For aim (iv) a similar analysis will be performed for the contribution of intake of discretionary choices between BMI and resource use. GLMs will specify a response distribution and link function as appropriate for the outcome, with model fit assessed using residual plots and other relevant plots and statistics. Results will be reported as parameter estimates with 95% confidence intervals, and statistical significance will be declared at the conventional 0.05 level for all analyses. Data manipulation and statistical analyses will be performed using SAS 9.4 (SAS Institute, Cary, NC, USA)™ software.

Discussion

Maternal obesity and poor diet quality are common in pregnancy and contribute to adverse perinatal outcomes [32, 34] that can contribute to greater utilisation of health care resources throughout the perinatal period [30, 31, 33, 35]. Current clinical guidelines recommend increased monitoring and management of pregnant women with obesity, compared to pregnant women

with healthy weight. This has resource use implications for the healthcare system. The planned study will investigate the association between obesity, dietary quality and resource use during the perinatal period. It will provide insight into economic implications of current antenatal care guidelines, the relationship between obesity and health service utilisation, and the contribution of diet quality on this relationship.

Limitations

The John Hunter Hospital antenatal outpatient clinic services both medium- and high-risk patients requiring ongoing management of GDM, pre-eclampsia, or those who have had previous adverse outcomes, women with babies in breech position or are attending the clinic drug and alcohol services or Indigenous health services. As such, the health outcomes and resource use of patients in this study is expected to be higher than typical values in the broader population of pregnant Australian women.

The current study does not consider health service resource use prior to the delivery admission. The John Hunter Hospital has five satellite antenatal clinics that patients can attend. Radiology and pathology can be performed at the hospital, in public or private clinics. Patients may attend private general practitioners, specialists, and care providers throughout the antenatal period. This investigative study did not allow for data linkage across all service providers. Data for health service provision prior to delivery was also unavailable. This investigative study did not allow for cost data linkage from service providers. Appropriate healthcare early in pregnancy may affect health outcomes for the mother and child, particularly the necessity for high health service costs associated with poor health outcomes. Interpretation of the results will account for these limitations.

Further limitations include the inherent bias associated with surveys. In particular, the AES responses and self-report measures of pre-pregnancy weight are expected to be subject to self-report bias. A measure of physical activity was not collected in the survey and as such was not included in the DAG.

6.5 Declarations

Ethics approval and consent to participate

The study has been approved by the University of Newcastle Human Research Ethics Committee, Australia, study reference number H-2017-0101. Hunter Area Research Ethics Committee in August 2016 reference number HREC/16/HNE/189. Opt-in consent to participate and access patient medical records was attained.

Consent for publication

The author(s) consent for publication of this paper.

Availability of data and materials

Data supporting the findings of this study will be made available with the corresponding outcomes manuscript.

Competing interests

CC is supported by an Australian National Health and Medical Research Council (NHMRC) Senior Research Fellowship and a University of Newcastle, Faculty of Health and Medicine, Gladys M brawn Senior Research Fellowship. The other author(s) declare(s) that there is no other conflicts of interest.

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Author's contributions

ZS, CC and MR developed the original research idea. ZS developed the recruitment strategy, managed the recruitment process and collection of trial data. SD, PR, NW, and EH provided expert statistical and economic advice and content. EH and NW conducted the statistical analysis. NW and ZS conducted the economic analysis. CC and MR provided nutrition content expertise. ZS and PR wrote the manuscript with the support and guidance of all other authors. All authors reviewed the final manuscript and provided feedback.

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Chapter 7

Diet quality and resource use in the antenatal period: economic evaluation of an observational study

7.1 Chapter Overview

Current dietary intakes of Australian women during pregnancy do not align with national nutrition guidelines [87]. The economic implications of suboptimal maternal nutrition are unknown. Chapter Six presented the protocol describing the planned economic and statistical analyses to explore the association between maternal dietary intake, weight status and health care resource use during the delivery period. Chapter Seven presents the findings from this observational cross-sectional study and the findings of the statistical and economic analyses described in Chapter Six.

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7.2 Published Manuscript

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MDPI

Article

Maternal Diet Quality, Body Mass Index and Resource Use in the Perinatal Period: An Observational Study

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Abstract: The impact of pre-pregnancy obesity and maternal diet quality on the use of healthcare resources during the perinatal period is underexplored. We assessed the effects of body mass index (BMI) and diet quality on the use of healthcare resources, to identify whether maternal diet quality may be effectively targeted to reduce antenatal heath care resource use, independent of women's BMI. Cross-sectional data and inpatient medical records were gathered from pregnant women attending publicly funded antenatal outpatient clinics in Newcastle, Australia. Dietary intake was self-reported, using the Australian Eating Survey (AES) food frequency questionnaire, and diet quality was quantified from the AES subscale, the Australian Recommended Food Score (ARFS). Mean pre-pregnancy BMI was 28.8 kg/m^2 (range: 14.7 kg/m^2–64 kg/m^2). Mean ARFS was 28.8 (SD = 13.1). Higher BMI was associated with increased odds of caesarean delivery; women in obese class II (35.0–39.9 kg/m^2) had significantly higher odds of caesarean delivery compared to women of normal weight, (OR = 2.13, 95% CI 1.03 to 4.39; $p = 0.04$). Using Australian Refined Diagnosis Related Group categories for birth admission, the average cost of the birth admission was $1348 more for women in the obese class II, and $1952 more for women in the obese class III, compared to women in a normal BMI weight class. Higher ARFS was associated with a small statistically significant reduction in maternal length of stay (RR = 1.24, 95% CI 1.00, 1.54; $p = 0.05$). There was no evidence of an association between ARFS and mode of delivery or "midwifery-in-the-home-visits".

Keywords: dietary assessment; pregnancy; nutrition; economic evaluation; directed acyclic graphs (DAGs); maternal and infant

1. Introduction

Obesity in pregnancy has become a major challenge for obstetric care in high-income countries [1]. Approximately 50% of women who become pregnant have overweight (body mass index (BMI) > 25 kg/m^2–30 kg /m^2) or obesity (BMI > 30 kg/m^2) [1], and the prevalence of obesity is rising [2]. High pre-pregnancy BMI has been strongly associated with excessive gestational weight gain [3], incidence of gestational diabetes mellitus, pre-eclampsia, pre-term delivery [3], large-for-gestational-age infants, caesarean delivery [4], miscarriage, antepartum stillbirth, complications at delivery and increased

postpartum weight retention [1,3,5]. Given the elevated risk to the mother and infant, obstetric and midwifery clinical practice guidelines recommend that healthcare facilities have well-defined pathways for the care of women with obesity, with increased care and monitoring relative to the antenatal care pathways of non-obese women [6,7]. This has resource use implications for the healthcare system. Clinical practice guidelines also provide "healthy eating in pregnancy" recommendations to address knowledge related to risk of diet-related conditions such as obesity [6]. However, there are no routine implementation interventions ensuring that clinical practice guideline recommendations for healthy eating in pregnancy are translated into practice [6]. This is a concern, as many Australian women fail to meet nationally recommended nutrient targets and do not appear to improve their diet quality when planning to become pregnant, or during pregnancy [8,9]. The economic implications of poor maternal nutrition, and its relationship with BMI and the use of healthcare resources (henceforth referred to as healthcare-resource use) is underexplored [10].

A recent World Health Organisation report, titled *Promoting Health and Preventing Disease: An Economic Case*, identified that improved maternal nutrition was as a potentially cost-effective target for health-promotion strategies aiming to improve maternal and infant health outcomes [11]. The volume of services and total expenditure on the delivery of maternity services means that relatively minor improvements in the cost per maternity patient could generate significant cost savings to public hospitals [12]. In particular, antenatal nutrition and gestational weight gain were identified as targets for health-promotion interventions aiming to improve maternal weight status and reduce demand on the healthcare system [13]. A recent study of infants born to mothers with overweight or obesity in the United Kingdom found that the usage rate for all healthcare services was significantly greater in infants born to mothers with obesity than infants born to mothers with healthy weight [14]. Infants born to mothers with obesity experienced a 39% higher rate of inpatient admissions and a 55% longer duration of inpatient stays, utilising, on average, 72% more resource costs [14]. Similarly, a cross-sectional comparative study of the short- and long-term effects of gestational diabetes mellitus (GDM) on healthcare costs found GDM was independently associated with an average additional cost of €817.60 (€2012) during pregnancy, due to additional delivery and neonatal care costs and an additional €680.50 in annual infant healthcare costs two to five years post-pregnancy [15]. A modelled economic evaluation exploring the short-term costs of maternal overweight, gestational diabetes and related macrosomia was conducted by Lenoir-Wijnkoop et al. [16] and found the average total additional costs for overweight was estimated to be $18,290 (USD) per pregnancy/delivery, which consists of an additional $13,047 for mothers with overweight and $5243 for their infants. Maternal diabetes was associated with an additional $15,593 per pregnancy/delivery, while foetal macrosomia was a significant risk factor for the development of obesity in childhood [16]. While overweight and obesity in women of child-bearing age and their offspring are of international concern, less attention has been paid to the economic consequences. At present, the cost of nutrition related perinatal health outcomes is unknown [10]. The range of potential targets for antenatal health promotion interventions, including nutrition interventions, is extensive, and healthcare-decision makers face growing pressure to optimize value, as well as quality, of healthcare [17].

Ensuring evidence-based healthcare is effective, as well as efficient and equitable, is critical if governments are to succeed in realising improved population health outcomes and contained per capita healthcare expenditure [18]. To identify technologies, interventions and models of care that provide the greatest value, healthcare providers are increasingly using health economic analyses to inform evidence-based decision-making [19]. Applied health economic evaluation informs evidence-based decision making by assisting healthcare-decision makers "identify, measure, and value activities with the necessary impact, scalability, and sustainability to optimize population health" [20]. High-quality cost and effectiveness data are a prerequisite for evidence-based decision-making. The highest cost of routine maternity care is incurred during the admission for birth (76%), followed by the non-admitted healthcare provided during the antenatal (17%) and postnatal (6%) periods [12]. However, the breakdown of these costs by population group is unknown. There is also insufficient evidence of the cost of nutrition

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interventions in pregnancy [10]. Given this absence of evidence, data on maternal dietary intake, obesity and their relationship with healthcare-resource use is needed to inform research, guidelines and decision makers of the economic impacts of current antenatal health promotion and clinical practice [21]. To address these evidence gaps, a cross-sectional population-based study was designed to quantify specific perinatal-healthcare-resource use associated with maternal weight status and diet quality in a sample of pregnant women attending a public hospital in New South Wales, Australia. The hypothesis was that high BMI and low diet quality would be associated with increased healthcare-resource use, with diet quality potentially having a direct effect, independent of BMI. The aims of this study were as follows:

i. Assess the diet quality of pregnant Australian women attending a public hospital antenatal clinic;
ii. Estimate the total effect of BMI, adjusted for diet quality, on healthcare-resource use during the delivery admission, including mode of delivery, length of stay, admission to intensive care and midwifery-in-the-home service;
iii. Estimate the total effect of maternal diet quality on healthcare-resource use during the delivery admission;
iv. Estimate the direct effect of maternal diet quality on healthcare-resource use during the delivery admission.

2. Materials and Methods

2.1. The Study

The study was an observational cross-sectional study in which patients attended public hospital antenatal outpatient clinics for routine antenatal care and were managed according to current clinical practice. The target sample size was 600 women with complete diet-quality scores, which were informed by investigator experience and feasibility. The study was advertised in the local newspaper and disseminated across university social media. Posters and fliers advertising the study were placed in the antenatal clinic, satellite clinics and birthing packs. Patients were also invited to complete the survey whilst in the waiting room, prior to their antenatal appointment, by trained volunteers.

All subjects gave their informed consent for inclusion before they participated in the study. The study was approved by the University of Newcastle Human Research Ethics Committee, Australia, study reference number H-2017-0101. Hunter Area Research Ethics Committee in August 2016 reference number HREC/16/HNE/189. The reporting adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

2.1.1. Study Population and Setting

Pregnant women aged 18 years or older, at 28–36 weeks of gestation (third trimester), and planning to deliver at the John Hunter Hospital were eligible to participate in the study. The time period of 28–36 weeks of gestation was selected, since the tool selected to measure diet, the Australia Eating Survey (AES), assesses intake over the previous three to six month, and we had previously shown significant correlations between dietary intake in early and late pregnancy [9]. The John Hunter Hospital, located in the Hunter New England Local Health District, New South Wales, Australia, is a large (550 bed) tertiary referral hospital, delivering around 4000 babies each year [22]. Participants were not excluded based on illnesses or known medical conditions.

2.1.2. The Survey

Self-reported demographic, health and diet quality data were collected at baseline (recruitment), and medical records data for the delivery admission were collected after discharge of mother and infant. The baseline survey consisted of four components: (1) consent and participant information statement; (2) participant information; (3) demographic data; and (4) the AES and could be completed

in about 25–35 min. All subjects gave their informed consent for inclusion before they participated in the study. Study data were collected and managed, using REDCap electronic data capture tools hosted at The University of Newcastle [23,24].

2.1.3. Study Recruitment

Trained volunteer research personnel (University students enrolled in the final years of a Bachelor of Nutrition and Dietetics) recruited study participants from the clinic between March 2018 and November 2018. All personnel undertook a mandatory workshop and further in-clinic training alongside a project officer. A brief and informative script was used by research personnel, to verbally screen women for eligibility, inform women of the survey content and purpose, and invite women to participate. Consenting participants then completed the survey on a tablet via the REDCap offline mobile application. Women at less than 28 weeks of gestation were invited via email to complete the survey when they reached 28 weeks' gestation. Women unable to complete the survey in the clinic due to fatigue, distractions (e.g., other children or feeling unwell) or being called to their appointment were emailed the remainder of their survey for later completion. An automated reminder email was sent seven days later, to all participants who had not finished the survey. All study participants had given birth by January 2019.

2.2. Statistical and Economic Analyses

The economic analysis took a healthcare provider's perspective to identify, measure and value outcomes associated with the provision of routine healthcare in the delivery period. The analysis excluded costs to patients and society. Since the time horizon for inclusion of relevant healthcare-resource use is set at less than 12 months, conversion or discounting of costs was not required [25].

2.2.1. Identification and Measurement of Exposure and Outcomes

Diet quality was quantified, using the previously validated Australian Recommended Food Score (ARFS) [26–28], derived from a subset of questions from the AES food frequency questionnaire for adults [26]. The AES is a 120-item semi-quantitative food-frequency questionnaire that was designed to assess usual dietary intake of individuals aged 18 years or older, based on a list of foods most commonly eaten by Australians. The AES has undergone comprehensive evaluation for validity and reliability, reported elsewhere [26]. The total ARFS score is calculated by summing the points for foods that are aligned with the core foods in the Australian Guide to Healthy Eating consumed at least weekly, with a total score ranging from 0 to 73 [26–28]. A higher score reflects greater alignment with recommendation in the Australian Dietary Guidelines.

Maternal clinical outcomes and healthcare-resource use from the delivery admission and associated home healthcare, Maternity Home Services, was collected from hospital databases using individual patient medical record numbers (MRN). Specific healthcare-resource use required for the management of maternal obesity was identified from the literature and reviewed by content experts (see Appendix A: Table A1). For the purpose of the current analyses, healthcare-resource use is defined as follows:

i. Mode of delivery: caesarean versus vaginal (natural, instrumental, breech, compound).
ii. Maternal length of stay: (count in days).
iii. Maternal admission to intensive care: (yes or no).
iv. Midwifery-in-the-home service utilisation: total number of follow-up care visits associated with maternal discharge post-delivery (count).

Establishing associations between an intervention target and an outcome is a mandatory precursor to economic evaluation [19]. For the current study, if associations between BMI or diet quality and mode of delivery or admission to intensive care were established, healthcare-resource use was then defined and costed, using the Australian Refined Diagnosis Related Group (AR-DRG) classification system for admitted acute episodes of care in Australian public and private hospitals. The AR-DRG codes classify

units of hospital output and group inpatient stays into clinically meaningful categories at similar levels of complexity (outputs) and consuming similar resources (inputs) [29]. Independent Hospital Pricing Authority national weighted activity unit (NWAU) calculators are used to estimate cost of care based on AR-DRG classifications. All costs were reported in 2020, Australian dollars ($AUD).

Mode of delivery and admission to intensive care have specific AR-DRG classifications. However, length of stay and midwifery-in-the-home care visits are non-clinical variables that do not have a diagnostic criterion. As such, length of stay and midwifery-in-the-home were reported in clinically relevant natural units, days and total number of visits, respectively.

2.2.2. Development and Use of Causal Diagrams

Many nutrition research studies aim to identify and quantify causal relationships between nutrition and health outcomes [30]. The limitations of traditional methods for assessing associations in observational studies and inferring causality are widely recognised [31]. However, the use of experimental design in the antenatal period needs careful ethical and practical consideration [31]. In order to investigate causality, observational data must be interrogated carefully, with attention to the potential for known and unknown confounders and other biases [31]. Incorrect casual inferences are more likely to occur in observational studies than clinical trials, due to confounding bias [31]. A common way to control for confounding bias in an observational study is to include confounders as covariates in a regression model; however, careful consideration of which variables should be adjusted for is required [30]. Adjustment is needed to ensure that the effect estimate for the exposure of interest is unconfounded. It is commonly believed that it is necessary to control for all potential confounders and that adjusting for more confounders cannot worsen causal inference; however, the inclusion of unnecessary covariates, or over-adjustment, carries the risk of introducing unintended bias and reducing statistical power [32].

For the current study, there exist complex preconception processes influence maternal and infant health outcomes and healthcare-resource use, and these may also influence diet quality (see Appendix A: Table A1). To depict the presumed causal relationships between the exposure, outcome and potential confounding variables related to the exposure and/or outcome, directed acyclic graphs (DAGs) were developed, using existing evidence (listed in Appendix A: Table A1) and expert opinion. DAGitty, a browser-based environment for creating, editing and analysing causal diagrams (DAGs) [33], was used to create a DAG, to visually depict the direct or total effects of interest for each aim: Aims (ii), (iii) and (iv). The three DAGs are included in the Supplementary Materials, along with the DAGitty code to reproduce them and the potential minimum adjustment sets that were identified.

A facility of DAGitty is its analysis of the DAG and provision of candidate "minimum adjustment sets" for estimating unconfounded effects of interest. Each adjustment set is minimal in the sense that it is sufficient to remove confounding bias for the effect of interest and includes no unnecessary variables. The inclusion of unnecessary covariates can reduce efficiency or introduce unintended bias. For a given effect of interest, there are potentially multiple minimum adjustment sets, any one of which could be used. The identified adjustment sets for each aim are listed below:

- Aim (ii) adjustment set: maternal age, maternal education, parity and ARFS.
- Aim (iii) adjustment set: maternal education,
- Aim (iv) adjustment set: maternal age, maternal education and BMI.

2.2.3. Statistical Methods

For Aim (i), the diet quality of pregnant Australian women attending a public hospital antenatal outpatient clinic was measured by using a diet-quality index and reported as total ARFS score, using descriptive statistics (mean with standard deviation or median with range for continuous variables, and frequency with percent for categorical variables). For estimating the effects in Aims (ii), (iii) and (iv), regression models were fitted within a generalized linear modelling (GLM) framework, with response distribution and link function as appropriate for each response.

Caesarean delivery was modelled by using logistic regression, assuming a binomial response distribution (for caesarean versus vaginal birth), and using the logit link function. Logistic models were estimated with Firth's penalised Maximum Likelihood [34], to reduce bias in parameter estimates due to data sparsity involving some response/explanatory variable combinations. Maternal length of stay and number of midwifery in the home visits were modelled as count responses, using Poisson regression with the log link function. Overdispersion was assessed by using hypothesis tests for the dispersion parameter. The proportion of participants admitted to higher-level care (0.6%) was too rare to perform regression analyses for this outcome.

During the modelling process, fit statistics were examined, to assess whether categorical variables could be simplified by combining categories. Based on the Akaike Information Criterion (AIC) and Likelihood Ratio Test (LRT), maternal education was reduced from seven categories to a binary variable (university versus not), and parity was reduced from a count variable to a binary variable indicating primiparous (parity = 0) versus not (parity > 0). We also considered reducing the number of BMI categories; however, based on an increased AIC and significant LRT, the six-level variable was retained. ARFS was rescaled (into quintiles) to aid interpretation of effect estimates. The validity of using ARFS quintiles has been reported elsewhere [28].

Results are reported as exponentiated parameter estimates with 95% Wald confidence intervals accompanied by *p*-values from Wald tests. Statistical significance was declared at the conventional 0.05 level, to two decimal places for all analyses. Data manipulation and statistical analyses were performed by using SAS 9.4 (SAS Institute, Cary, NC, USA)™ software.

3. Results

3.1. Study Recruitment

A total of 1117 individuals commenced the survey (see Figure 1). Of these, two withdrew during survey completion. A total of 148 did not consent to participate or partially completed the consent questions, and 61 participants did not meet the eligibility criteria. A total of 670 consenting participants were eligible to participate and were linked to medical records data.

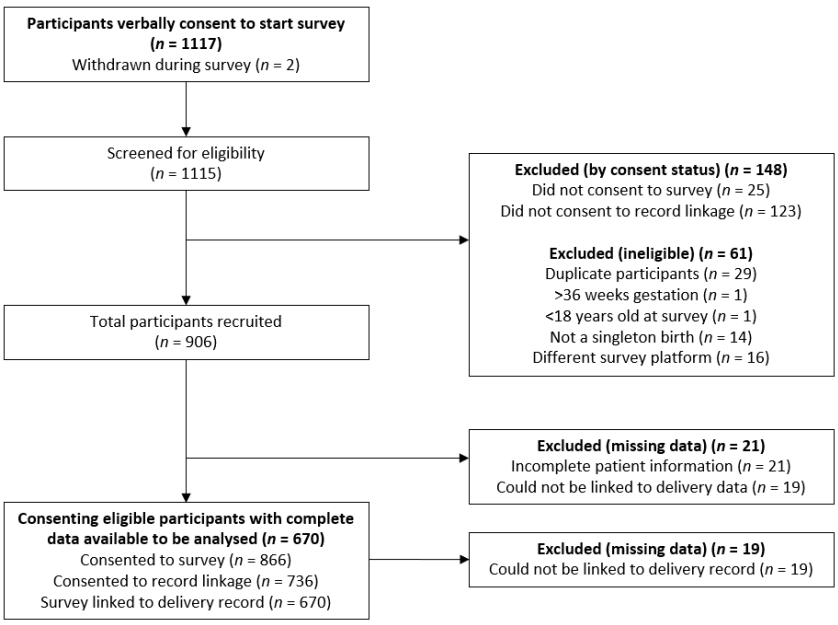

Figure 1. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) flow diagram of participant inclusion and exclusion.

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3.2. Participant Demographics

The mean age of participants was 30 years (range: 18.4–53.0), and the mean gestation length at time of survey was 32 weeks. Most participants were born in Australia (90%) and spoke English at home (93%). A total of 6.8% of participants identified as Aboriginal or Torres Strait Islander. A total of 85% of participants were married or in a de facto relationship, 11% were single mothers and 3.3% were divorced or separated. The most frequent level of educational attainment was ≤year 12 (or equivalent) level of education (37.1%). The most frequent annual household income category was ≥$104,000 (27%), and a further 25% of participants reported incomes of $65,000 to $104,000. The mean pre-pregnancy BMI was 28.8 kg/m^2 (range: 14.7 kg/m^2–64 kg/m^2), with 59% of participants having overweight or obesity, 37% having normal weight and 4.5% having underweight. Just over half (54%) of participants said they had received pregnancy diet advice from a health professional during the current pregnancy. Table 1 summarises study participant demographic and health data.

Table 1. Summary of study participant demographic and health data.

Participant Demographic and Health Data		
Characteristic	**Statistic or Class**	**Total (*N* = 670)**
Age at survey	mean (SD)	30.3 (5.5)
	median (min, max)	30.1 (18.4, 53.0)
Aboriginal or Torres Strait Islander	No	600 (93%)
	Yes	44 (6.8%)
Born in Australia	No	62 (9.6%)
	Yes	581 (90%)
Marital status	Married/de facto	548 (85%)
	Divorced/separated	21 (3.3%)
	Single	73 (11%)
Language spoken at home	English only	598 (93%)
	Other	44 (6.9%)
Highest educational qualification	No formal qualifications	20 (3.1%)
	Year 10 or equivalent	107 (17%)
	Year 12 or equivalent	111 (17%)
	Trade/Apprenticeship	29 (4.5%)
	Certificate/Diploma	176 (27%)
	University undergraduate	151 (23%)
	University postgraduate	50 (7.8%)
Annual household income	Less than $20,800	32 (5.1%)
	$20,800 to less than $41,600	44 (7.0%)
	$41,600 to less than $65,000	68 (11%)
	$65,000 to less than $104,000	158 (25%)
	$104,000 or more	172 (27%)
	Not provided	153 (24%)
Weeks of gestation at survey	mean (SD)	32 (3)
	median (min, max)	31 (28, 36)

Table 1. *Cont.*

Participant Demographic and Health Data		
Characteristic	**Statistic or Class**	**Total (*N* = 670)**
Received pregnancy diet advice from health professional	Yes	325 (54%)
	No	263 (44%)
	Unsure	15 (2.5%)
Pre-pregnancy body mass index (BMI) measured	mean (SD)	28.8 (8.3)
	median (min, max)	26.8 (14.7, 64.0)
	Underweight (<18.5 kg/m^2)	30 (4.5%)
	Normal (18.5–24.9 kg/m^2)	247 (37%)
	Overweight (25.0–29.9 kg/m^2)	139 (21%)
	Obese Class I (30.0–34.9 kg/m^2)	116 (17%)
	Obese Class II (35.0–39.9 kg/m^2)	64 (9.6%)
	Obese class III (≥40 kg/m^2)	74 (11%)
Number ANC visits	mean (SD)	12.1 (5.3)
	median (min, max)	11.0 (1.0, 40.0)
Alcohol risk score	mean (SD)	0.1 (0.5)
	median (min, max)	0.0 (0.0, 9.0)
Number term pregnancies	mean (SD)	1.3 (1.1)
	median (min, max)	1.0 (0.0, 8.0)
Number preterm pregnancies	mean (SD)	0.1 (0.4)
	median (min, max)	0.0 (0.0, 3.0)
Number living children	mean (SD)	1.3 (1.1)
	median (min, max)	1.0 (0.0, 10.0)
History of endocrine disease	No	534 (80%)
	Yes	136 (20%)
History of hypertension	No	606 (90%)
	Yes	64 (9.6%)
Maternal risk factor—diabetes	No	488 (73%)
	Yes	182 (27%)
Maternal risk factor—hypertension	No	607 (91%)
	Yes	63 (9.4%)
Maternal risk factor—anaemia	No	448 (67%)
	Yes	222 (33%)
Maternal risk factor—smoke during pregnancy	No	568 (85%)
	Yes	102 (15%)

3.3. Aim (i): Diet Quality of Pregnant Women

Diet quality was assessed using the ARFS, with a mean ARFS of 28.8 (SD 13.1) points. The mean ARFS for those with a pre-pregnancy BMI in the normal weight category was 31.2 (SD 13.1). The mean ARFS was lower for women outside the normal BMI category, and ranged from 27.1 to 28.3 points (Table 2).

Table 2. Maternal-diet quality, measured using the Australian Recommended Food Score (ARFS), and specific healthcare-resource use by BMI category (N = 670).

Characteristic	Statistic or Class	Underweight (n = 30)	Normal (n = 247)	Overweight (n = 139)	Obese Class I (n = 116)	Obese Class II (n = 64)	Obese Class III (n = 74)
Diet quality (ARFS)	mean (SD)	27.2 (13.8)	31.2 (13.1)	27.2 (14.3)	27.1 (12.7)	28.3 (9.8)	28.2 (12.9)
	median (min, max)	28.0 (4.0, 56.0)	34.0 (1.0, 54.0)	30.0 (1.0, 50.0)	29.0 (2.0, 52.0)	29.5 (9.0, 46.0)	29.0 (1.0, 51.0)
Maternal length of stay (days)	mean (SD)	1.6 (1.5)	1.9 (1.6)	2.1 (1.6)	2.2 (1.5)	2.2 (1.6)	2.2 (1.6)
	median (min, max)	1.0 (0.0, 5.0)	2.0 (0.0, 9.0)	2.0 (0.0, 7.0)	2.0 (0.0, 8.0)	2.0 (0.0, 9.0)	2.0 (0.0, 7.0)
Number of "midwifery-in-the-home" visits	mean (SD)	1.8 (1.0)	1.6 (0.9)	1.6 (0.9)	1.6 (0.9)	1.6 (0.7)	1.5 (0.8)
	median (min, max)	2.0 (0.0, 5.0)	2.0 (0.0, 6.0)	2.0 (0.0, 4.0)	2.0 (0.0, 4.0)	2.0 (0.0, 3.0)	2.0 (0.0, 3.0)
Delivery mode	Vaginal birth	21 (70%)	167 (68%)	79 (57%)	65 (56%)	33 (52%)	36 (49%)
	Caesarean section	9 (30%)	80 (32%)	60 (43%)	51 (44%)	31 (48%)	38 (51%)

3.4. Aim (ii): Estimate of the Total Effect of BMI on Healthcare-Resource Use

Results from the analyses investigating the total effect of BMI on specific healthcare-resource use are shown in Table 4. The mean gestational age at birth was 38.4 weeks (SD 1.4 weeks), and 93% of infants were delivered at term (>37 weeks). The most common birth type was normal vaginal birth (50%), a further 40% of the babies were delivered via caesarean section and 10% had an abnormal vaginal birth (including instrumental, breech and compound birth). Four women required higher level care or were admitted to intensive care (refer to Table 3).

Table 3. Participant demographics and healthcare-resource use summary statistics.

Characteristic	Statistic or Class	Total (N = 670)
Infant birthweight (grams)	mean (SD)	3359.4 (515.1)
	median (min, max)	3390.0 (1450.0, 4830.0)
Gestational age at birth (weeks)	mean (SD)	38.4 (1.4)
	median (min, max)	38.0 (31.0, 41.0)
Maternal length of stay (days)	mean (SD)	2.1 (1.6)
	median (min, max)	2.0 (0.0, 9.0)
Mode of delivery	Normal vaginal birth	334 (50%)
	Caesarean section	269 (40%)
	Abnormal vaginal birth	67 (10%)
Pre-term birth (<37 weeks)	No	626 (93%)
	Yes	44 (6.6%)
Gender of infant	Male	326 (49%)
	Female	344 (51%)
Birthweight category	Low birth weight (<2500 g)	35 (5.2%)
	Normal range	568 (85%)
	Macrosomia (>4000 g)	67 (10%)
Midwifery-in-the-home care visits	mean (SD)	1.6 (0.9)
	median (min, max)	2.0 (0.0, 6.0)
Maternal admission to higher level care (intensive care)	No	664 (99%)
	Yes	4 (0.6%)

The mean maternal postnatal length of stay was 2.1 (SD 1.6) days, and the median was 2.0 (range: 0.0, 9.0), inclusive of the four women admitted to intensive care. The mean length of stay for women in the normal BMI weight class was 1.9 (SD 1.6) days and was slightly lower in the underweight BMI category, at 1.6 (SD 1.5) days. Amongst overweight and obese women, the mean length of stay was 2.1 (SD 1.6) in the overweight class and 2.2 (SD 1.6) for women in the BMI category obese class III. The mean number of midwifery-in-the-home care visits was 1.6 (SD 0.9), and the median was 2.0 (range: 0.0, 6.0). The mean number of midwifery-in-the-home care visits for women in the overweight category was 1.6 (SD 0.9), and the range did not vary substantially across pre-pregnancy BMI categories obese class I–III (1.55–1.5).

Women in the overweight and obese categories had increased odds of caesarean delivery, relative to women in the normal BMI category. The magnitude of this effect increased with increasing BMI category. The association for obese class II (35.0–39.9 kg/m^2) reached 0.05 significance (OR = 2.13, 95% CI 1.03 to 4.39; $p = 0.04$), indicating that women in obese class II had about double the odds of caesarean delivery, compared to women with normal BMI (Table 4).

Table 4. Estimates of the effect of diet quality and pre-pregnancy BMI on healthcare-resource use.

	Caesarean Delivery		Maternal Length of Stay		MITH Visits	
	Odds Ratio (95% CI)	***p*-Value**	**Rate Ratio (95% CI)**	***p*-Value**	**Rate Ratio (95% CI)**	***p*-Value**
Aim (ii)—total effect of BMI *						
Underweight	0.58 (0.16 to 2.08)	0.40	0.78 (0.49 to 1.23)	0.28	0.95 (0.63 to 1.44)	0.82
Normal	(ref)		(ref)		(ref)	
Overweight	1.57 (0.91 to 2.71)	0.11	1.04 (0.86 to 1.26)	0.71	0.95 (0.78 to 1.18)	0.66
Obese Class I	1.18 (0.65 to 2.16)	0.58	1.07 (0.87 to 1.32)	0.51	0.89 (0.70 to 1.12)	0.31
Obese Class II	2.13 (1.03 to 4.39)	0.04	1.11 (0.87 to 1.42)	0.41	0.99 (0.75 to 1.30)	0.92
Obese class III	1.92 (0.98 to 3.73)	0.06	1.10 (0.87 to 1.39)	0.41	0.90 (0.69 to 1.16)	0.41
Aim (iii)—total effect of ARFS **						
Quintile 1	1.08 (0.64 to 1.85)	0.77	1.20 (1.00 to 1.44)	0.05	1.02 (0.83 to 1.26)	0.85
Quintile 2	1.16 (0.69 to 1.96)	0.58	1.10 (0.91 to 1.32)	0.33	1.09 (0.89 to 1.34)	0.41
Quintile 3	0.72 (0.42 to 1.24)	0.24	1.05 (0.87 to 1.27)	0.60	1.01 (0.82 to 1.25)	0.91
Quintile 4	0.93 (0.54 to 1.62)	0.80	1.12 (0.92 to 1.35)	0.26	0.99 (0.79 to 1.22)	0.90
Quintile 5	(ref)		(ref)		(ref)	
Aim (iv)—direct effect of ARFS ***						
Quintile 1	1.23 (0.71 to 2.16)	0.46	1.27 (1.05 to 1.53)	0.01	1.00 (0.81 to 1.24)	0.99
Quintile 2	1.25 (0.72 to 2.17)	0.43	1.14 (0.94 to 1.37)	0.19	1.07 (0.87 to 1.32)	0.52
Quintile 3	0.74 (0.42 to 1.29)	0.29	1.07 (0.88 to 1.29)	0.50	1.00 (0.81 to 1.24)	0.96
Quintile 4	0.97 (0.55 to 1.71)	0.92	1.13 (0.93 to 1.37)	0.21	0.98 (0.78 to 1.21)	0.83
Quintile 1	(ref)	.	(ref)	.	(ref)	.

* Adjusted for ARFS, maternal age, maternal university education (yes versus no) and primiparous (yes versus no). ** Adjusted for maternal university education (yes versus no). *** Adjusted for BMI, maternal age and maternal university education (yes versus no). (ref): reference category used.

The association was very similar for women in obese class III, who also had about a two-fold higher odds of caesarean delivery (OR 1.92; 95% CI 0.98 to 3.73; $p = 0.056$).

A total of 666 patients had AR-DRG classification for their birth admission. Of these, there were 242 (99%) women in the normal weight category and 62 (98%) women in obese class II and III.

The AR-DRG cost for birth admission did not vary by length of stay or maternal age. In general, there was a higher rate of complex deliveries among women with obesity. Among women in the normal BMI category, 32% had a caesarean delivery and 11% had a birth classified as having "major complexity". Rates were higher for women in obese class II, with 50% having caesarean delivery and 18% having a "major complexity" birth. Rates were slightly higher again for women in obese class III, with 53% having caesarean delivery and 25% having a "major complexity" birth.

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We have reported and compared costs of delivery for women with normal BMI (reference) and women in obese class II and obese class III, due to high similarity of effect estimates and likely clinical importance of results for both obesity classes (see Table 5). The average cost per patient for women in normal weight was $7962. The average cost per patient for women in obese class II was $9309. The incremental difference in admitted patient cost was $1348. That is, in this sample, the birth admission for women in BMI category Obese class II cost $1348 more than women in normal weight class. The average cost of the delivery admission for women in obese class III was $9914, which was $1952 more than for women in the normal weight class and $605 more than women in obese class II.

Table 5. Maternal birth admission Australian Refined Diagnosis Related Group (AR-DRG) classification (with description and price ($AUD, 2020) and mean cost per patient for study participants in BMI categories normal and obese class II and III.

AR-DRG			Normal		Obese Class II		Obese Class III	
Code	**Description**	**NWAU Cost**	***n* * = 242**	**Cost ($) ****	***n* = 62**	**Cost ($) ****	***n* = 72**	**Cost ($) ****
O01A	Caesarean delivery, major complexity	$17,170	5	$85,850	2	$34,340	10	$171,700
O01B	Caesarean delivery, intermediate complexity	$12,310	39	$480,090	14	$172,340	15	$184,650
O01C	Caesarean delivery, minor complexity	$10,074	34	$342,516	15	$151,110	13	$130,962
O02A	Vaginal delivery with operating room procedures, major complexity	$12,691	3	$38,073	0	$0	0	$0
O02B	Vaginal delivery with operating room procedures, minor complexity	$9119	6	$54,714	3	$27,357	0	$0
O60A	Vaginal delivery, major complexity	$8967	19	$170,373	9	$80,703	8	$71,736
O60B	Vaginal delivery, intermediate complexity	$6206	82	$508,892	15	$93,090	22	$136,532
O60C	Vaginal delivery, minor complexity	$4560	54	$246,240	4	$18,240	4	$18,240
Cost per patient ***				**$7962**		**$9309**		**$9914**

* Number of participants with AR-DRG available. ** Cost ($) = number of participants × NWAU cost (by AR-DRG classification). *** Cost ($) per total number of patients, by BMI category. NWAU: National Weighted Activity Unit.

3.5. Aim (iii): Estimate of the Total Effect of Maternal Diet Quality on Healthcare-Resource Use

Results from the analyses investigating the total effect of maternal diet quality on healthcare-resource use during the delivery admission are shown in Table 4. There were no significant effects of ARFS on mode of delivery or the number of midwifery-in-the-home visits a patient required. Women in ARFS Quintile 1 had a 20% increase in the mean length of stay relative to Quintile 5 (RR 1.20; 95% CI 1.00 to 1.44; $p = 0.05$). That is, women with poor diet quality had an increase in average length of stay, when compared to women with the highest level of diet quality.

3.6. Aim (iv): Estimate of the Direct Effect of Maternal Diet Quality on Healthcare-Resource Use

Results from the regression analyses investigating the direct effect of maternal diet quality on healthcare-resource use during the delivery admission are shown in Table 4. Women in ARFS Quintile 1 had a 27% increase in the mean length of stay relative to Quintile 5 (RR 1.27; 95% CI 1.05 to 1.53; $p = 0.01$). That is, independent of a woman's BMI, those with an ARFS score in Quintile 1 (lowest diet quality) had a 27% increase in average length of stay when compared to women with an ARFS score in Quintile 5 (highest diet quality). There was no significant direct effect of ARFS on caesarean delivery or midwifery in the home visits.

Given there was no statistically significant association between ARFS and mode of delivery, admission to intensive care and midwifery in the home visits, analysis of the economic impact of ARFS on these outcomes was not conducted.

4. Discussion

This observational study sought to quantify specific perinatal-healthcare-resource use associated with maternal weight status and diet quality, in a sample of pregnant women attending a public hospital in NSW, Australia. It was hypothesized that high BMI and low diet quality would be associated with increased healthcare-resource use, with diet quality potentially having a direct effect, independent of BMI. This study found the odds of caesarean delivery was about two-fold higher for women in obese class II than for women of normal weight. In this sample, the effect size for the association between BMI category obese class III was very similar, but did not quite reach the nominal 0.05 significance threshold (OR 1.92; 95% CI 0.98 to 3.73; $p = 0.056$). With consideration for the real-world impacts of BMI on healthcare-resource use, given similarity of the effect sizes, in a larger sample size, both obese class II and III would likely have achieved statistical significance. Based on these findings and evidence-based guideline recommendations for increased routine monitoring for women classified as obese [6], the impact of both obese class II and obese class III on caesarean delivery is expected to be clinically important. As such, the impact of both obese class II and III on average inpatient cost was explored.

AR-DRG classifications include an estimate of case complexity, which is a classification system within the AR-DRG classifications, to "better explain the variation in costs occurring in the admitted patient data within the ARDRG classification" [35]. There were higher rates of caesarean delivery and cases with "major complexities" for women in BMI category obese class II and III, relative to women with a BMI in the normal-weight category. The birth admission for women in BMI category obese class II cost $1348 more than women in normal-weight class. The average cost of the birth admission for women in obese class III was $1952 more than for women in the normal-weight class and $605 more than for women in obese class II. Within the perinatal period alone, small improvements in maternal pre-pregnancy BMI could deliver substantive economic benefits to the healthcare system and community. Aside from the economic impact, obesity and increased case complexity have procedural complications for clinicians and the healthcare system. For example, complications from anaesthesia are higher in obese patients compared to normal weight patients [36]. There is increased risk of incorrectly placing an epidural in obese patients as the distance to the epidural space is greater with increased BMI [36,37], risk of difficult intubation is increased in obese patients, monitoring and positioning obese patients under anaesthesia can also pose specific challenges [36]. Obesity is also associated with an increased risk of maternal mortality and anaesthesia-related maternal mortality [37]. From a midwife's perspective, a 2011 study of midwives and other health professionals caring for obese childbearing women in NSW, Australia, found midwives were concerned about the rapid impact of the obesity epidemic on maternity services and that study participants felt increased pressure in the management of obese pregnant women and the complications associated with their BMI [38]. Pre-pregnancy public health interventions to reduce maternal pre-pregnancy BMI may prevent the onset or mitigate complications in the delivery period and reduce the obesity related risks to mothers, clinicians and the healthcare system.

This study also found that diet quality had a direct effect on maternal length of stay, independent of BMI. Women in ARFS Quintile 1 had a 27% increase in the mean length of stay relative to Quintile 5 (RR 1.27; 95% CI 1.05 to 1.53; $p = 0.01$). That is, independent of a woman's BMI, those with an ARFS score in Quintile 1 (lowest diet quality) had a 27% increase in average length of stay when compared to women with an ARFS score in Quintile 5 (highest diet quality). The method in which diet quality acts on length of stay is also unknown. The investment required to improve maternal diet quality is unknown [10]. Further investigation is required, given that poor dietary patterns are common among this population [39] and that current systematic review indicate interventions to improve maternal

BMI and pregnancy outcome show inconsistent finding in regard to cost-effectiveness [40,41]. This study found no significant association between pre-pregnancy BMI and maternal length of stay or midwifery-in-the-home care visits. Analyses also showed that maternal diet quality had no direct effect on caesarean delivery or midwifery-in-the-home care visits. Greater understanding of the economic impact of maternal-health behaviours and specific dietary components on healthcare-resource use and health outcomes is warranted [10].

Strengths and Limitations

The limitations of traditional methods for assessing associations in observational studies and inferring causality are widely recognised [31]. In order to investigate causality, observational data must be interrogated carefully, with attention to the potential for known and unknown confounders and other biases [31]. Use of DAGs in observational nutrition research allows for stronger causal inferences, as compared to conventional statistical adjustments alone. A strength of the current study was the extensive DAG development process informed by the relevant literature, and expert opinion to inform assumptions underpinning the statistical and economic models.

This observational study was conducted in the John Hunter Hospital, NSW, where admitted inpatient-cost data are not stored in administrative hospital datasets and, hence, were outside the data available for this analysis. In the absence of individual patient-cost data, the AR-DRG classification was used as a proxy for admitted-inpatient costs [29]. For the purpose of future research, individual patient-cost data may provide greater specificity regarding the association between patient outcomes, resource use and cost. The John Hunter Hospital antenatal outpatient clinic services high-risk patients requiring ongoing management of GDM, pre-eclampsia, those who have had previous adverse outcomes, women with babies in breech position or those who are attending the clinic drug and alcohol services or Indigenous health services. A limitation of the current study is that the sample of women is expected to have worse health outcomes and thus higher healthcare-resource use compared to the broader population of pregnant Australian women. The current analysis also did not allow for data linkage across all service providers. The John Hunter Hospital has five satellite antenatal clinics that patients can attend, but radiology and pathology can be performed at the hospital, in public or private clinics, and patients may attend private general practitioners, specialists and care providers throughout the antenatal period. Data for health service provision prior to delivery were also unavailable. The inherent recall bias associated with retrospective self-report surveys is recognised as a limitation. Further, the AES food frequency questionnaire, although previously used in pregnancy [42], has not been validated in this population group, and, therefore, the findings of this study need to be interpreted in this context.

5. Conclusions

The current study aimed to quantify specific perinatal-healthcare-resource use associated with maternal weight status and diet quality, in a sample of pregnant women attending a public hospital in New South Wales, Australia. This study found that the odds of caesarean delivery more than doubled for those in obese class II relative to normal weight women, with pre-pregnancy BMI positively associated with an increased risk of caesarean delivery. On average, the birth admission for women in BMI category obese class II costs $1348 more than women in normal weight class, and women in obese class III cost $1952 more than women in the normal weight class. Both obese classes II and III had a higher incidence of caesarean section and complex cases, compared to women in the normal weight class. Our analyses showed that, independent of a woman's BMI, those with an ARFS score in Quintile 1 (lowest diet quality) had a 27% increase in average length of stay when compared to women with an ARFS score in Quintile 5 (highest diet quality). Maternal-diet quality had no direct effect on caesarean delivery or midwifery-in-the-home care visits. Poor dietary patterns are common during pregnancy [39]; thus, interventions to improve maternal BMI and diet quality could deliver substantive economic benefits to the healthcare system and community.

Supplementary Materials: The following are available online at http://www.mdpi.com/2072-6643/12/11/3532/s1, Identifiable healthcare data were used in this study and not appropriate for circulation.

Author Contributions: Z.S., C.C. and M.R. developed the original research idea. Z.S. developed the recruitment strategy, managed the recruitment process and collection of trial data. S.D., P.R., N.W. and E.H. provided expert statistical and economic advice and content. C.C. and M.R. provided nutrition and dietary assessment expertise. N.W. and E.H. conducted the statistical analyses. Z.S., N.W. and E.H. wrote the manuscript, with the support and guidance of all authors. All authors have read and agreed to the published version of the manuscript.

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Appendix A

Table A1. List of characteristics collected via patient medical records and evidence of association on preconception process influencing health outcomes and healthcare-resource use.

Study Data	Description	Preconception Process
Demographics		
Maternal age	Age in years	- Increased incidence of maternal hypertension and gestational diabetes mellitus, non-elective caesarean delivery and instrumental delivery and preterm delivery and neonatal intensive care admission among mothers of advanced maternal age [43–45]. - Mothers of advanced maternal age have increased pregnancy risk when compared to younger mothers [43,46].
Education	Maternal education level acquired: high school, TAFE, tertiary education, post-graduate	- Lower-educated women are more likely to smoke, have passive smoking exposure, have low health control beliefs, and not attend antenatal classes or take supplements [47]. - Low educational attainment has been associated with higher rates of pre-pregnancy obesity [48].
Partner status	Relationship status: single, married, de facto, divorced	- Partner (marital) status has been used previously in antenatal diet quality studies [8,49], serving as a participant specific metric for socioeconomic advantage and disadvantage [50].
Insurance status	Health insurance status: no insurance, private health insurance, private insurance without obstetrics	- The inter-sector difference in obstetric practice [51,52] and maternal and infant health outcomes are well documented [53,54]. - Studies have shown increased rates of caesarean section and pre-labour caesarean section amongst patients with private health insurance [51,55].
Lifestyle		
Cigarette smoking	Did the mother smoke nicotine during this pregnancy?	- Antenatal smoking is strongly correlated with preterm birth, low birth weight and adverse infant outcomes [56].
Alcohol consumption	AUDIT-C score	- Antenatal alcohol and substance use are strongly correlated with adverse maternal and infant health outcomes [57,58]. - Older women were significantly more likely than younger women to report drinking while pregnant, but equally likely to reduce their consumption when they became pregnant as their younger counterparts [59].
Diet Quality	Maternal ARFS during current pregnancy	- Suboptimal eating patterns during pregnancy contribute to EGWG, gestational hypertension, pre-eclampsia, GDM, pre-term birth, low and high birth weight, birth defects and still birth [8,9].

Table A1. *Cont.*

Study Data	Description	Preconception Process
Previous Medical History		
Body mass index	At booking visit (20 weeks gestation)	- Clinical practice guidelines recommend that healthcare facilities have well-defined pathways for the care of pregnant obese women, with increased monitoring and management in comparison to the pathways for the care of healthy-weight women [7]. - High pre-pregnancy BMI has been shown to be strongly associated with EGWG [3] and increased resource use in the antenatal period [3,60,61]. - There is a linear trend between maternal pre-pregnancy BMI and risk for both elective and unplanned caesarean section [62,63].
Previous mode of delivery	Total number of previous caesarean sections	- Attempting vaginal birth after a previous caesarean section, or repeat elective caesarean section, carries additional risks to the mother and baby [64].
Parity	Number of previous pregnancies	- Parity has been associated with advanced maternal age, sociodemographic status and educational attainment [45].
Assisted reproductive therapy required? (ART)	Did the mother require ART or IVF to conceive this pregnancy?	- Perinatal risks that may be associated with assisted reproductive technology (ART) and ovulation induction include multifetal gestations, prematurity, low birth weight, small for gestational age, perinatal mortality, caesarean delivery, placenta previa, abruptio placentae, preeclampsia and birth defects [65].
Diabetes	Has the mother been diagnosed with type I or type II diabetes?	- Patients with pre-gestational diabetes (types 1 and 2) are more prone to higher rates of pre-eclampsia, prematurity and caesarean section. - Pregnancy may accelerate maternal and infant complications of diabetes [66].
Recent Antenatal Period		
Weight change	Did the patient gain an appropriate amount of weight during pregnancy?	- EGWG are risk factors for GDM, pregnancy-induced hypertension and pre-eclampsia, venous thrombo-embolism, labour induction and caesarean delivery [67].
Hypertensive disorders	Was the mother diagnosed with hypertensive disorders?	- High maternal-diet quality may reduce the risk of gestational hypertension for the mother [49]. - Current clinical guidelines for management of hypertensive disorders in pregnancy recommend diagnosis of hypertensive disorders "should lead to increased observation and vigilance" [68].

Table A1. *Cont.*

Study Data	Description	Preconception Process
Gestational diabetes:	Was the mother diagnosed with GDM?	- Prevalence is affected by maternal factors such as history of previous GDM, ethnicity, advanced maternal age, family history of diabetes, pre-pregnancy weight and EGWG [66]. - Potential maternal complications during pregnancy and delivery include pre-eclampsia and higher rates of caesarean delivery, birth injury and postpartum haemorrhage [66]. - For the neonate, complications can include macrosomia (large for gestational age) growth restriction, birth injuries, respiratory distress, hypoglycaemia and jaundice [66]. - GDM is diagnosed at any time throughout the pregnancy, and management includes a prescriptive diet which is expected to be different from the mother's diet pre-GDM diagnosis [69].
Plurality	Number of infants born (2, 3, 4, . . . , x)	- Guidelines advise of additional care that should be offered to women with twin and triplet pregnancies above that are routinely offered to all women during pregnancy [70].
Gestation	Number of weeks at delivery	- Gestational age at birth is an important predictor or infant mortality and length of stay [71].
Infant birth weight	Infant birth weight in grams	- Birthweight is a key indicator of infant health and a principal determinant of infant mortality [50]. - Factors that contribute to low birthweight include extremes of maternal age, illness during pregnancy, low socioeconomic position, multiple pregnancy, maternal history of spontaneous abortion, harmful behaviours such as smoking or excessive alcohol consumption, poor nutrition during pregnancy and poor antenatal care [50]. - Low birth weight is a risk factor for inadequate foetal development and amplified risk of chronic disease throughout life [50].
Mode of delivery	Caesarean; surgical intervention (including internal manoeuvres); vaginal birth	- It is considered self-evident that the cost of caesarean delivery is more expensive than natural birth. - Even amongst similar cases, the charges associated with mode of delivery vary widely [72]
Mother length of stay	Mothers length of stay in days	- It is considered self-evident that length of stay and admission to intensive care accrues higher healthcare-resource use and total cost of admission than those without. - Neonatal service levels range from no planned service, Level 1 to Level 6 [73]. Level 6 neonatal care is provided in specialist children's hospitals where neonatal surgery and complex genetic and metabolic services are located. It is considered self-evident that Level 6 care will accrue higher costs than Level 1 care, due to the complexity of care provided.
Infant length of stay	Infant length of stay in days	
Infant admission to nursery	Neonatal intensive care admission	

ART, Assistive reproductive therapy; AUDIT-C, Alcohol Use Disorders Identification Test; EGWG, excessive gestational weight gain; GDM, gestational diabetes mellitus; TAFE, Technical and Further Education.

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Chapter 8

Summary of findings, discussion, and future research directions

8.1 Chapter Introduction

This chapter summarises and evaluates the results of this doctoral research with consideration of the broader research context. The first section recaps the primary aims and objectives of the research undertaken to address them. The second section summarises the key findings from the individual studies and associated learning's in methods development. The third section provides an interpretation of the research findings in the broader context of health and medical research, considers their implications, limitations, and offers future directions for related research.

8.2 Thesis aims and objectives

The research question of this thesis was: what is the economic impact of improving the modifiable maternal health risk behaviours, alcohol and dietary intake, on health care resource use during the antenatal period? To address this question, the thesis aims were:

1. Identify and synthesize evidence regarding the costs and impacts of antenatal nutrition and alcohol interventions and their associated implementation strategies.
2. Assess the cost, cost-consequence, and cost-effectiveness of a multi-strategy practice change intervention in increasing antenatal care addressing the consumption of alcohol by pregnant women.
3. Assess the economic impact of maternal diet quality and weight status of pregnant women and their impact on resource use in the delivery period.

The review presented in Chapter Three identified a paucity of economic evidence regarding the cost and cost-effectiveness of antenatal nutrition and alcohol interventions and related investment in implementation. In response to this gap in the literature, the second aim was to examine the costs, consequences, and cost-effectiveness of an implementation intervention targeting maternal alcohol consumption in the antenatal period. Given the additional cost of managing and treating health conditions associated with maternal health risk behaviours, the third aim was to examine the economic impact of a specific health behaviour, dietary intake. The second and third aims were addressed via a program of work presented in multiple chapters of this thesis. For the second aim, an economic evaluation was designed and undertaken alongside a randomised controlled trial (RCT) of a multi-strategy practice change intervention to support antenatal care staff to provide a model of care that is consistent with clinical guideline recommendations for alcohol consumption in pregnancy. For the third aim, examining maternal dietary intake and health care resource use, an observational study was conducted – including recruitment of N=1119 pregnant participants – to measure maternal weight status and collect comprehensive data regarding dietary intake. These data were then used to examine the economic impact of maternal diet quality on resource use in the antenatal period.

8.3 Results: Summary of key findings in relation to the study questions

8.3.1 Chapter Three: A systematic review of economic evaluations of antenatal nutrition and alcohol interventions and their associated implementation interventions

In stark contrast with the wealth of epidemiological evidence on the adverse outcomes associated with poor diet, excess body weight, and alcohol consumption in pregnancy, little attention has been paid to quantifying the economic impact of these behaviours [52]. The first systematic review identified just 12 economic evaluations of nutrition and alcohol interventions in pregnancy since the year 2000. Of the identified studies, ten were economic evaluations of nutrition interventions and two were economic evaluations of alcohol interventions targeting pregnant women. There were notably few trial-based analyses (n=2) highlighting a scarcity of real world, prospectively, collected economic data available to inform policy and practice. The second systematic review presented in Chapter Three identified no economic evaluations of antenatal health promotion intervention implementation strategies.

Direct comparison between the results of the identified studies or meta-analysis was not feasible given significant study heterogeneity stemming from differences in the objectives, design, methods, and outcomes of included studies. None of the included studies considered the investment required to implement these interventions into routine practice. Although the prominence of translational research and implementation science in health services is increasing [109], the findings of this review highlighted that little attention has been paid to an important aspect of implementation practice: that implementation activity requires funding, and thus has a cost [109]. Most of the nutrition and alcohol interventions included in this review were found to be cost-effective or cost saving. However, the size of the investment in implementation required to translate these interventions into clinical practice remains unknown. This knowledge gap is a limitation for decision makers looking to adopt health promotion interventions based on efficiency and return on investment via reduced resource use and improved patient health outcomes.

8.3.2 Chapters Four and Five: Economic evaluation of a randomised, stepped-wedge controlled trial for practice change support to increase routine provision of antenatal care for maternal alcohol consumption

To our knowledge, the economic evaluation described in Chapters Four and Five represents the first study to estimate the cost, cost-consequence, and cost effectiveness of a practice change intervention in antenatal care. The intervention was delivered in three sectors within a geographically diverse local health district, the Hunter New England Local Health District (HNELHD)

(i.e. Hunter New England, Lower Mid North Coast and Peel), Australia. The resources invested to increase compliance with the guideline-based model of care were wholly additional to usual practice; as such, the intervention was found to be more effective and more costly than usual care. Specifically, the total cost of the practice change intervention across all three sectors was calculated to be $367,646, of which $40,871 (11%) were development costs and $326,774 (89%) ($AUD, 2019) were intervention delivery costs.

Of the total costs associated with the practice change intervention, the cost of health service staff labour time was the main cost driver for the intervention, comprising 70% of the total cost. The average cost of delivering the practice change intervention per eligible clinician was calculated to be $993 (range: $640–1928). The cost per woman who received all guideline elements of care was calculated to be $591 (range: $329–$940). Variation in the average cost per woman was associated with variation in the average number of women attending each antenatal outpatient clinic, per month between sectors.

The trial's primary efficacy outcome was the proportion of antenatal appointments for which women reported: (1) being assessed for alcohol consumption, (2) being provided with brief advice related to alcohol consumption during pregnancy, (3) receiving relevant care for addressing alcohol consumption during pregnancy, and (4) being assessed for alcohol consumption and receiving relevant care [26]. Based on this outcome, the estimated incremental cost-effectiveness ratio (ICER) per one percent increase in the proportion of women receiving all guideline elements was calculated to be $32,570 (95% CI: $32,566–$36,340). The incremental cost per one percent increase in the proportion of women receiving all guideline elements ranged from $15,951 (range: $13,109–$20,365) in Sector one and $5,618 (range: $4,261–$8,25) in Sector two. Assessing the downstream impact of this intervention on referral to services and uptake of available services was beyond the scope of the implementation intervention and economic evaluation.

8.3.3 Chapters Six and Seven: Diet quality and resource use in the delivery period: an observational study

Given the absence of economic evidence regarding maternal health behaviors in the local health district or Australia more broadly, a cross-sectional, observational study was designed and conducted to measure maternal dietary intake and resource use during the delivery period (defined as the period from admission to discharge for childbirth). Self-report dietary data and inpatient medical records were gathered and extracted for a total 670 pregnant women attending tertiary antenatal outpatient clinics in Newcastle, Australia.

The mean diet quality score of this sample was 28.8 (SD 13.1) points. Interpretation of the Australian Recommended Food Score (ARFS) is relative as diet quality indices are typically used for population-based studies where estimated average requirements are the standard measure. In comparison to existing literature, one recent study used the Australian Eating Survey (AES) to measure dietary intake amongst pregnant Indigenous Australian women and found the ARFS

was 28 (IQR: 21-36) [110]. Similar to the study in Chapter Eight, both studies report the ARFS of pregnant women is lower than that of the general population [111]. This contrasts the findings by Hure et al., that pregnant women and those who had given birth in the previous 12-months had marginally higher ARFS compared to 'other' women [23]. Hure et al. used the Dietary Questionnaire for Epidemiological Studies to calculate the ARFS, in comparison to the AES [23]. It is possible that the method of dietary assessment accounts for the variation in ARFS reported by Hure et al. and that reported in Chapter Seven. Alternatively, a recent systematic review and critical appraisal of diet quality indices identified and critically appraised all diet quality indices within Australia and New Zealand [112]. The appraisal reviewed indices based on dimensions of nutritional adequacy, moderation and balance, indicator selection, scoring criteria, and evaluation [112]. This review found the ARFS is the most frequently used diet quality index, however recommend the Dietary Guideline Index, Dietary Guideline Index-2013, Total Diet Score, Healthy Eating Index for Australian Adults-2013, and Aussie-Diet Quality Index as preferable indices for use in Australian adult populations [112].

In assessments of the relationship between maternal diet and maternal weight, the mean ARFS for those with a pre-pregnancy body mass index (BMI) in the normal weight category was found to be slightly higher (31.2 (SD 13.1)) than the mean ARFS for women outside (above and below) the normal BMI category (range 27.1 to 28.3 points). This difference was statistically significant, indicating a positive relationship between healthy pre-pregnancy weight and healthy diet in pregnancy.

The mean length of stay for women with a normal weight BMI was 1.9 (SD 1.6) days. The mean length of stay was slightly lower among women who were underweight, and slightly higher amongst overweight and obese BMI categories. Women in the overweight and obese categories had increased odds of caesarean delivery, relative to women in the normal BMI category. Obesity class II and III had about double the odds of caesarean delivery, compared to women with a normal weight BMI. The increased length of stay amongst those in overweight and obese categories is likely due to the increased rates of caesarean section in this population, given surgical intervention requires increased care and monitoring compared to spontaneous birth. Women with poor diet quality had a 20% increase in average length of stay, when compared to women with the highest level of diet quality. Independent of a woman's BMI, those with the lowest diet quality had a 27% increase in average length of stay when compared to women with an ARFS score with the highest diet quality. There are multiple dietary factors that may explain this association, for example, dietary fats and fatty acid intakes are associated with reduced preterm births [113, 114] and by extension, length of stay [115].Another possible factor is insufficient gestational weight gain, which is associated with low birth weight [116], and increased length of stay for the infant [117]. This study found no significant relationship between diet quality measured using ARFS and mode of delivery or the number of midwifery-in-the-home visits a patient required. Whilst statistical significance was not identified, greater understanding

of the minimally important clinical difference in this relationship may be significant from a health service perspective. A reliable estimate of the size of the effect was not measurable in the sample population (n=670), however a clinically important relationship between poor diet quality and health service resource use may be identifiable in larger sample sizes.The minimal clinically important difference is the smallest difference in score in any domain or outcome of interest that patients can perceive as beneficial or harmful. It links the magnitude of change to treatment decisions in clinical practice and emphasizes the primacy of patient's perception [118]. Greater understanding of the minimally important clinical difference in maternal diet quality is required to inform future research, guideline implementation interventions and health service decision making. However, measuring and quantifying the minimally important clinical difference associated with care process outcome measures was beyond the scope of this thesis.

8.4 Discussion

To facilitate effective integration of clinical practice guidelines into national decision making and clinical practice in the health sector, guidelines must be informed by both clinical and economic evidence [119]. As described in Chapter One, only five of the 183 (2.7%) current *"Clinical Practice Guidelines: Pregnancy Care"* [4] recommendations have been informed by an economic evaluation. Within these guidelines there are recommendations for 'lifestyle considerations' (health behaviours) that include nutrition, nutritional supplementation, physical activity, tobacco smoking, and alcohol recommendations [4]. Of those, only tobacco has had an economic evaluation informing the cost-effectiveness of smoking cessation recommendations and interventions [42]. Considering the specific, significant economic gaps identified in the literature review in Chapter Three and guidelines, this thesis included two distinct economic analyses of maternal health promotion targets: maternal alcohol consumption, and maternal nutrition. These independent analyses build on the findings of the literature review, providing much needed original research. What is evident across all results chapters of this thesis is that the application of economics to antenatal health promotion is a nascent area of research, challenged by a paucity of real-world evidence and complex sociodemographic, physiological, and behavioural factors unique to the antenatal period.

8.4.1 Maternal alcohol consumption during pregnancy

The economic evaluation in Chapters Four and Five assessed the cost and cost-effectiveness of an implementation intervention from a health care provider perspective. As such, the inputs (costs) included in the analyses were focused on those collected within-trial and the outcomes were focused on those experienced within the trial follow up period. The profile of costs and benefits is consistent with implementation science, specifically guideline implementation interventions, which are conducted on the assumption that the guideline recommendations have been assessed

for cost-effectiveness [52, 5]. As such, the costs are appropriate focused on measuring practice change and do not allow for downstream economic benefits to be captured [109].

It has been recognised that the long-term health and economic benefits that contribute the greatest return on investment for health promotion interventions occur across the lifespan, beyond trial time horizons and budget reporting cycles [52]. For example, the benefits from alcohol cessation (or reduction) occur from birth, when a child can first be diagnosed with foetal alcohol spectrum disorder (FASD). These benefits can then be measured throughout an infant's life including: prevention or reduction in avoidable neurodevelopmental disabilities resulting in learning and behavioural impacts, increased health care requirements, increased contact with the justice system, and productivity losses [120]. When the outcomes of antenatal alcohol exposure manifest, the costs related to greater health service utilisation and associated social support are considerably higher than those without FASD [120, 57]. Popova et al. used cost-of-illness analysis to examine the impact of FASD on the material welfare of Canadian society in 2013 by analysing the direct costs of resources expended on health care, law enforcement, children and youth in care, special education, supportive housing, long-term care, prevention, and research, as well as the indirect costs of productivity losses of individuals with FASD due to their increased morbidity and premature mortality [58]. Estimating the cost-of-illness per FASD case in Australia could be used as a benchmark for future economic evaluations of alcohol implementation interventions, where the intervention cost, estimated reduction in cases of FASD associated with this intervention, and the lifetime cost of illness are incorporated into a single modelled cost-effectiveness analysis. Given the wholly additional, upfront cost profile associated with investment in implementation interventions, identifying, measuring, and valuing the associated downstream benefits may more accurately reflect the true costs and benefits associated with investment in policy implementation.

As described in Chapters Four and Five, maternal alcohol consumption in Australia is higher than other high-income countries. Popova and colleagues estimated the prevalence of alcohol use and drinking amongst the general population in Canada and the United States and found approximately 10% and 15% of pregnant women in the general population consume alcohol, respectively, [121]. Furthermore, about 3% of women engage in binge drinking during pregnancy in both countries [121]. The economic cost of alcohol consumption in Canada was conservatively estimated as $1.8 billion (range: $1.3 billion - $2.3 billion) in 2013, of which 10% were health care costs ($128.5-$226.3 million) [58]. In comparison, Australian national surveys and prospective cohort studies report the prevalence of maternal alcohol consumption at any time during pregnancy to be between 35% and 72% [26]. Despite the much higher rates of drinking during pregnancy in Australia, and the already substantial economic impact of antenatal alcohol consumption in Canada, the economic impact of antenatal alcohol consumption in Australia has not been evaluated [120, 59]. This represents an important gap in the evidence regarding the potential return on investment associated with interventions aiming to reduce maternal alcohol

consumption, addressed in Future Directions below.

8.4.2 Maternal nutrition and weight status

The literature review in Chapter Three identified nine interventions involving diet supplements, of which none considered the investment required to implement these interventions into routine health care practice to ensure clinicians and/or patients adhere to guideline or intervention recommendations. For example, the fish-oil [115], calcium [122], and vitamin-C [123] supplementation interventions did not consider who would be required to pay for the antenatal supplement. Whilst adherence to supplement regimens was explored in sensitivity analyses for its impact on the intervention's effectiveness, the drivers of supplement adherence, such as whether a mother (or household) could afford the supplement, were not considered in any study [84]. Cost is a common contributor to implementation failure [124]. Barriers that reduce adherence to supplement recommendations and interventions in pregnancy include forgetfulness, lack of time, access, maternal age, maternal education, whether the pregnancy was planned or not, and the costs, side-effects and physical difficulties associated with taking tablets [125]. Given that none of the economic evaluations of supplemental nutrition interventions considered the investment required to implement the intervention into practice or promote adherence, it is likely that the investment required to improve antenatal health outcomes reported in the studies identified in Chapter Three is underestimated and conclusions regarding the cost-effectiveness of each intervention may be biased in favour of the intervention.

Greater understanding of the barriers to supplemental nutrition interventions and the investment required to address them is warranted. Future economic evaluations of antenatal supplementation interventions could consider the distribution of economic benefits associated with health promotion interventions, from the perspective of both health care providers and individual families. The upfront cost of supplements and implementations strategies that promote supplement adherence has the potential to be offset by improved health outcomes and decreased resource use during the delivery period and across the infant's lifespan. For example, A recent Cochrane systematic review on omega-3 fatty acid supplementation (or dietary addition) during pregnancy found preterm birth (<37 weeks) and early preterm birth (<34 weeks) were reduced in women receiving omega-3 long chain poly-unsaturated fatty acid compared with no omega-3 [126]. There was also a possible reduction in risk of perinatal death and of neonatal care admission, a reduced risk of low birth weight infants, and possibly a small increased risk of large for gestational age babies with omega-3 long chain poly-unsaturated fatty acid [126]. Reductions in preterm birth, neonatal care admissions, length of stay, and low birth weight are associated with reductions in demand for health care services both during infancy, and across the lifespan [52]. Greater understanding of the willingness-to-pay for guideline recommended, antenatal micronutrient supplements by health care providers and patients could also inform health care decision making and investment allocation.

Despite rising levels of obesity amongst women who are pregnant or trying to become pregnant and increases in gestational weight gain, few studies have assessed the impact of maternal weight status on hospital resource use and cost in the short term (delivery period) using linked health care data [52]. The study described in Chapters Six and Seven found that maternal weight status is associated with increased resource use in the delivery period, and it increases with increasing BMI weight category. The findings in this study are consistent with international literature, for example, a recent study by Solmi et al. found women in the United Kingdom with overweight and obese pre-pregnancy BMI incur higher average hospital costs of childbirth [127]. Based on data from the Millennium Cohort Study (n=7564) delivery costs incurred by those whose BMI category was overweight or obese category I, II, and III were higher than those incurred by women whose BMI was in the normal range, with mode of delivery, pre-term delivery, and length of stay accounting for the observed difference [127]. This is comparable to the results presented in Chapter Seven where a pre-pregnancy BMI in the obese category II and III had higher length of stay and increased odds of caesarean delivery compared to those with a BMI in the normal weight class. Given the Solmi et al. study had substantially larger sample size compared to the study in Chapter Seven, it is possible that with continued data collection and increased sample size, greater understanding of the impact of overweight and obese class I on resource use in the HNELHD could be gained. Maternal weight status during pregnancy is a potential target for future interventions aiming to improve health outcomes and reduce health care resource use in the delivery period. In addition to increased motivation amongst pregnant women, interventions addressing maternal weight gain during pregnancy have the potential to reduce excessive gestational weight gain, which is associated with adverse health impacts to both mother and infant and increased health care costs [128]. Given the findings of Chapter Seven, helping women in obese class II and III or preventing excessive gestational weight gain, may result in improved health outcomes for mothers and infants as well as decreased resource use.

8.5 Implications, limitations and future directions

8.5.1 Implications

The findings of this thesis have relevance for a broad range of clinical and research fields, including health promotion research and clinical practice, nursing and midwifery clinical practice, allied health practice, dietetics practice and research, economic analysis and methodology, and health care funder decision making.

Given the positive trial findings in Chapter Four, further research and monitoring is required to assess the sustainability of intervention effectiveness and whether economies of scale or reduced costs of intervention delivery without reductions in impact can be achieved. Furthermore, it is possible that increased screening and patient advice may increase the detection

of risky alcohol consumption, increase referrals to services, and increase the demand on clinical staff downstream from the antenatal appointments. Gathering evidence of the downstream consequences of the intervention detailed in Chapters Four to Six may assist with developing a business case advocating for adequate resourcing (e.g. staff hours, clinic times, and administerial support) by New South Wales Get Healthy in Pregnancy Service and the Hunter New England Drug and Alcohol Clinical Service to deal with increased demand.

At an international [52] and national [5] level there have been calls for increased identification, measurement, and valuation of the economic impacts associated with health risk behaviours, and their prevention. There is a need to understand the effectiveness, efficiency, and affordability of antenatal health promotion interventions and their associated implementation strategies. For example, effectiveness at sufficient scale must be established prior to conducting a cost-effectiveness analysis, and efficiency must be established prior to evaluation intervention affordability [50]. If a health technology or model of care is cost-effective, economic pre-modelling can be conducted prior to conducting an implementation intervention, using existing evidence of costs, to determine the 'tipping point' for cost-effectiveness for the implementation intervention – the point where an implementation intervention is no longer dominant or the willingness to pay is unacceptable. Economic pre-modelling can inform decision makers of the affordability of investment in implementation.

For health service policy and decision makers, the findings of this research provide an evidence base to better inform decision making regarding the needs of pregnant women who consume alcohol and have sub-optimal nutrition, and the health care systems required to manage the associated adverse outcomes. With sound evidence supporting the efficiency and affordability of guideline implementation into routine antenatal care, and potential downstream benefits, there is a strong argument for increased funding to support antenatal alcohol guideline implementation interventions. The method of identifying barriers to guideline care provision, comprising the development of tailored implementation strategies to address barriers (experienced by care providers, managers, and within the health system) could be extended to other health promotion recommendations included in the *"Clinical Practice Guidelines: Pregnancy Care"*, such as pregnancy specific micro-nutrients or antenatal weight status [4]. The findings of this research also identified specific gaps in the evidence surrounding the sustainability of the practice change intervention and the cost, efficiency, and affordability of nutrition guideline implementation interventions. While there is a current paucity of implementation evidence and deficiencies in the application of economic evaluation methods, this is a growing field with a recently published guideline for the conduct and reporting of economic evaluations of implementation interventions in public health [62]. Health economic analyses makes a critical contribution to antenatal health promotion research via its evaluation of the cost-effectiveness of antenatal nutrition and alcohol health promotion interventions and their implementation for policy and investment decision makers. Additionally, in Australia's largely taxpayer funded health care system, taxpayers rely

on government bodies to make informed funding and policy decisions. Economic evaluation of antenatal health promotion interventions is also of interest to the taxpaying public, who want good health, access to health care when required, and assurances that tax dollars are being used efficiently [5].

Finally, the implications of this thesis for pregnant women, their infants, and families are that there has been an increase in routine screening, advice, and referral for maternal alcohol consumption in the HNELHD. Given the cost profile and system-level changes associated with this practice change intervention, the new model of care is expected to be retained within the health care system into the future. Additionally, maternal weight status and diet quality have been identified as targets for improving maternal and infant health outcomes and decreased resource use during the delivery period. The findings should encourage women to maintain a healthy weight during pregnancy and seek pregnancy specific nutrition advice from their health care providers. Given the potential cost savings associated with reducing pre-pregnancy BMI, there is also potential for nutrition education and weight loss counselling, via a Medicare subsidised public health program, to be more accessible for women in obese class II and III. Abstaining from alcohol consumption and maintaining a healthy weight in pregnancy will improve maternal health outcomes in the delivery period and improve an infant's health outcomes throughout their lives [3]. These benefits will have a flow-on effect for the health care system and society.

8.5.2 Limitations

The literature review reported in Chapter Three was updated in September 2021 to identify any texts published since conducting the review and writing this discussion. This update found no additional published analyses which would have been included in either review in Chapter Three. There has been one protocol published for an economic evaluation of a diet and physical activity intervention to prevent gestational diabetes. The outcomes of this economic evaluation protocol may be suitable for inclusion in a future update of the published review in Chapter Three [129]. There has also been a series of modelled economic evaluations of antenatal 'lifestyle' interventions [130, 131], however they do not report on diet only interventions and therefore the incremental contribution of nutrition interventions cannot be assessed and remains a gap in the literature. The update also identified that in May 2019 new Australian guidelines for alcohol have been published [24]. The recommendations for pregnancy have not changed, however there is thus a need to continually review and update the evidence based on current guidelines and recommendations. As such, the economic evidence base for the role of nutrition in improving health and preventing disease is currently incomplete and requires more research.

The outcome measures in Chapters Four and Five are process measures (i.e. guideline adherent receipt of care) and assume that the guidelines themselves are cost-effective. However, the efficiency of the maternal alcohol guideline recommendations is unknown, as described in Chapter One. Understanding what an acceptable cost is to improve care processes or a decision

makers willingness to pay for guideline adherent care processes is unknown, and is debated within the literature [132, 64].Given the implementation efforts described in Chapter Four and Five are wholly additional to usual care they are both more expensive and more effective than usual care. However, the willingness to pay for this care process measure is unknown.

There were limitations with the AES instrument and the ARFS metric used to measure diet quality in Chapter Seven. Firstly, the AES is a food frequency questionnaire used to estimate usual dietary intakes of Australian adults [107, 133]. The AES does not ask participants questions regarding portion size, rather, states "portion sizes are predetermined based on average portion size of the relevant food based on age and for adults' gender" [134]. Regarding the ARFS, optimal diet quality is defined as 'alignment of an individual's usual dietary intake with the ADG and includes the concepts of nutrient intake adequacy and food variety within key healthy food groups. Poor diet quality is defined as lower intakes of nutrient dense foods and higher intakes of energy-dense' [111]. The ADG recommend people enjoy a wide variety of nutrition foods (from the five food groups) and limit intake of foods containing saturated fat, added salt, added sugars, and alcohol [13]. The ARFS is calculated by summing intakes whereby most foods are awarded one point for a reported consumption of greater than or equal to once per week and the total scores can range from zero to 73 [111]. The AES for all adult Australians is scored out of 73 and includes a question regarding alcohol consumption. The AES has been adjusted for pregnant populations [117], and as a result the alcohol question is not included and the total ARFS is scored out of 72. This thesis has presented strong evidence that Australian women consume alcohol whilst pregnant and some continue to consume alcohol once they knew they were pregnant [26]. The exclusion of the alcohol specific question in the AES is not expected to impact the ARFS index, however, demonstrates that the assumptions underpinning the tool may benefit from further assessment before future use in pregnant populations. Future economic evaluations of nutrition interventions addressing weight status should consider using clinically meaningful metrics that are sensitive to not just diversity, but energy or adherence to dietary guidelines.

Second, although standard for commercialised food frequency questionnaires, the AES is a patented tool and the algorithm for calculating the ARFS, energy intake from food, macronutrient and micronutrient intake is not publicly available; as such, the assumptions and methods underpinning application of the algorithm are not transparent. Transparent documentation of assumptions is a recommendation in the economic evaluation reporting guidelines, the *"Consolidated Health Economic Evaluation Reporting Standard"* (CHEERS) Checklist [106]. For those considering using the AES and ARFS in economic evaluation, greater transparency around the assumptions underpinning the algorithm used to calculate nutrition intake should be sought prior to use so that assumptions can be accounted for and limitations addressed prospectively.

8.5.3 Future directions

As more research is conducted on the impact of health promotion interventions on maternal health risk behaviours, data to examine intervention cost, cost-effectiveness, and budget impact should also be collected. Ideally, existing practices and models of care need to be updated based on effectiveness as well as efficiency and affordability. Future health promotion research should involve collaboration with health economists at the research design phase in order to ensure the required data is collected and the research design, including longer follow-up, will support rigorous economic evaluation of relevant outcomes.

Given the complete absence of economic evaluation informing antenatal clinical practice guideline recommendations for nutrition and alcohol [42], improving the state of evidence surrounding the economic costs and benefits associated with antenatal nutrition interventions will allow decision makers to invest in health promotion according to its comparative cost effectiveness [5]. The three-part series by Mastrigt et al. [81, 135, 136] on how to conduct a systematic review of economic evaluations could inform those unfamiliar with economics regarding how to: 1) initiate a systematic review of economic evaluations; 2) identify full economic evaluations; 3) complete data extraction, risk of bias, and transferability assessments; 4) report results; and 5) discuss and interpret research findings. For those looking to report the findings the CHEERS checklist and elaboration statement can be used as a reporting guideline for publications [106, 83]. Finally, for researchers looking to collect economic evidence the costing methods proposed by Saldana et al. [124] and Cidav et al. [137] provide pragmatic methods for time drive activity based costing which can be applied to both implementation studies and dietetic interventions.

The protocol in Chapter Four included a cost, cost-consequence, CEA, and budget impact assessment (BIA) of the maternal alcohol implementation intervention. As described in Chapter Three of this thesis, while there exist national guidelines for conducting and reporting BIA of medicines, medical devices, and diagnostics there are no such guidelines for conducting BIA at the local level of health care, where the majority of health care is provided [49]. A BIA of the maternal alcohol intervention will be conducted outside the scope of this thesis, alongside a local level BIA guideline development project being conducted by the Health Research Economics (HRE) team at the Hunter Medical Research Institute (HMRI). A BIA using the economic evidence collected in Chapter Five will be published alongside the HMRI HRE guidelines, to provide information to decision and policy makers regarding the budget impact and affordability of a practice change intervention to support the introduction of a model of care for addressing alcohol consumption by pregnant women. This work will answer the research question first proposed in the protocol in Chapter Four, from the Australian health care system perspective: "Is a practice change intervention to increase routine provision of antenatal care for maternal alcohol consumption compared to usual practice an affordable model for local health services?". Once published, this work will provide a published example of how the HMRI HRE guidelines can be applied to local, state, and potentially federal health care evaluations to inform investment

and decision making. These guidelines are expected to be published in 2022.

Midwives and nurses can be instrumental in encouraging pregnant women to improve their nutrition [138]. The *"Clinical Practice Guidelines: Pregnancy Care"* recommend, where appropriate, midwives and nurses provide specific nutrition advice and refer pregnant women to allied health professionals for weight management services [4]. Pregnant women have reported an increased interest in nutrition [138]; in addition, trust in antenatal health care providers [48] and frequent antenatal care visits [4] are considered facilitators of nutrition communication by midwives and nurses during this time. However, it has been reported that health professionals do not routinely discuss a woman's weight or diet during antenatal visits [139, 140, 141] and report providing 'general' healthy eating advice rather than specific advice relevant during pregnancy [142, 143]. To address this, an implementation intervention addressing excessive gestational weight gain is being conducted. The methods used to identify, measure, and value the economic and financial costs associated with the implementation intervention in Chapters Four and Five have since informed economic data collection for this nutrition guideline implementation study. Specifically, the data set used for the cost, cost-consequence, and cost-effectiveness evaluation in Chapter Five directly informed the development of a prospective time-drive activity-based cost capture tool in REDCap and a supporting data dictionary. Using an electronic web-form for data collection is expected to improve consistency of reporting across intervention sectors, the use of "required" data points (which include electronic prompts for completion) is expected to reduce missing data and require less data management (cleaning) prior to analysis.

The trial-based economic evaluation revealed the challenges associated with identifying, measuring, and valuing economic data. Where possible, prospective time-based activity costing could be used in RCT's to collect economic evidence to support assessment of efficiency and affordability. Referral data, including measures of the number of referrals provided and the number of referrals accepted, from sources such as administrative hospital databases, could be used to strengthen the estimate of efficiency and affordability. The use of administrative hospital data sets for economic evaluation may also allow for extrapolation of the economic impact over a longer time horizon to capture the impact of the intervention and provide evidence of intervention sustainability.

8.6 Conclusion

The research included in this doctoral thesis addressed an important gap in the evidence base to inform greater understanding of the cost and cost-effectiveness of current nutrition and alcohol recommendations in pregnancy. The evidence presented and discussed in this thesis suggests that despite guideline recommendations, women are not meeting guideline recommendations for nutrition and alcohol, increasing the risk of adverse health outcomes for both the mother and infant and incurring avoidable health care system cost. Whilst implementation interventions can change clinician behaviour to ensure women receive evidence-based care addressing

alcohol consumption, this thesis identified, measured, and valued the investment in implementation required from health care providers. This thesis also included the collection of evidence to quantify specific health care resource use associated with maternal weight status and diet quality. This thesis demonstrated that interventions to improve maternal compliance with dietary guideline recommendations could deliver substantive economic benefits to the health care system and community. However, improved economic data collection methods for trial-based health promotion interventions are required if the economic impact of preventing adverse health outcomes is to be accurately measured, and the impact of economic evaluations on public health promotion interventions and policy enhanced. The work reported in this thesis has contributed to advancing applied health economic research and practice.

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Appendices

Chapter 3 Appendices

Appendix 3.1: Systematic Review Search Terms for Medline

Table 1. Medline search strategy and PICO categories for review (i): Economic evaluations of antenatal health promotion interventions	
(P) Population	33. pregnancy/ 34. pregnan*.tw. 35. pregnant women/ 36. (child adj3 bearing).tw. 37. childbearing.tw. 38. matern*.tw. 39. prenatal.mp. 40. antenatal.mp. 41. perinatal.mp. or Perinatal Care/ 42. premature birth/ or pregnancy complications/ or infant, newborn/ 43. Infant, Newborn/ or Pregnancy/ or gestation*.mp. 44. maternal outcome*.mp. 45. infant outcome*.mp. 46. Prenatal Care/ or Prenatal Education/ or prenatal.mp. 47. 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 59. (developing countr* or third world or underdeveloped countr* or under developed countr*).mp. 60. exp africa/ or americas/ or exp caribbean region/ or exp central america/ or latin america/ or mexico/ or exp south america/ 61. exp europe, eastern/ or exp transcaucasia/ 62. New Guinea/ or asia/ or exp asia, central/ or asia, southeastern/ or borneo/ or cambodia/ or east timor/ or indonesia/ or laos/ or malaysia/ or mekong valley/ or myanmar/ or philippines/ or thailand/ or vietnam/ or asia, western/ or bangladesh/ or bhutan/ or india/ or middle east/ or afghanistan/ or iran/ or iraq/ or jordan/ or lebanon/ or oman/ or saudi arabia/ or syria/ or turkey/ or yemen/ or nepal/ or pakistan/ or sri lanka/ or far east/ or china/ or tibet/ or exp korea/ or mongolia/ 63. (Afghanistan or Africa or Albania or Algeria or Angola or Antigua or Argentina or Armenia or Azerbaijan or Bangladesh or Barbados or Barbuda or Belarus or Belize or Brazil or Bhutan or Bolivia or Bosnia or Botswana or Bulgaria or Burkina Faso or Burundi or Cambodia or Cameroon or Central African Republic or Chad or Chile or Colombia or Comoros or Congo or Costa Rica or Croatia or Cuba or Czech* or Congo or Djibouti or Dominica or Dominican or East Timor or Ecuador or Egypt or El Salvador or Equatorial Guinea or Eritrea or Estonia or Ethiopia or Fiji or Gabon or Gambia or Ghana or Grenada or Guatemala or Guinea-Bissau or Guyana or Haiti or Honduras or Hungary or India or Indonesia or Iran or Iraq or Ivory Coast or Jamaica or Jordan or Kazakhstan or Kenya or Kiribati or Kyrgyzstan or Laos or Latvia or Lebanon or Lesotho or Liberia or Libya or Lithuania or Madagascar or Malawi or Malaysia or Maldives or Mali or Marshall Islands or Mauritania or Mauritius or Mexico or Micronesia or Moldova or Mongolia or Montenegro or Morocco or Mozambique or Myanmar or Namibia or Nepal or New Guinea or Nicaragua or Niger or Nigeria or Korea or Oman or Pakistan or Palau or Panama or Papua New Guinea or Paraguay or Benin or China or Peru or Philippines or Poland or Cape Verde or Georgia or Kosovo or Macedonia or Yemen or Romania or Russia or Rwanda or Saint Kitts or Saint Vincent or Saint Lucia or Sao Tome Principe or Saudi Arabia or Senegal or Serbia or Seychelles or Sierra Leone or Slovak* or South Africa or Solomon Islands or Somalia or Sri Lanka or Sri-Lanka or Sudan or Suriname or Swaziland or Syria or Tajikistan or Tanzania or Thailand or Togo or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or Uganda or Ukraine or Uruguay or Uzbekistan or Vanuatu or Venezuela or Vietnam or Samoa or Zambia or Zimbabwe).af. 64. 59 or 60 or 61 or 62 or 63 65. (developed countries or european union).af. 66. Europe/ or andorra/ or austria/ or belgium/ or exp france/ or exp germany/ or exp united kingdom/ or greece/ or ireland/ or exp italy/ or liechtenstein/ or luxembourg/ or monaco/ or netherlands/ or portugal/ or exp "scandinavian and nordic countries"/ or spain/ or switzerland/ or exp australia/ or new zealand/ 67. North america/ or exp canada/ or exp united states/ 68. (united kingdom or england or scotland or wales or denmark or finland or iceland or norway or sweden).af.

	69. (north america or canada or oecd or united states).af. 70. (europe or andorra or austria or belgium or france or germany or greece or ireland or italy or liechtenstein or luxembourg or monaco or netherlands or portugal or spain or switzerland or australia or new zealand).af. 71. 64 or 65 or 66 or 67 or 68 or 69 or 70 72. animals/ not (humans/ and animals/) 73. 64 and 72 74. 13 and 47 and 58 and 71 75. 74 not 73 76. limit 75 to yr="2000 -Current"
(I) Intervention	15. Weight Gain/ 16. weight gain*.tw. 17. Weight Loss/ 18. weight loss*.tw. 19. weight change*.tw. 20. Overweight/ 21. overweight*.tw. 22. diet*.mp. or Diet/ 23. Body Mass Index/ 24. bmi.tw. 25. Nutrition/ 26. diabet*.ti,ab,kf. 27. body weight.ti,ab,kf. 28. vitamin*.mp. 29. obes*.tw. 30. (Fortifi* adj5 (food* or diet* or nutrit*)).ti,ab,kf. 31. (supplement* adj5 (food* or diet* or nutrit*)).ti,ab,kf. 32. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 48. Alcohol-Related Disorders/ 49. Alcoholic intoxication/ 50. Alcoholism/ 51. Binge Drinking/ or Alcohol drinking/ 52. (alcohol* adj1 (use* or abuse* or misuse* or depend* or reduc* or addict* or therap* or treatment* or excess* or harmful or risk* or hazardous or problem* or unhealthy or consum*)).ti,ab. 53. ((harmful* or risk* or hazardous or problem* or binge* or heavy or excessive or unhealthy) adj (drink* or alcohol*)).ti,ab. 54. (alcohol* adj5 (scale* or inventor* or questionnaire* or survey* or index* or checklist* or interview*)).ti,ab. 55. AUDIT-C.ti,ab. 56. f?etal alcohol spectrum disorder.tw,kw. or Fetal Alcohol Spectrum Disorders/ or fasd.tw,kw. 57. 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 58. 32 or 57
(C) Control	Any comparator intervention including no intervention and ‘usual care’ or ‘treatment as usual’

(O) Outcomes	1. Economics/ or health economic*.ti,kf,ab. 2. "Costs and Cost Analysis"/ 3. Economics, Medical/ 4. "Fees and Charges"/ 5. budget*.ti,ab,kf. 6. (economic* or cost*).ti,kf,ab. 7. (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ti,kf. 8. exp models, economic/ 9. economic model*.ti,ab,kf. 10. exp Decision Theory/ 11. (decision* adj2 (tree* or analy* or model*)).ti,ab,kf. 12. (cochrane or (health adj2 technology assessment) or evidence report).jw. 13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12

Table 2. Medline search strategy and PICOS categories for review (ii): economic evaluations of antenatal public health implementation interventions	
(P) Population	33. pregnancy/ 34. pregnan*.tw. 35. pregnant women/ 36. (child adj3 bearing).tw. 37. childbearing.tw. 38. matern*.tw. 39. prenatal.mp. 40. antenatal.mp. 41. perinatal.mp. or Perinatal Care/ 42. premature birth/ or pregnancy complications/ or infant, newborn/ 43. Infant, Newborn/ or Pregnancy/ or gestation*.mp. 44. maternal outcome*.mp. 45. infant outcome*.mp. 46. Prenatal Care/ or Prenatal Education/ or prenatal.mp. 47. 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 59. (developing countr* or third world or underdeveloped countr* or under developed countr*).mp. 60. exp africa/ or americas/ or exp caribbean region/ or exp central america/ or latin america/ or mexico/ or exp south america/ 61. exp europe, eastern/ or exp transcaucasia/ 62. New Guinea/ or asia/ or exp asia, central/ or asia, southeastern/ or borneo/ or cambodia/ or east timor/ or indonesia/ or laos/ or malaysia/ or mekong valley/ or myanmar/ or philippines/ or thailand/ or vietnam/ or asia, western/ or bangladesh/ or bhutan/ or india/ or middle east/ or afghanistan/ or iran/ or iraq/ or jordan/ or lebanon/ or oman/ or saudi arabia/ or syria/ or turkey/ or yemen/ or nepal/ or pakistan/ or sri lanka/ or far east/ or china/ or tibet/ or exp korea/ or mongoli 63. (Afghanistan or Africa or Albania or Algeria or Angola or Antigua or Argentina or Armenia or Azerbaijan or Bangladesh or Barbados or Barbuda or Belarus or Belize or Brazil or Bhutan or Bolivia or Bosnia or Botswana or Bulgaria or Burkina Faso or Burundi or Cambodia or Cameroon or Central African Republic or Chad or Chile or Colombia or Comoros or Congo or Costa Rica or Croatia or Cuba or Czech* or Congo or Djibouti or Dominica or Dominican or East Timor or Ecuador or Egypt or El Salvador or Equatorial Guinea or Eritrea or Estonia or Ethiopia or Fiji or Gabon or Gambia or Ghana or Grenada or Guatemala or Guinea-Bissau or Guyana or Haiti or Honduras or Hungary or India or Indonesia or Iran or Iraq or Ivory Coast or Jamaica or Jordan or Kazakhstan or Kenya or Kiribati or Kyrgyzstan or Laos or Latvia or Lebanon or Lesotho or Liberia or Libya or Lithuania or Madagascar or Malawi or Malaysia or Maldives or Mali or Marshall Islands or Mauritania or Mauritius or Mexico or Micronesia or Moldova or Mongolia or Montenegro or Morocco or Mozambique or Myanmar or Namibia or Nepal or New Guinea or Nicaragua or Niger or Nigeria or Korea or Oman or Pakistan or Palau or Panama or Papua New Guinea or Paraguay or Benin or China or Peru or Philippines or Poland or Cape Verde or Georgia or Kosovo or Macedonia or Yemen or Romania or Russia or Rwanda or Saint Kitts or Saint Vincent or Saint Lucia or Sao Tome Principe or Saudi Arabia or Senegal or Serbia or Seychelles or Sierra Leone or Slovak* or South Africa or Solomon Islands or Somalia or Sri Lanka or Sri-Lanka or Sudan or Suriname or Swaziland or Syria or Tajikistan or Tanzania or Thailand or Togo or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or Uganda or Ukraine or Uruguay or Uzbekistan or Vanuatu or Venezuela or Vietnam or Samoa or Zambia or Zimbabwe).af. 64. 59 or 60 or 61 or 62 or 63 65. (developed countries or european union).af. 66. Europe/ or andorra/ or austria/ or belgium/ or exp france/ or exp germany/ or exp united kingdom/ or greece/ or ireland/ or exp italy/ or liechtenstein/ or luxembourg/ or monaco/ or netherlands/ or portugal/ or exp "scandinavian and nordic countries"/ or spain/ or switzerland/ or exp australia/ or new zealand 67. North america/ or exp canada/ or exp united states/ 68. (united kingdom or england or scotland or wales or denmark or finland or iceland or norway or sweden).af.

	69. (north america or canada or oecd or united states).af. 70. (europe or andorra or austria or belgium or france or germany or greece or ireland or italy or liechtenstein or luxembourg or monaco or netherlands or portugal or spain or switzerland or australia or new zealand).af. 71. 64 or 65 or 66 or 67 or 68 or 69 or 70
(I) Intervention	15. Weight Gain/ 16. weight gain*.tw. 17. Weight Loss/ 18. weight loss*.tw. 19. weight change*.tw. 20. Overweight/ 21. overweight*.tw. 22. diet*.mp. or Diet/ 23. Body Mass Index/ 24. bmi.tw. 25. Nutrition/ 26. diabet*.ti,ab,kf. 27. body weight.ti,ab,kf. 28. vitamin*.mp. 29. obes*.tw. 30. (Fortifi* adj5 (food* or diet* or nutrit*)).ti,ab,kf. 31. (supplement* adj5 (food* or diet* or nutrit*)).ti,ab,kf. 32. 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 48. Alcohol-Related Disorders/ 49. Alcoholic intoxication/ 50. Alcoholism/ 51. Binge Drinking/ or Alcohol drinking/ 52. (alcohol* adj1 (use* or abuse* or misuse* or depend* or reduc* or addict* or therap* or treatment* or excess* or harmful or risk* or hazardous or problem* or unhealthy or consum*)).ti,ab. 53. ((harmful* or risk* or hazardous or problem* or binge* or heavy or excessive or unhealthy) adj (drink* or alcohol*)).ti,ab. 54. (alcohol* adj5 (scale* or inventor* or questionnaire* or survey* or index* or checklist* or interview*)).ti,ab. 55. AUDIT-C.ti,ab. 56. f?etal alcohol spectrum disorder.tw,kw. or Fetal Alcohol Spectrum Disorders/ or fasd.tw,kw. 57. 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 58. 32 or 57
(C) Control	Any comparator intervention including no intervention and ‘usual care’ or ‘treatment as usual’
(O) Outcomes	1. Economics/ or health economic*.ti,kf,ab. 2. "Costs and Cost Analysis"/ 3. Economics, Medical/ 4. "Fees and Charges"/ 5. budget*.ti,ab,kf.

	6. (economic* or cost*).ti,kf,ab. 7. (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ti,kf. 8. exp models, economic/ 9. economic model*.ti,ab,kf. 10. exp Decision Theory/ 11. (decision* adj2 (tree* or analy* or model*)).ti,ab,kf. 12. (cochrane or (health adj2 technology assessment) or evidence report).jw. 13. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 72. implement*.mp. 73. Implement* strat*.mp. 74. Dissemination.mp. 75. (organi?ational adj change*).mp. 76. (system adj2 change*).mp. 77. Quality improvement.mp. 78. ((adherent or complian*) adj3 policy).mp. 79. ((polic* or practic* or progra* or innovat*) adj5 (perform* or feedback or prompt* or reminder* or incentive* or penalt* or communic* or change manag* or train* or audit*)).mp. 80. (intervention$ or prevent* or polic* or program$).mp. 81. 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 82. 13 and 47 and 58 and 81 83. 82 not 71 84. limit 83 to yr="2000 -Current"

Appendix 3.2: Systematic Review PRISMA 2009 Checklist

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6/7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	10
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary material 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	9

Appendix 3.2: Systematic Review PRISMA 2009 Checklist

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10/11
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	29
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Chapter 5 Appendices

Appendix 5.1: Implementation Strategy Summary

Appendix 5. Table 1. Implementation Strategy Summary

Intervention component	Component details	Resource use details	Data collection method for costing
Leadership and management	• Monthly meetings were held with management from antenatal services to elicit support. • Service managers distributed resources to staff and attended training sessions. • Performance measures related to the provision of the model of care were monitored and reported on.	**Labour time:** • Health district implementation support officer and manager. • Health service antenatal clinical staff and management.	• Resource use capture template
Local clinical practice guidelines	• A service level guideline and procedure document detailed the model of care, including assessment, brief advice and referral pathways. • The document was uploaded onto the health service's policy directory, disseminated by managers to all staff via email and hard copies were placed in staff common areas.	**Materials:** • Guideline and procedure document development and provision. **Miscellaneous:** • Electronic dissemination. **Labour time:** • Health district implementation support officer and manager. • Health service antenatal clinical staff and management.	• Resource use capture template
Electronic prompt and reminder system	• Existing point-of-care and medical record systems used by maternity clinicians were modified to electronically prompt use of the AUDIT-C alcohol screening tool. • Brief advice scripts were displayed on the point-of-care system based on the woman's AUDIT-C risk score and prompts and tools for referral to appropriate services.	**Materials:** • Computer-based intervention component. **Labour time:** • Health district implementation support officer and manager. • Health service antenatal clinical staff and management.	• Resource use capture template
Local opinion leaders/champions	• Project-specific Clinical Midwife Educators were appointed to support staff to uptake the model of care	**Labour time:**	• Resource use capture template

	and provide support at a one-on-one, team and service level. • Additional local antenatal clinical leaders were engaged to provide encouragement and demonstrate required behaviours as required.	• Health district implementation support officer. • Clinical midwife educator (CME) change champion.	
Educational meetings and materials	• Training was provided to all antenatal service clinicians via a 30-minute online training module and face-to-face sessions. Clinical Midwife Educators facilitated clinicians completing the online training and coordinate face-to-face training sessions. This included lecture style sessions, interactive, case-study based sessions and one-on-one sessions. • Clinicians were provided with written resources (hardcopy and electronic) to support the model of care, including standard drink measure charts and point-of care written prompts/reminders (e.g. stickers in charts).	**Labour time:** • Health district implementation support officer. • CME change champion. • Health service clinical staff. • Expert clinicians. **Materials:** • Educational tools and resources	• Resource use capture template • REDCap database
Academic detailing	• Data from both medical records and telephone surveys conducted with women who attended the antenatal services were used to provide feedback on adherence to the agreed model of care. • The Clinical Midwife Educators visited service teams in their antenatal clinics to provide feedback data and developed action plans to improve adherence.	**Labour time:** • Project support officer. • CME change champion. • Clinical service staff time.	• Resource use capture template • REDCap database
Monitoring and accountability	• Antenatal service managers reported, interpreted and monitored performance measures for the model of care. • These results were disseminated to antenatal service staff through team meetings, emails and other usual communication mechanisms. • Performance measures were built into the existing monitoring and accountability frameworks for antenatal services.	**Labour time:** • Health district implementation support officer. • Health service antenatal clinical staff and management. **Miscellaneous:** • Electronic dissemination.	• Resource use capture template

Chapter 6 Appendices

Appendix 6.1: Prepared Media Content for the Study

HMRI Website – Research Project Listings Page (links to Research Project Details Page)

The association between diet quality during pregnancy and maternal and infant health and health care costs

Are you pregnant? Researchers are looking for volunteers to participate in an online survey that looks at your usual eating habits.

Click here to find out more: http://bit.ly/hmriantediet

HMRI Website - Research Projects Details Page

The association between what you eat during pregnancy and the health of mothers and their babies as well as health care costs is important, but often overlooked.

Are you pregnant? Researchers are looking for volunteers to participate in an online survey that looks at your usual eating habits.

Details:

The purpose of the research is to examine the dietary patterns of pregnant women and the association between dietary intake during pregnancy and childbirth related health and health care costs.

Who can volunteer?

Pregnant women who are 28- 36 weeks pregnant (in their third trimester) from the Hunter New England and planning to have their baby at the John Hunter Hospital.

In addition to the above this study would be suitable for you if you:

- Are aged 18 years and above
- Are able to complete an online survey which includes the Australian Eating Survey on usual dietary intake.
- Are proficient in the English language

How do I find out more information?

If you are interested or for further information and to find out if you are eligible please go to http://bit.ly/hmriantediet or alternatively contact the research team on 02 4921 5646.

For further information contact Professor Clare Collins

T +61 2 4921 5646

E Clare.Collins@Newcastle.edu.au

This project has been approved Hunter New England Reference Number: 16/07/20/4.03

Approval Number: HREC/16/HNE/314

HMRI Social Media Wording (all posts will link to appropriate landing page on HMRI website via the following link: http://bit.ly/diethmri)

1) Are you pregnant? Researchers are looking for volunteers to participate in an online survey that looks at usual eating habits.

2) Are you pregnant? Researchers are seeking volunteers to participate in an online survey that looks at usual eating habits.

3) Researchers are seeking pregnant women to complete a survey of usual dietary intake to examine associations with pregnancy and birth outcomes and health care costs.

4) Researchers are seeking volunteers to examine the diet quality of pregnant women in relation to health and healthcare costs.

5) Researchers are seeking volunteers to examine the usual eating habits of pregnant women.

6) Help researchers study the links between dietary patterns pregnancy, birth and healthcare outcomes and costs. Pregnant volunteers needed for online survey.

7) Researchers are seeking volunteers to examine the diet quality of pregnant women – complete online survey of dietary patterns, pregnancy, birth and healthcare outcomes and costs.

8) Researchers are seeking volunteers to examine the eating habits of pregnant women – complete online survey.

9) Researchers are recruiting pregnant women to participate in an online survey that looks at usual eating habits and pregnancy, birth and healthcare outcomes and costs.

10) Researchers are seeking pregnant women to participate in an online survey that looks at usual eating habits.

Photos for use on HMRI website and social media

Appendix 6.2: "About the Study": In-service for Antenatal Clinic Staff

THE UNIVERSITY OF NEWCASTLE AUSTRALIA

Diet quality in pregnancy and maternal and infant outcomes: a cross-sectional survey

Zoe Szewczyk (PhD Student)

Professor Clare Collins
Professor in Nutrition and Dietetics, The University of Newcastle
Co-Director Priority Research Centre in Physical Activity and Nutrition
Global *e*Health Research & Innovation Cluster

Who are the researchers?

- Prof Clare Collins (UoN)
- Dr Felicity Park (Neonatal and Foetal Medicine; JHH)
- Dr Megan Rollo (UoN)
- Dr Chris Oldmeadow (Senior Statastician; HMRI)
- Dr Andrew Searles (Health Research Economist; HMRI)
- Dr Kristine Pezdirc (UoN)
- Mr Simon Deeming (Health Research Economist; HMRI)
- Dr Catherine Chojenta (UoN)
- DR Melinda Hutchesson (UoN)
- Ms Zoe Szewczyk (PhD student)

Project Summary

- Online survey for pregnant women in their third trimester.
- Examining the relationship between diet quality and pregnancy and birth outcomes.
- 600 females aged 18 years and over from the Hunter New England Area
- Diet Quality will be collected via food frequency questionnaire
- Clinical outcomes, and costs related to hospital admission will be collected via the medical record and ObsetriX

Background

- Poor pregnancy eating patterns are common
- Contribute to excessive gestational weight gain, hypertension, preeclampsia, gestational diabetes (GDM), preterm birth, perturbations in birth weight, birth defects and caesarean section.
- Adverse clinical outcomes incur major healthcare and personal costs, yet the economic impact of poor diet and excess gestational weight gain (GWG) has been neglected in research.
- In addition the direct comparison of diet quality and infant and maternal outcomes in terms of healthcare cost has not been undertaken in Australia.
- Our own research has shown pregnancy diet is related to foetal body composition, infant blood pressure and cognitive outcomes to age four.

Hypothesis

- Pregnant women who had a poor diet quality will have higher healthcare costs and poorer maternal and infant outcomes

Recruitment Methods

- Recruitment Flyer in booking information
- Flyers distributed at the antenatal clinics (John Hunter Hospital only)
- Media releases (including social media).

Research study

THE UNIVERSITY OF NEWCASTLE AUSTRALIA

Are you pregnant? We are looking for volunteers to participate in an online survey that looks at your usual eating habits.

Details:
The purpose of the research is to examine the diet quality of pregnant women and the association between diet quality, pregnancy and birth outcomes and health care costs.

Who can volunteer?
- Pregnant women who are 28-36 weeks gestation (third trimester) from the Hunter New England area
- In addition to the above this study would be suitable for you if you:
  - Are aged 18 years and above
  - Are able to complete an online survey and the Australian Eating Survey.
  - Are proficient in the English language

How do I find out more information?
If you are interested or for further information and to find out if you are eligible please go to (insert survey link) or alternatively contact the research team on 02 4921 5646.

CONTACT
T +61 2 4921 5646
E Clare.Collins@Newcastle.edu.au

This project has been approved Hunter New England
Reference: x06/xxx.xx , Approval Number

Version 2 dated 24/8/16

What is required from the participant?

- Give online Consent
- Complete Two Survey's:
- Questionnaires will be completed covering demographics (income, language spoken at home , self reported medical history and medications (including supplements), parity, past weight history, information on diet during pregnancy, other relevant information
- They will also complete a web-based Australian Eating Survey (AES) to assess their dietary intake

Australian Eating Survey (AES)

- Validated food frequency questionnaire
- Assess dietary intake.

What information will be collected from Medical Records/ObstetriX

- Birth complications
- Birth outcomes
- Length of gestation
- Birth weight and length
- Preeclampsia,
- Hypertension,
- Preterm birth,
- Cesarean section,
- Shoulder dystocia, macrosomia
- Small for gestational age (SGA), Large for gestational age(LGA)
- Length of stay (for mother and infant)
- Gestational weight gain and postpartum weight retention
- Breastfeeding.

Ethical considerations

- Participation in this study is entirely voluntary
- Participants will be informed about what is involved in the study and will have the opportunity to have any questions answered prior to consenting to participate. (via email)
- Participants will be free to withdraw from the study at any time without fear of consequence or any detriment to their relationship.

Harm Vs. Benefit

- Harm:
  - Potential distress to pregnant women caused by recognition of poor diet

- Benefit:
- The results of the cross-sectional survey will inform a future NHMRC grant in 2017 to develop an nutrition therapy intervention for pregnant women to improve health and infant cognition.

What is required of clinicians?

- Your support
- Awareness of the study
- Allowing a member of the research team to visit clinic waiting rooms

References

1.Thangaratinam S, Rogozińska E, Jolly K, Glinkowski S, Duda W, Borowiack E, et al. Interventions to reduce or prevent obesity in pregnant women: a systematic review. Health Technol Assess. 2012;16(31):1191.

2.Guelinckx I, Devlieger R, Beckers K, Vansant G. Maternal obesity: pregnancy complications, gestational weight gain and nutrition. Obes Rev. 2008;9(2):14050.

3.Brenseke B, Renee Prater M, Bahamonde J, Claudio Gutierrez J. Current Thoughts on Maternal Nutrition and Fetal Programming of the Metabolic Syndrome. J Pregnancy. 2013;2013:113.

4.Sui Z, Turnbull DA, Dodd JM. Overweight and Obese Women's Perceptions About Making Healthy Change During Pregnancy: A Mixed Method Study. Matern Child Health J. 2013;17(10):187987.

5.Blumfield M, Hure A, MacDonaldWicks L, Smith R, Simpson S, Giles W, et al. Dietary balance during pregnancy is associated with fetal adiposity and fat distribution. Am J Clin Nutr. 2012;96(5):103241.

6.Blumfield M, Nowson C, Hure A, Smith R, Simpson S, Raubenheimer D, et al. Lower proteintocarbohydrate ratios in maternal diet are associated with increased childhood systolic blood pressures up to 4 years of age. submitted. 2015.

7.Collins C, Hure A, Blumfield M, Drysdale K, Smith R. Higher proteintocarbohydrate ratios in maternal diet are associated with higher intelligence quotient at 4 years. Abstract submitted to DoHAD Australia 2015 (Melbourne April) id# 181389694. 2015.

8.Ulker A. Body size at birth, physical development and cognitive outcomes in early childhood: evidence from the Longitudinal Survey of Australian Children. Educ Econ. 2014.

Appendix 6.3: Study Recruitment Flyer placed in Antenatal Outpatient Clinic

Research study

THE UNIVERSITY OF NEWCASTLE AUSTRALIA

Are you pregnant? We are looking for volunteers to participate in an online survey that looks at your usual eating habits.

Details:

The purpose of the research is to examine the diet quality of pregnant women and the association between diet quality, pregnancy and birth outcomes and health care costs.

Who can volunteer?

- Pregnant women who are 28- 36 weeks gestation (third trimester) from the Hunter New England area
- In addition to the above this study would be suitable for you if you:
  - Are aged 18 years and above
  - Are able to complete an online survey and the Australian Eating Survey.
  - Are proficient in the English language

How do I find out more information?

If you are interested or for further information and to find out if you are eligible please go to http://bit.ly/pregdq5 or alternatively contact the research team on 02 4921 5646.

CONTACT

T +61 2 4921 5646
E Clare.Collins@Newcastle.edu.au

This project has been approved Hunter New England
Reference Number: 16/07/20/4.03
Approval Number: HREC/16/HNE/314

Version 2 dated 24/8/16

Appendix 6.4: Volunteer Position Description

Content for volunteer recruitment advertisement: EOI for N&D blackboard:

Professor Clare Collins and a team of researchers are seeking 3rd and 4th year N&D student volunteers who enjoy talking to patients and working in the hospital environment.

In 2018 Professor Clare Collins and her team will be recruiting 600 pregnant women from the John Hunter Hospital antenatal clinic to participate in a study into diet quality and resource use. We will be asking participants complete a survey on their dietary intake in pregnancy.

Whats involved?

The John Hunter Hospital antenatal clinic is open four hours a day, five days a week. We are seeking student volunteers to be present in the clinic and invite pregnant women to complete the survey on their mobile devices or ipads (provided by UoN). As well as provide people in the waiting room with information about the study and how to participate.

Requirements:

- Training and induction: Date TBA (May 2018)
- Available for clinic times:
    - Monday, Tuesday: 1:30pm – 5:30pm
    - Wednesday, Thursday, Friday: 9am – 1pm
- Vaccination status

Desirable applicant attributes:

- Confident and comfortable approaching patients
- Mindful of patient concerns and confidentiality
- Aware of sensitivity of research topic and environment

We understand the importance of university study and practical placement and are committed to working around student schedules and will offer a flexible, rotating volunteer roster.

This is a fantastic opportunity for students to gain experience in a clinical, outpatient setting talking to patients and being in a busy hospital environment. Volunteers will receive a certificate confirming their contribution and experience working on the study.

For more information, or to apply please send your resume and cover letter to:

Zoe Szewczyk (PhD student)
Zoe.szewczyk@uon.edu.au

Appendix 6.5: Volunteer Recruitment Interview Questions

Name:	
Date:	**Time:**
Interview questions	
Why do you want to be involved in this study?	
When have you had to speak with new/unfamiliar people about sensitive topics? - Are you comfortable/uncomfortable in this situation?	
What do you think you need to keep in mind when speaking with pregnant women regarding their health, pregnancy and dietary habits?	

Notes:

_____
_____
_____
_____
_____
_____

Availabilities (considering placement, semester timetable, work, other):

_____
_____
_____
_____

Appendix 6.6: Volunteer Training and Induction Workshop Presentation

THE UNIVERSITY OF NEWCASTLE AUSTRALIA

Diet quality in pregnancy and maternal and infant outcomes: a cross-sectional survey.

Zoe Szewczyk
Ba. N&D, PhD candidate

Professor Clare Collins
Professor in Nutrition and Dietetics, The University of Newcastle Co-Director Priority Research Centre in Physical Activity and Nutrition
Global eHealth Research & Innovation Cluster

Workshop overview

- About the project
  - Who are the researchers
  - Background to the research project
  - Recruitment
- Volunteer training materials
- Project logistics and the role of volunteers
- Safety and ethical considerations
- Recruitment role playing scenarios
  - Lets practice!

Who are the researchers?

- Prof Clare Collins (UoN)
- Dr Felicity Park (Neonatal and Foetal Medicine; JHH)
- Dr Megan Rollo (UoN)
- Dr Chris Oldmeadow (Senior Statastician; HMRI)
- Dr Andrew Searles (Health Research Economist; HMRI)
- Dr Kristine Pezdirc (UoN)
- Mr Simon Deeming (Health Research Economist; HMRI)
- Dr Catherine Chojenta (UoN)
- DR Melinda Hutchesson (UoN)
- Ms Zoe Szewczyk (PhD student)

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- Adverse clinical outcomes incur major healthcare and personal costs, yet the economic impact of poor diet and excess gestational weight gain (GWG) has been neglected in research.
- In addition the direct comparison of diet quality and infant and maternal outcomes in terms of healthcare cost has not been undertaken in Australia.
- Our own research has shown pregnancy diet is related to foetal body composition, infant blood pressure and cognitive outcomes to age four.

Hypothesis

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- Media releases (including social media).

What is required from the participant?

- Give online Consent
- Complete Two Survey's:
- Questionnaires will be completed covering demographics (income, language spoken at home , self reported medical history and medications (including supplements), parity, past weight history, information on diet during pregnancy, other relevant information
- They will also complete a web-based Australian Eating Survey (AES) to assess their dietary intake

Australian Eating Survey (AES)

- Validated food frequency questionnaire
- Assess dietary intake.

What information will be collected from Medical Records/ObstetriX

- Birth complications
- Birth outcomes
- Length of gestation
- Birth weight and length
- Preeclampsia,
- Hypertension,
- Preterm birth,
- Cesarean section,
- Shoulder dystocia, macrosomia
- Small for gestational age (SGA), Large for gestational age(LGA)
- Length of stay (for mother and infant)
- Gestational weight gain and postpartum weight retention
- Breastfeeding.

Ethical considerations

- Participation in this study is entirely voluntary
- Participants will be informed about what is involved in the study and will have the opportunity to have any questions answered prior to consenting to participate. (via email)
- Participants will be free to withdraw from the study at any time without fear of consequence or any detriment to their relationship.

Harm Vs. Benefit

- Harm:
  - Potential distress to pregnant women caused by recognition of poor diet

- Benefit:
- The results of the cross-sectional survey will inform a future NHMRC grant in 2017 to develop an nutrition therapy intervention for pregnant women to improve health and infant cognition.

What is required of clinicians?

- Support
- Awareness of the study
- Allowing a member of the research team to visit clinic waiting rooms

References

1.Thangaratinam S, Rogozińska E, Jolly K, Glinkowski S, Duda W, Borowiack E, et al. Interventions to reduce or prevent obesity in pregnant women: a systematic review. Health Technol Assess. 2012;16(31):1191.

2.Guelinckx I, Devlieger R, Beckers K, Vansant G. Maternal obesity: pregnancy complications, gestational weight gain and nutrition. Obes Rev. 2008;9(2):14050.

3.Brenseke B, Renee Prater M, Bahamonde J, Claudio Gutierrez J. Current Thoughts on Maternal Nutrition and Fetal Programming of the Metabolic Syndrome. J Pregnancy. 2013;2013:113.

4.Sui Z, Turnbull DA, Dodd JM. Overweight and Obese Women's Perceptions About Making Healthy Change During Pregnancy: A Mixed Method Study. Matern Child Health J. 2013;17(10):187987.

5.Blumfield M, Hure A, MacDonaldWicks L, Smith R, Simpson S, Giles W, et al. Dietary balance during pregnancy is associated with fetal adiposity and fat distribution. Am J Clin Nutr. 2012;96(5):103241.

6.Blumfield M, Nowson C, Hure A, Smith R, Simpson S, Raubenheimer D, et al. Lower proteintocarbohydrate ratios in maternal diet are associated with increased childhood systolic blood pressures up to 4 years of age. submitted. 2015.

7.Collins C, Hure A, Blumfield M, Drysdale K, Smith R. Higher proteintocarbohydrate ratios in maternal diet are associated with higher intelligence quotient at 4 years. Abstract submitted to DoHAD Australia 2015 (Melbourne April) id# 181389694. 2015.

8.Ulker A. Body size at birth, physical development and cognitive outcomes in early childhood: evidence from the Longitudinal Survey of Australian Children. Educ Econ. 2014.

Questions?

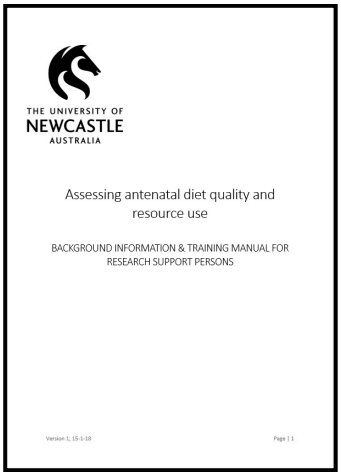
- Does anyone have any questions or comments from the previous content?

Next…

Volunteer training materials

Volunteer training materials

- For your personal use
- Please feel free to make notes
- A reference copy will be available in resource kits
- Please review this manual before your first session and bring any questions or suggestions with you.


THE UNIVERSITY OF NEWCASTLE AUSTRALIA

Assessing antenatal diet quality and resource use

BACKGROUND INFORMATION & TRAINING MANUAL FOR RESEARCH SUPPORT PERSONS

Version 1, 15-1-18 Page | 1

Next…

Project logistics and the role of volunteers

Your role within the project

You have three key roles within the clinic:

- Recruit patients to complete the survey in the waiting room.
- Assist participants to complete the survey using a touch-screen iPad.
- Maintain a study log-book and resource kit

Role 1: Recruit

You will be located in the John Hunter Hospital antenatal clinic waiting room - only! To recruit eligible women into the study we will ask you to:

- Approach women in the clinic waiting rooms and confirm they are eligible to participate. You may have to ask a few screening questions. These may include:
  - Are you over 18 years of age?
  - Have you completed our survey before?
  - You will be able to judge yourself if the participant can comfortably speak and read English, and if they are comfortable and well enough to participate.
  - Inform the patient that they need to provide their medical reference number (MRN) which is located on their medical documentation that they will provide to their health professional.

Role 1: Recruit

For women who do not want to complete the survey in the waiting room, invite them to join our mailing list and we can send them the link to the survey and they can complete it in their own time

Diet quality in pregnancy and maternal and infant outcomes: a cross sectional survey.			
By providing your name and contact details you are consenting to being emailed a link to the diet quality in pregnancy survey.			
Name:	How many weeks pregnant are you:	Date of birth:	Email address:

Role 2: Assist

- Assist participants to complete the survey using a touch-screen iPad.
- Keep iPads/tablets secure
- Answer participants questions
- Report any issues with the survey, tablets or recruitment

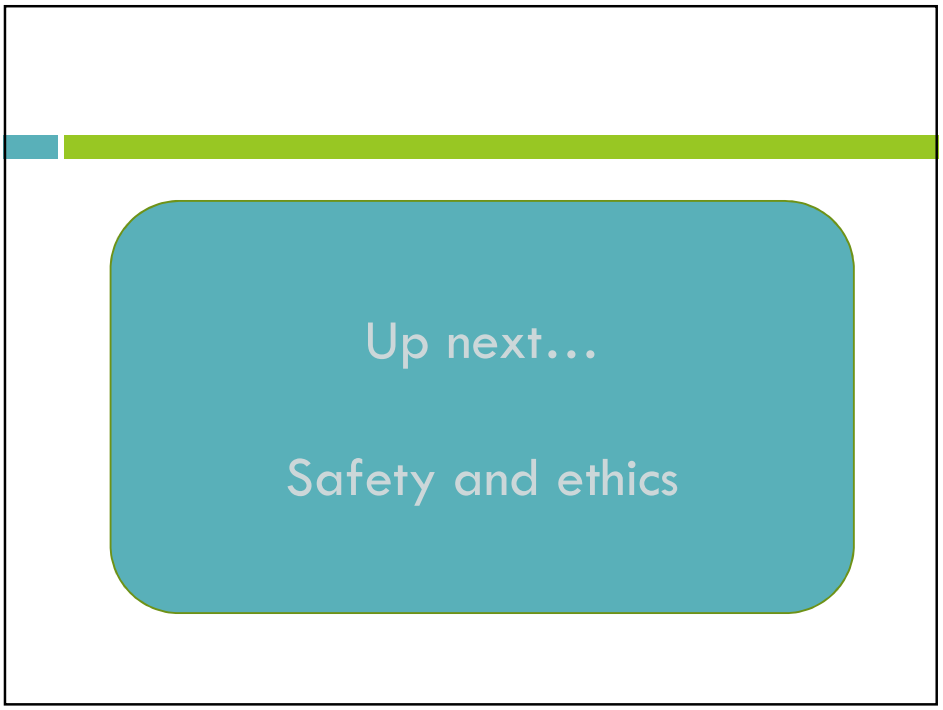
Role 3: Maintain

- Maintain a study log-book
- Collect and return iPads/tablets to the resource kit and leave it with Zoe or in an allocated place.
- Report any iPad/tablet issues
- Report any issues with survey
- Return contact and response log data to Zoe:

Contact and response log					
Volunteer name:		Clinic attendee responses			
Date:	Number eligible women approached	Not interested	Completed survey	Start but didn't finish	Added to mailing list

Questions?

- Does anyone have any questions or comments from the previous content?



Safety and hazards when volunteering

- Travelling
- Distressed patients
- Physical contact with patients
- Illness
- Clinic locations
- Clinic operations

Ethical considerations and obligations

- Contact details for Hunter New England Human Research Ethics Committee and for investigators
- Obligated to follow the recruitment procedures approved by the ethic's committees
- Obligated to report any adverse events, and an annual progress report

- Voluntary and can end the survey at any time without providing a reason
- Private and confidential
- No impact on their care

Scheduling logistics

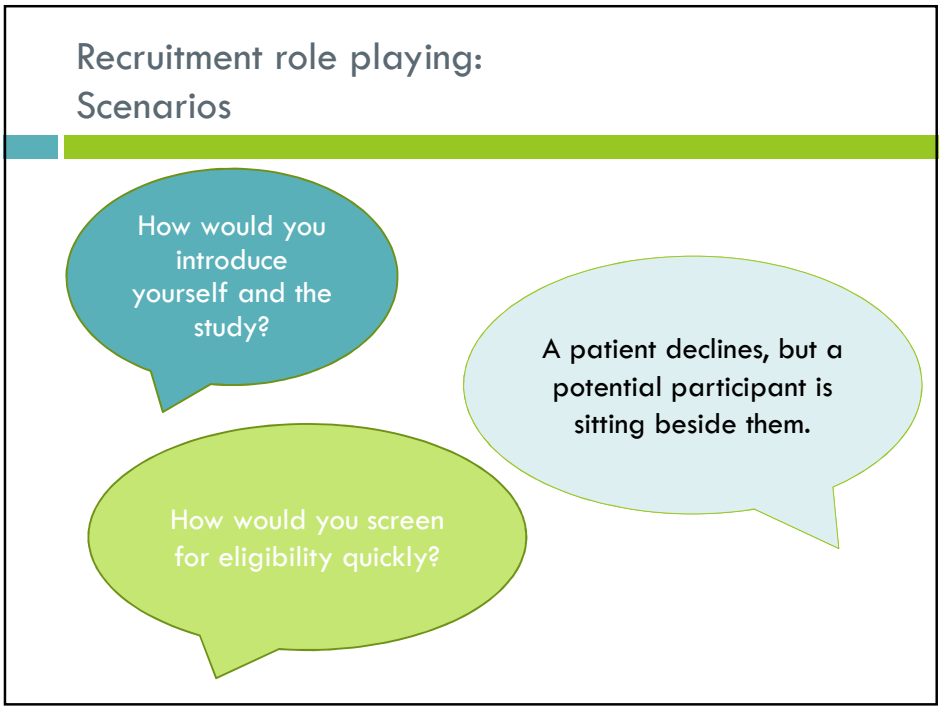
- Zoe is responsible for scheduling.
- Will be based on your preferences.
- Contact Zoe in advance if you know you will be unavailable.
- Please do not visit any out-patient clinics while feeling ill.
- We will ask you to visit an out-patient clinic at least once a week.
- We will work around your placement and work schedule

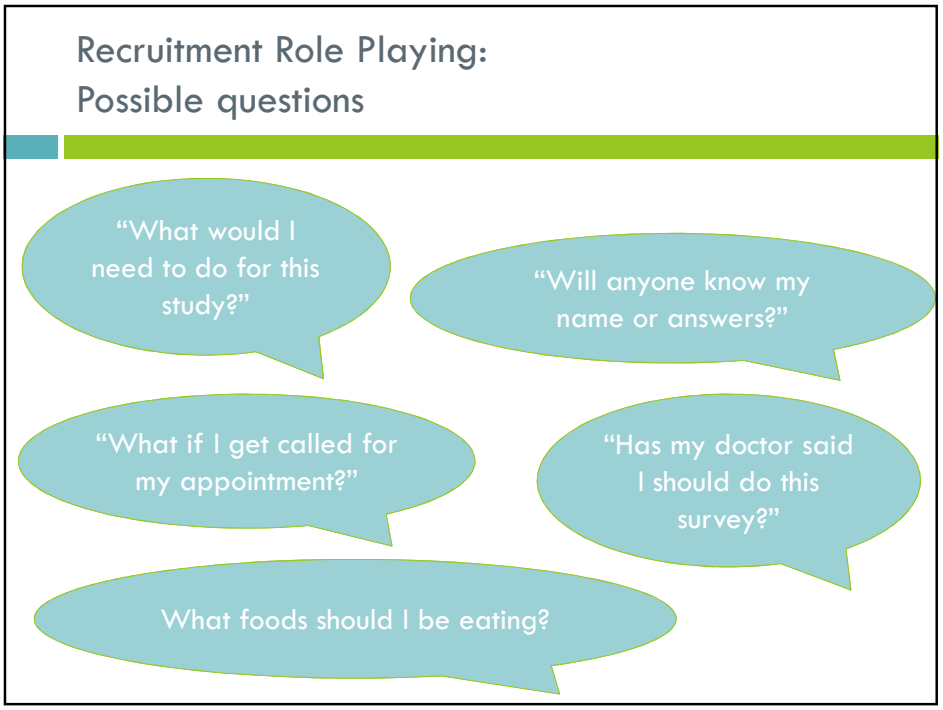
Immunizations and parking

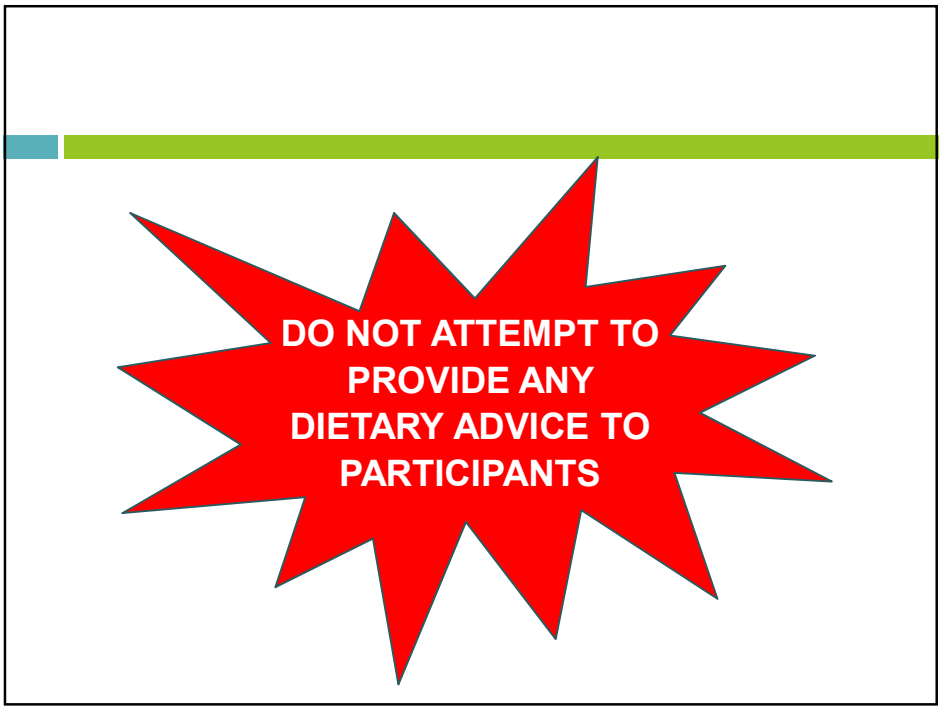
- Please provide a record of your immunizations (the same you use for placement)
- Parking at HMRI carpark
  - Unfortunately this is not guaranteed, we will endeavour to have parking available.
  - Use public transport where possible

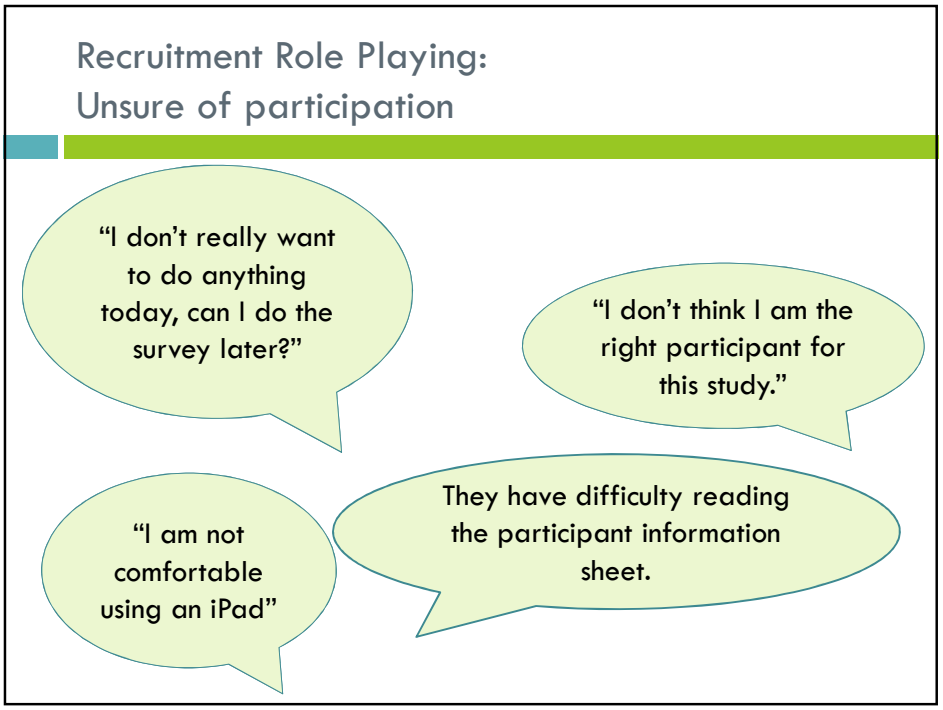
Up next…

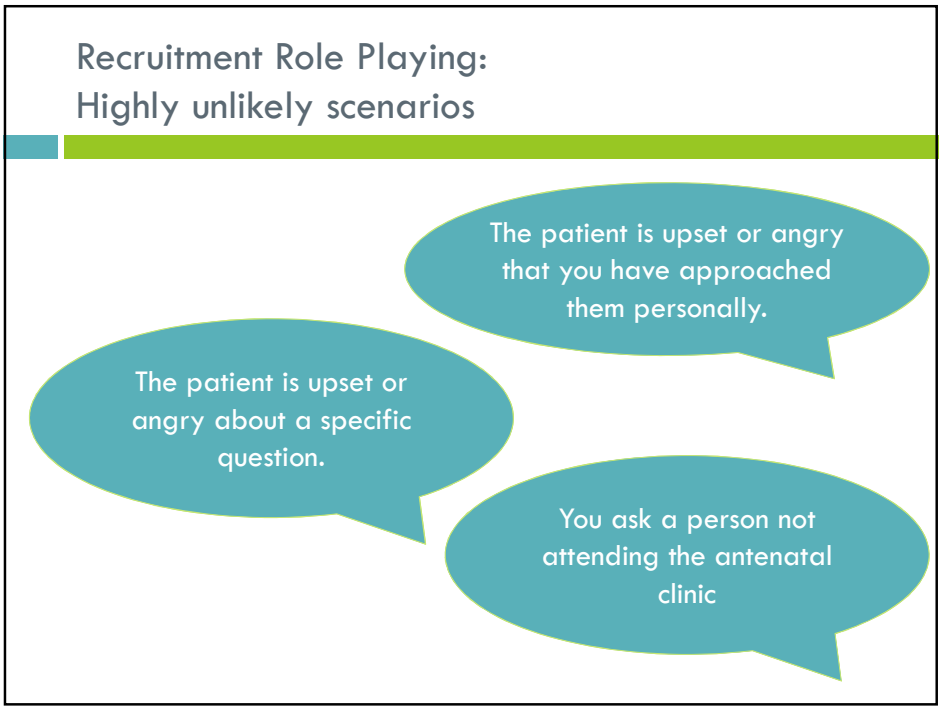
Recruitment role playing scenarios

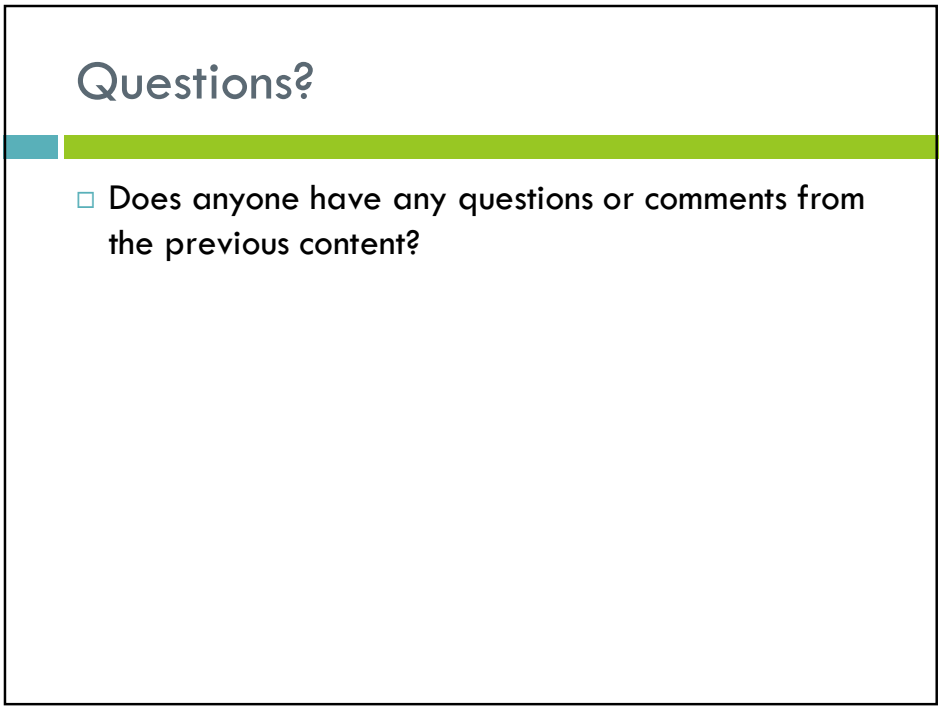

Recruitment role playing:
Scenarios
How would you introduce yourself and the study?
A patient declines, but a potential participant is sitting beside them.
How would you screen for eligibility quickly?

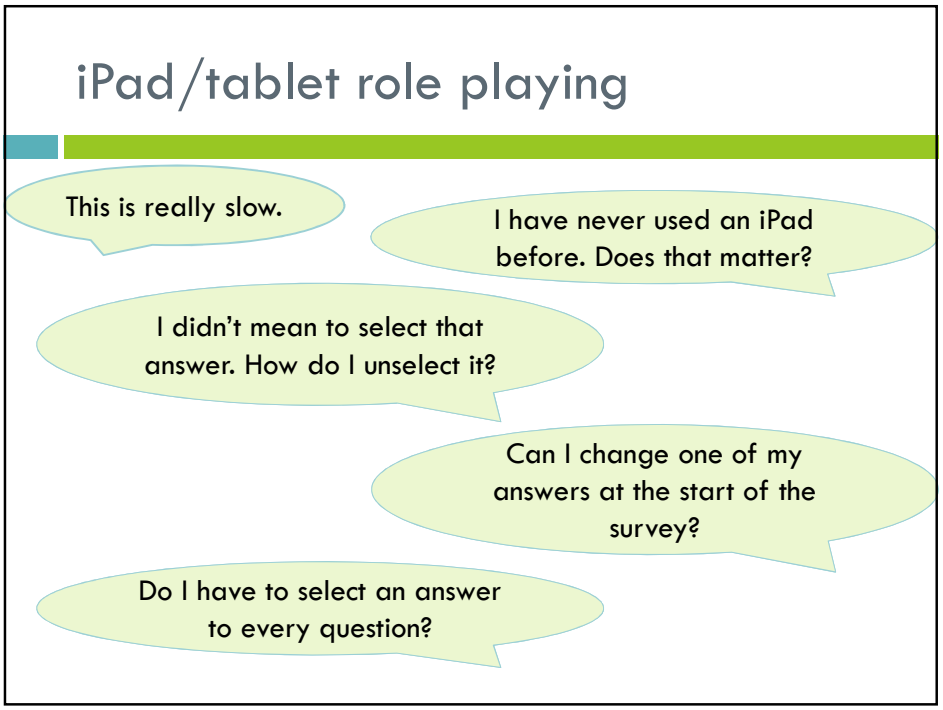

Recruitment Role Playing:
Possible questions
"What would I need to do for this study?"
"Will anyone know my name or answers?"
"What if I get called for my appointment?"
"Has my doctor said I should do this survey?"
What foods should I be eating?

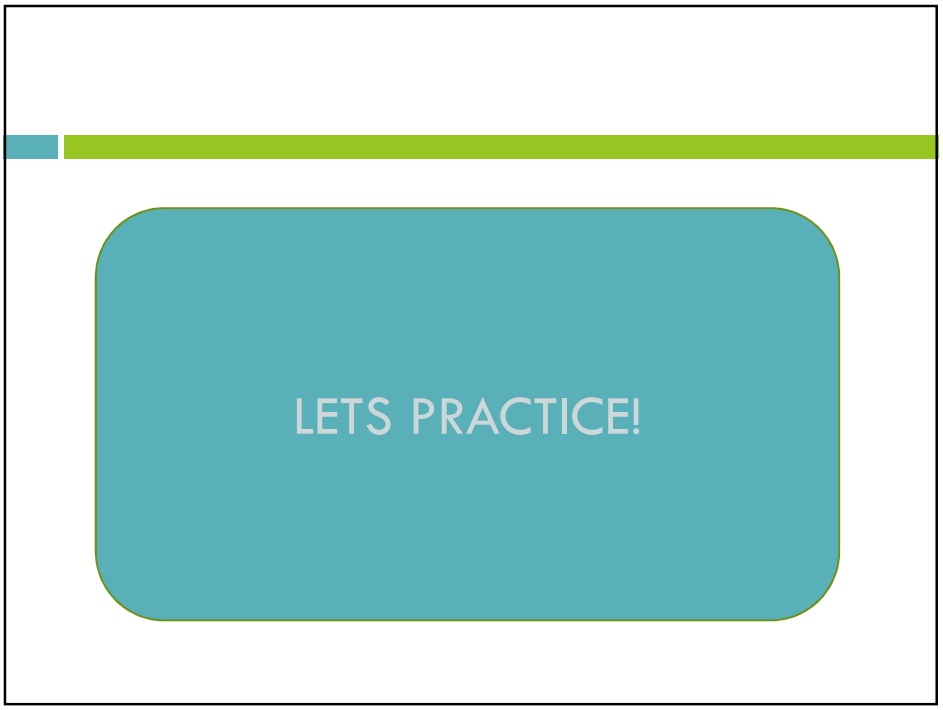

DO NOT ATTEMPT TO PROVIDE ANY DIETARY ADVICE TO PARTICIPANTS

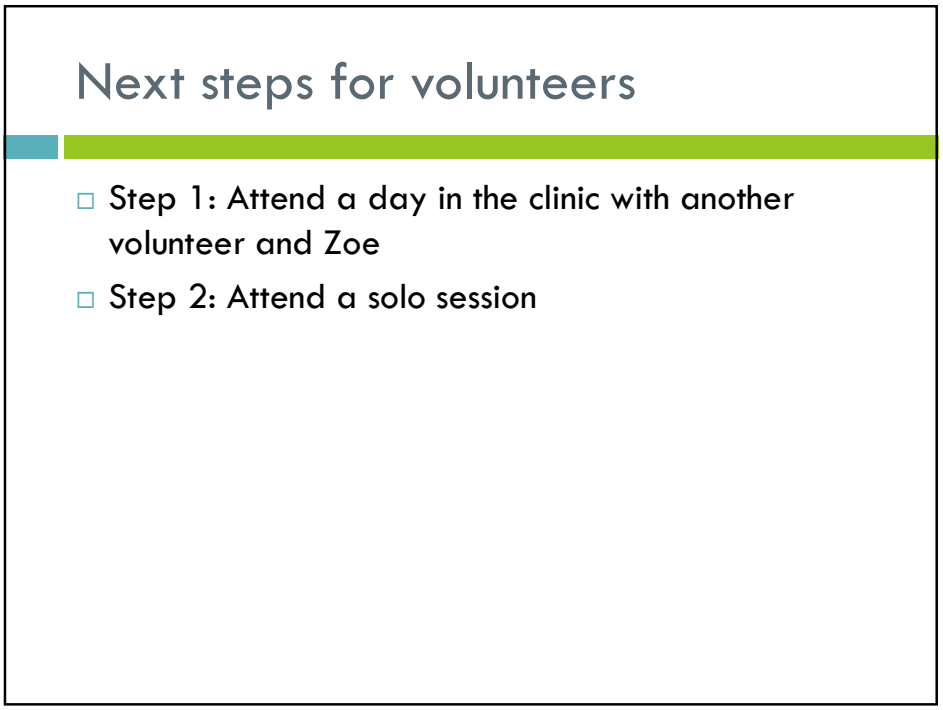

Recruitment Role Playing:
Unsure of participation
"I don't really want to do anything today, can I do the survey later?"
"I don't think I am the right participant for this study."
"I am not comfortable using an iPad"
They have difficulty reading the participant information sheet.

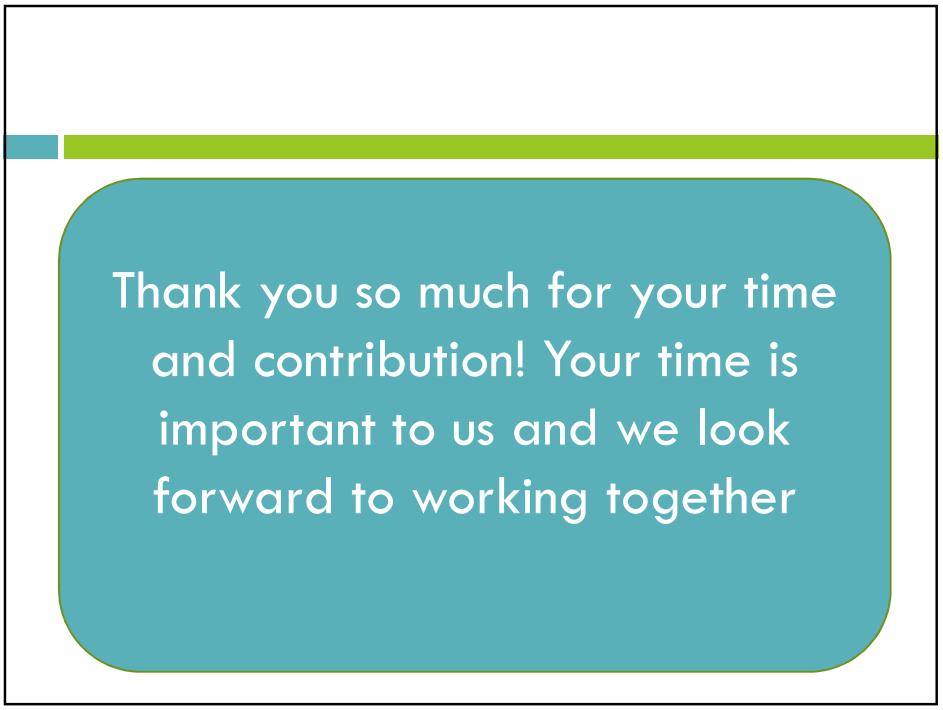

Recruitment Role Playing:
Highly unlikely scenarios
The patient is upset or angry that you have approached them personally.
The patient is upset or angry about a specific question.
You ask a person not attending the antenatal clinic


Questions?
Does anyone have any questions or comments from the previous content?


iPad/tablet role playing
This is really slow.
I have never used an iPad before. Does that matter?
I didn't mean to select that answer. How do I unselect it?
Can I change one of my answers at the start of the survey?
Do I have to select an answer to every question?


LETS PRACTICE!


Next steps for volunteers
Step 1: Attend a day in the clinic with another volunteer and Zoe
Step 2: Attend a solo session


Thank you so much for your time and contribution! Your time is important to us and we look forward to working together

Appendix 6.7: Volunteer Recruiter Manual

Assessing antenatal diet quality and resource use

BACKGROUND INFORMATION & TRAINING MANUAL FOR RESEARCH SUPPORT PERSONS

Contents

Introduction

Thank you for helping us with recruitment for our study "Diet quality in pregnancy and maternal and infant health outcomes: a cross sectional survey". The manual outlines the background and rationale behind this study and your role in assisting with data collection.

Your role is crucial to the success of this study. The data collected is very important and will be used by a team of University of Newcastle researchers and local health care professionals. It is hoped the results will help to understand how a mother's diet during pregnancy affects maternal and infant health outcomes and resource use.

This manual aims to provide you with information that will help you to complete your tasks in a way that ensures consistency across all volunteers, and meets ethical and safety obligations. Please keep this manual for your personal reference, and feel free to write notes on any of the pages.

If you have any questions about the information provided in this manual, please contact Zoe Szewczyk

Phone: 0422955392
Email: zoe.szewczyk@uon.edu.au

The research study team

This research project is being conducted by investigators from the School of Health Sciences at the University of Newcastle, and the Hunter Medical Research Institute (HMRI). The research is led by Professor Clare Collins, Dr Megan Rollo and Dr Kristine Pezdirc, Dr Melinda Hutchesson, Dr Catherine Chojenta from the Faculty of Health and Medicine at the University of Newcastle, Dr Chris Oldmeadow, Dr Andrew Searles, Zoe Szewczyk and Simon Deeming from Hunter Medical Research Institute and Dr Felicity Park from the John Hunter Hospital.

Background

Poor pregnancy eating patterns are common(1) and contribute to excessive gestational weight gain, hypertension, preeclampsia, gestational diabetes (GDM), preterm birth, perturbations in birth weight, birth defects and caesarean section.(2) Calls have been made for trials of personalised diet interventions in pregnancy (3) to educate pregnant women about diet related maternal and infant risks.(4) We urgently need novel, scalable ways to assist pregnant women to make nutrient rich, healthy food choices. Our own research has shown pregnancy diet is related to foetal body composition,(5) infant blood pressure(6) and cognitive outcomes to age four.(7) The Longitudinal Study of Australian Children found a robust relationship between birth size and cognitive scores to age 67 years, even after controlling for physical development.(8) Adverse clinical outcomes incur major healthcare and personal costs, yet the economic impact of poor diet and excess gestational weight gain (GWG) has been neglected in research. In addition, the direct comparison of diet quality and infant and maternal outcomes in terms of healthcare cost has not been undertaken in Australia. Therefore, this study will look at examining the cost implications of poor diet quality in pregnancy on maternal and infant outcomes.

A cross sectional survey will be conducted amongst pregnant women 28-36 weeks (third trimester) to examine the relationship between diet quality and pregnancy and birth outcomes. We will simulate the healthcare costs and compare the costs for those with high versus low diet quality.

600 females aged 18 years and over will be invited to participate in the study from the Hunter New England Area. Clinical pregnancy and infant outcomes will be obtained from their medical records and Obsetrix following birth of their infant. In addition cost outcomes related to hospital admissions will be collected from their medical record numbers.

References:
1. Thangaratinam S, Rogozińska E, Jolly K, Glinkowski S, Duda W, Borowiack E, et al. Interventions to reduce or prevent obesity in pregnant women: a systematic review. Health Technol Assess. 2012;16(31):1191.
2. Guelinckx I, Devlieger R, Beckers K, Vansant G. Maternal obesity: pregnancy complications, gestational weight gain and nutrition. Obes Rev. 2008;9(2):14050.
3. Brenseke B, Renee Prater M, Bahamonde J, Claudio Gutierrez J. Current Thoughts on Maternal Nutrition and Fetal Programming of the Metabolic Syndrome. J Pregnancy. 2013;2013:113.
4. Sui Z, Turnbull DA, Dodd JM. Overweight and Obese Women's Perceptions About Making Healthy Change During Pregnancy: A Mixed Method Study. Matern Child Health J. 2013;17(10):187987.
5. Blumfield M, Hure A, MacDonald Wicks L, Smith R, Simpson S, Giles W, et al. Dietary balance during pregnancy is associated with fetal adiposity and fat distribution. Am J Clin Nutr. 2012;96(5):103241.
6. Blumfield M, Nowson C, Hure A, Smith R, Simpson S, Raubenheimer D, et al. Lower protein to carbohydrate ratios

About the study

Who is eligible to complete the survey?

Women will be eligible to complete the survey if they are:

- Pregnant: Women can complete the survey between 28-36 weeks gestation. Women less than 28 weeks will be invited to join the mailing list and receive an email reminder when they reach 28 weeks gestation.
- Are over 18 years
- Will give birth at the John Hunter Hospital
- Can read and write in English
- Can provide informed consent. Informed consent means that the patient knows:
    - Their participation is voluntary
    - What they will be asked to do
    - Any risks or benefits to participating.

What will participants do?

At each antenatal clinic, women will be recruited by volunteer Research Support Persons (You!). Patients will be:

- Provided an information sheet describing the study and can ask you any questions.
- Invited to complete the iPad survey.
- If they agree to participate, women will complete the iPad survey in the waiting room before their appointment. The survey will take approximately 25-35 minutes.

Patient information statement

Once participants have completed the screening questions and are invited to complete the Australian Eating Survey, they will be presented with the following participant information statement. Please familiarise yourself with this statement before your first shift.

The association between diet quality during pregnancy and maternal and infant health and health care costs

INFORMATION STATEMENT FOR PARTICIPANTS

Document Version; 5 dated 28/02/201704/10/20/16

Introduction

You are invited to participate in the study identified above which is being conducted by Professor Clare Collins, Dr Megan Rollo and Dr Kristine Pezdirc, Dr Melinda Hutchesson,,Dr Catherine Chojenta from the Faculty of Health and Medicine at the University of Newcastle, Dr Chris Oldmeadow, Dr Andrew Searles, Zoe Szewczyk and Simon Deeming from Hunter Medical Research Institute and Dr Felicity Park from the John Hunter Hospital.

What is the research about?

The purpose of the study is to examine the diet quality of pregnant women and the association between diet quality, pregnancy and birth outcomes and health care costs.

Who can participate in the study?

We are seeking pregnant women who are between 28 and 36 weeks gestation, aged 18 years and above and who are proficient in the English language participate in this study. We would like to enrol women who are from the Hunter New England Area.

What choice do you have?

Participation in this study is entirely your choice. You will be only included in the study if you have provided informed consent online. Whether or not you decide to participate, your decision will not disadvantage you. If you do decide to participate, you may withdraw from the study at any time without giving a reason and have the option of withdrawing any data that identifies you.

What would you be asked to do if you agree to participate?

If you agree to participate in this study, you will then be asked to complete two surveys. The first online survey will ask you some questions about your background (e.g. age, education), health status, current and previous pregnancies and pregnancy-related healthcare. The second survey (the Australian Eating Survey) will ask you about your usual food intake.

Your role in the study

You have three key roles within the clinic:

1. Recruit participants to complete the survey in the waiting room.
2. Assist participants to complete the survey using a touch-screen iPad.
3. Maintain project resources

What we need before commencing your first shift

- Student ID and photo ID for verification
- Proof of enrolment or qualifications
- Vaccination record card for health care workers and students
- Mandatory training and induction

Project materials required at every shift

- Name badge/ID
- Contact and response log
- Pen
- Recruitment flyers: to be offered to all participants before they begin the survey.
- iPad
- Copy of participant information statement

Please note that all documents and project materials will be supplied by The University of Newcastle, and stored at the Hunter Medical Research Institute. There will be a copy of all necessary resources available in the research project kit, stored in the antenatal clinic locker.

What to wear in whilst volunteering

Please wear your standard placement uniform whilst working in this volunteer position. You must wear your student ID at all times whilst working in the clinic as a volunteer.

Clinic location

The antenatal clinic is located within the outpatient clinic at the John Hunter Hospital.

Enter the clinic via the main hospital entrance (next to the major bus stop on Kookaburra circuit). Once entering the hospital entrance glass sliding doors, there is a long corridor to the left that takes visitors past a bathroom, the HAPS pathology waiting room and into a large waiting room with a reception desk on the left hand side – this is one of the two waiting rooms patients will be located in during their visit to the antenatal clinic.

Please note, if you have enter the hospital entrance glass sliding doors and pass a second set of doors and a café, you have gone too far – turn around.

Clinic hours

Clinic hours are the same as rostered shifts.

Monday 1pm – 5pm

Tuesday 1pm – 5pm

Wednesday 9am – 1pm

Thursday 9am – 1pm

Friday 9am – 1pm

These hours are set and do not change. They are the times that the specialist doctors have rooms booked in the outpatient clinic. It is advisable you arrive at the clinic 10 minutes prior to the start time so you can pick up the iPad, put your bags away and check the iPads are working and ready to go.

Your role in recruiting patients

You will be located in the John Hunter Hospital antenatal clinic waiting room (only!), where you will talk to eligible women. To recruit eligible women into the study we will ask you to:

1. Approach women in the clinic waiting rooms and confirm they are eligible to participate. You may have to ask a few screening questions. These may include:

- Are you over 18 years of age?
- Is this your first time to the clinic?
- You will be able to judge yourself if the participant can comfortably speak and read English, and if they are comfortable and well enough to participate.

Inform the patient that they need to provide their medical reference number (MRN) which is located on their medical documentation that they will provide to their health professional.

2. Describe the study and provide the appropriate information sheet:

The flyer has been approved by ethics committees, and has detailed information on: what the participants will be asked to do and, why this study is important. This document will help the patient decide if they would like to complete the survey.

3. If the patient is willing to participate, please start the iPad and hand it to the patient.
4. If the patient wishes to stop the survey early or is called to an appointment you are to take the iPad back from them and press 'exit'. This will save their results so far and generate an email response encouraging them to complete their survey later. DO NOT EXIT THE APPLICATION AT ANY STAGE DURING A SURVEY - this will delete all their survey responses.

It is recommended you highlight that the survey is voluntary, confidential, will not affect the care they receive and they can stop the survey at any time.

Some advice before you commence your shift

Remember all conversations should be brief and focused on the research. Whilst it may seem natural to share experiences or stories with participants, these types of conversations could interfere with the results of the research. If a participant wants to discuss personal issues or feelings at length, you should suggest that they talk to their family, the midwives, doctors or dietitians providing their care.

In situations where participants ask for medical advice regarding health conditions, please refer participants to speak to their healthcare provider.

Suggested text for approaching patients

Example 1:

Hi, my name is _____. I am helping the University of Newcastle conduct some research. I am here today to ask patients if they are willing to complete a survey before their appointment.

Are you happy for me to discuss it with you?

Here is a flyer about the survey (provide copy of flyer). The survey will help researchers from the University better understand how the food you eat affects your health and the health of your baby, in terms of your needs whilst in hospital. It is confidential, will not affect the care that you receive, and you can stop doing the survey at any time. It would be great if you could look over the flyer and let me know if you are interested.

If interested give them an iPad to complete the survey. Explain that if they get called into their appointment they can save the survey and complete it when they finish their appointment or online at home.

If patients decline, ask if they *would be interested in having the survey sent to their email address and can fill it in later.* If the patient agrees, provide them with the participant log and a pen to provide their contact details.

Example 2:

Hi, my name is _____. I am helping the University of Newcastle survey pregnant women about the foods they eat. Are you interested in completing a survey whilst you wait?

No. *That's ok, thanks for your time.*

Yes. *We are surveying women about the foods they eat whilst they are pregnant and how that impacts the care they need when their baby is born. Are you planning on having your baby here at the John Hunter Hospital?*

No. *Unfortunately we are only surveying women who will be delivering here at the JHH. Thanks for your interest.*

Yes. *Great! There are a few other questions in the survey that will check if you are eligible to be included in the study. If you do complete the study, you can choose to have a personalised report of your diet sent to you once your baby is born. *Hand over iPad with survey open* you will need your medical record number to complete the survey, it is located on your hospital forms.*

If you have any questions just ask, and I will happily help you out. When you're finished you can just hand the iPad back. If you get called to your appointment or need to leave, please don't close the application, just hand the iPad back to a volunteer and we will close the survey for you.

Example 3 - write your own:

_____
_____
_____
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Example 4 - write your own:

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Using the iPads

The iPads and project resource kit will be stored in the antenatal clinic nurses lockers. Volunteers will be using the top right locker with the black number lock. The locker key is **248.** Under no circumstances is anyone apart from volunteers and Nurse Unit Manager Irene Chapman to access this locker.

Zoe will show you where the lockers are on your first shift. If you are unsure, please ask the staff to direct you to the lockers. At the start of each shift, collect your materials from here.

Getting started

Turn on the iPad using the home button (button at the center, bottom of the iPad).

The password is: **8663** (the letters UNND)

If battery is less than 10% do not use, please find a power point and charge the iPad. Do not leave the iPad unsupervised whilst charging.

If you have a quiet period in the clinic, please charge the iPad. Please make a note on the contact and response log that you needed to charge the iPad during clinic hours.

iPad password:
UNND

Locker code:
248

REDCap PIN:

866318

How to assist participants to complete surveys

1) Access the iPad with the password 8663 (or the letters UNND)
2) Select the 'REDCap' application
3) Login with the following details:
   Username: **uon**
   Password: **866318**
4) Select 'My Projects'
5) Select the 'Diet Quality and Resource Use Survey'
6) You will be directed to the 'Diet Quality and Resource Use Survey' homepage.
   I. Please note the 'Last Full Sync' time and date. If the device has not been synced by the last person, please do this immediately.
7) Select 'Collect Data'
8) Select 'Screening Questionnaire'
9) Select 'Create new record'

10) Hand iPad to patient and instruct them at the end of each page to select 'form status – complete' and 'save and go to next instrument'.
11) Once the participant has completed the survey collect the iPad, check that she has saved the form (you may have to select "save record" and return to the instrument home page).
    I. Note: if the participant leaves the survey part way through the survey you will return to that instrument home page. You may need to select the back arrow '<' button at the top left corner of the screen to return to the survey home page.

Please note:

- "Save Record" takes you back to the home screen. When you upload the data to the database his will generate the automated email to those who did not complete the entire survey. If the participant accidentally selects this option, you can click on their survey ID number and are taken back to where you left off.
- "Save and continue" saves where you are at and lets you select that you would like to continue to the next instrument.
- "Save and go to Next Instrument" is the box you want to click to finish one page of the survey and continue onto the next.

Please remain within the clinic whilst the patient is completing the survey on the iPad, and assist with any questions they have.

If a patient has to leave the waiting room and has not completed the survey, take the iPad from the patient. Select "Save record" at the bottom of the survey page. It is crucial that you save the data, and exit the survey at the point the patient has finished at, as it will send an automated email with the remained of the survey to that patient.

Uploading saved surveys to the database:

The iPad allows us to collect and store participant data directly on the iPad without having internet connectivity. This means that you will be carrying saved patient data on the iPad, and must upload it to the server throughout the shift and at the end of every shift. To upload saved patient surveys to the network you will be required to return to the HMRI, or within range of the UON-wifi that is located at the HMRI.

1) Return to HMRI or within range of HMRI-UON wifi.
2) Check that you have internet connection, the wifi symbol will be displayed in the top left hand corner of the iPad screen, and should have all three bars of connectivity. (See image)
    a. If you do not have internet connection, you can connect manually via the settings.
3) Select the 'back arrow' **<** button on the top left corner of the iPad until you return to the "Diet Quality and Resource Use Survey" homepage. Here you will see the number of records you are going to upload to the database.
4) Select "Send Data to Server"
5) Select "Begin Send of All Data"
6) Allow upload to complete
7) Wait until you see "Sync successfully completed" in green
8) Select "Refresh setup and data (recommended)"
9) It will ask you "Do you want to delete your local copy of the project data and configurations and then install new current versions?" select "**Proceed**"

10) It will then ask you "This will delete ALL DATA on the app for this project. Are you sure?" select "**Proceed**"
11) If asked do you want to download all [#] records from the project, or do you want to leave the project blank in the app?" select "**Do NOT Download Records"**
12) At this point you will return to the home screen, select "**Collect Data"** and continue with collecting new patient data.

At the end of your shift:

Please return the iPads to the lockers and complete the Contact and Response Log. If there have been any issues throughout your shift report them to Zoe.

Contact and response log

There will be a study log book in the project resource kit. Ensuring that the study log book is completed accurately is important because the research team will use this to monitor the study's progress. It is also another form of research data because it provides information on how many patients were ineligible or unwilling to participate. The log is to be completed and returned to the project resource kit at the end of each shift.

The contact and response log will look like this:

Contact and Response Log					
Volunteer name:		Clinic attendee responses			
Date:	Number eligible women approached	Not interested	Completed survey	Start but didn't finish	Added to mailing list

Did you have any issues with participant recruitment or the iPad equipment?

_____
_____
_____
_____
_____

Safety and hazards

- Travelling: Be careful travelling to and from the clinic
- Distressed patients: Refer distressed patients to clinic staff
- Illness: Do not come to work if ill.
- Clinic operations: Tell clinic staff that you are there and why. The midwife managers and service managers know that we will be there.

Frequently asked questions by volunteer researchers

What will this information be used for?

This information will contribute towards multiple research projects at the University of Newcastle and Hunter Medical Research Institute. This research is one of a number of projects being run by the University of Newcastle and Professor Clare Collins. This study will focus on the relationship between dietary intake and resource use.

Can I switch shifts with a fellow volunteer?

Yes, you can organise your own roster changes and inform Zoe once they are confirmed between both students.

What if I need to leave early or start late?

If it can be avoided, we would like to minimise shortened hours. It would be preferable to reschedule your shift rather than leave early or late.

What if I am running late to a shift?

Cars break down, buses don't turn up, and life gets in the way. If you're running late send Zoe a text message and arrive safely when you can.

What if I am sick on the morning of my shift?

If you are unwell, please do not attend your shift. Contact Zoe and inform her you are unable to attend your shift. Stay home, rest up and return when you are ready.

Where will I park?

Due to limited parking within the JHH grounds, we encourage you to use public transport wherever possible. There is street parking available on

Where do I get study materials from?

These are kept in the project resource kit which is kept in the antenatal clinic locker.

How do I demonstrate the iPad operation and survey navigation?

Students will be trained in using the iPad and navigating survey. Students are not to attend clinic without attending a training session.

What if the participant is called into their appointment before finishing?

We have to be very careful not to interfere with patients' appointments and the clinic staff. If the participant is called into their appointment, you will need to pause the survey. Let them know they have the choice to return after their appointment and complete the survey, but they are not

obligated. Please do not approach patients after their appointment, but wait for them to return to you if they are willing. If they do not return and they provided their email address, they will be contacted via email to complete the remainder of their survey.

What if I am unwell throughout my shift?

If you are unwell, go home! Contact Zoe to let her know you are leaving and arrange for the other student to hand back the iPad's.

Is there any funding available for paid work?

Unfortunately, not at this stage.

What do I gain from volunteering?

Volunteering is an opportunity for students to gain professional experience and develop an array of skills which will benefit their education and employment opportunities. In this volunteer role, students will spend the vast majority of their time in a hospital and clinical environment speaking with patients, midwives and hospital staff. In this environment students are provided the opportunity to develop interpersonal communication skills. It will require you to approach new people, and practice motivational interviewing skills in a crowded and public environment. Experience and confidence in the clinical environment is highly desirable to employers, particularly for those students planning to work as clinical dietitians.

This role will also expose students to the tasks required for higher degrees in research and academia. Volunteers are an important part of data collection and study recruitment processes. In this role, volunteers will have the opportunity to be exposed to the realities of working in research.

At the end of your time as a volunteer you will receive a certificate confirming your role and work experience in this role.

Questions frequently asked by patients

How long will it take?

It is expected that the survey will take approximately 25-35 minutes to complete.

Why should I participate in this research project?

This survey will be used to gain a better understanding of how the food women eat during pregnancy, impacts their health outcomes and the health outcomes of their baby. If you would like more detail, I would be happy to review the study flyer and participant information statement with you.

How will the researchers use the information collected?

The research will be used by a team of local researchers and clinicians and be published. Your personal information will not be identifiable in any published documents. If you would like more detail, I would be happy to review the participant information sheet with you.

Will my information be kept private?

If you choose to complete the surveys, your privacy will be protected. Individual participants will not be identified in any of the information. Your data would be stored securely and only the research

team will have access to these details. If you would like more detail, I would be happy to review the participant information sheet with you.

Can you provide me with any advice?

In situations where participants ask for medical advice regarding health conditions, please refer participants to speak to their healthcare provider (dietitian, doctor, nurse etc).
If patients ask for directions on how to see a dietitian in the antenatal clinic, ask them to speak with their Doctor for a referral.

Students are not to provide dietary advice or forward patients to particular health care professionals.

Will the doctor/ hospital see my answers?

Your doctor and hospital will not see individual responses. Any identifying information will be stored securely in a password protected file and will only be accessed by the researchers.

Can I complete the survey later?

If you are not able to complete the survey at your appointment today, you can place your name and email on a contact list and we will email the survey to you.

Diet quality in pregnancy and maternal and infant outcomes: a cross sectional survey.			
By providing your name and contact details you are consenting to being emailed a link to the diet quality in pregnancy survey.			
Name:	**How many weeks pregnant are you:**	**Date of birth:**	**Email address:**

Adverse events

An adverse event is any instance where participation in the research distressed a patient. It is very important that adverse events are reported to the research team. Ethics committees are concerned with patient welfare, and have carefully reviewed this project before giving approval. We have approval from our ethics committees, and are required to report any adverse events.

What do I do when a participant becomes upset or distressed?

If a participant becomes upset, ask them if they would like to stop the survey. Encourage the participant to talk to their midwife about what has upset them. Ensure that the participant knows who they can contact if they have concerns about the research. The contact details Zoe Szewczyk and Clare Collins are provided on the information statement. Please contact a member of the research team and let them know of instances where a patient has become upset or has a complaint about the research.

What do I do when a patient wishes to withdraw from the study after starting the survey?

If the patient wishes to withdraw from the study completely:

- Thank the patient for taking the time to complete what they have,
- Clarify if they wish to withdraw all of their data, or are happy to leave their completed data in the survey
- If the patient wishes to withdraw their data, note the time and their birthdate and a member of the research team will erase the data.
- If the participant does not want their partially completed information erased, submit the data using the bar in the top right corner.
- If the patient mentions the reason they are withdrawing please inform the research team of this.

What do I do when I am unable to answer a patient's question?

For assistance with patient enquiries, please contact Zoe Szewczyk and she will direct your question to the appropriate key contact. If the request is not urgent, send an email detailing your enquiry.

Your ethical rights and responsibilities

The *National Statement on Ethical Conduct in Human Research (2007)* provides guidelines on the requirement for consent. These guidelines state that '*consent should be a voluntary choice, and should be based on sufficient information and adequate understanding of both the proposed research and the implications of participation in it.'*

This requires an adequate understanding of the purpose, methods, demands, risks and potential benefits of the research. The process of communicating information to participants and seeking their consent aims to achieve mutual understanding between researchers and participants which requires an opportunity for participants to ask questions and to discuss the information and their decision with others if they wish.

Ethics:

This project has been approved by Hunter New England Human Research Council HREC/16/HNE/189 and by John Hunter Hospital Governance.

Key contacts

A member of the research team will be in regular contact with you. Please let them know if you experience any problems, or if you notice that participants are having difficulty with particular parts of the surveys. Please feel free to phone a member of the research team at any time should you have a question or concern.

FIRST CONTACT: Zoe Szewczyk (0422955392; zoe.szewczyk@uon.edu.au)
SECOND CONTACT: Megan Rollo (Megan.Rollo@newcastle.edu.au)
THIRD CONTACT: Clare Collins (Clare.Collins@newcastle.edu.au)

Chapter 7 Appendices

Appendix 7.1: Manuscript Supplementary File

Supplementary content to be viewed along with the methods section of the manuscript:

There are three roles that variables can assume in a DAG: confounder, mediator, or collider. A confounder is ancestor to both the exposure and the outcome, where an ancestor is a variable that has temporal precedence and a suspected causal influence. For example, in Figure 2, diet quality is a confounder with respect to the relationship between the exposure BMI and the outcome resource use. An unconfounded estimate of the direct effect of BMI on resource use can thus be calculated by adjusting statistically for diet quality in this simplified situation. On the other hand, with respect to the relationship between diet quality as the exposure and the outcome resource use, BMI is a mediator which is a variable that is on a causal pathway leading from the exposure to the outcome. The third type of variable is a collider, which is a variable that is causally influenced by two other variables and lies on a path starting with an arrow leading to the exposure and ending with an arrow leading to the outcome. Crucially, colliders should not be adjusted for statistically as doing so can bias the estimate of the effect of interest [32].

Figure 1. is the colour-coded legend provided by DAGitty to inform model building.

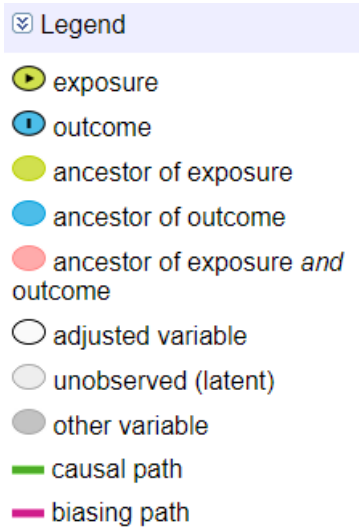

Figure 1. Legend provided in DAGitty used to inform development of DAGs.

Finally, the use of DAGs in causal inference relies on the assumption that the DAG is correct and that no variables with a causal influence have been omitted. There is a further assumption that adjusting for a given confounder completely reduces its bias, which may not be true if residual bias exists due to imperfect measurement of the confounder [32].

Aim ii) estimate the total unconfounded effect of BMI on specific health care resource use during the delivery admission

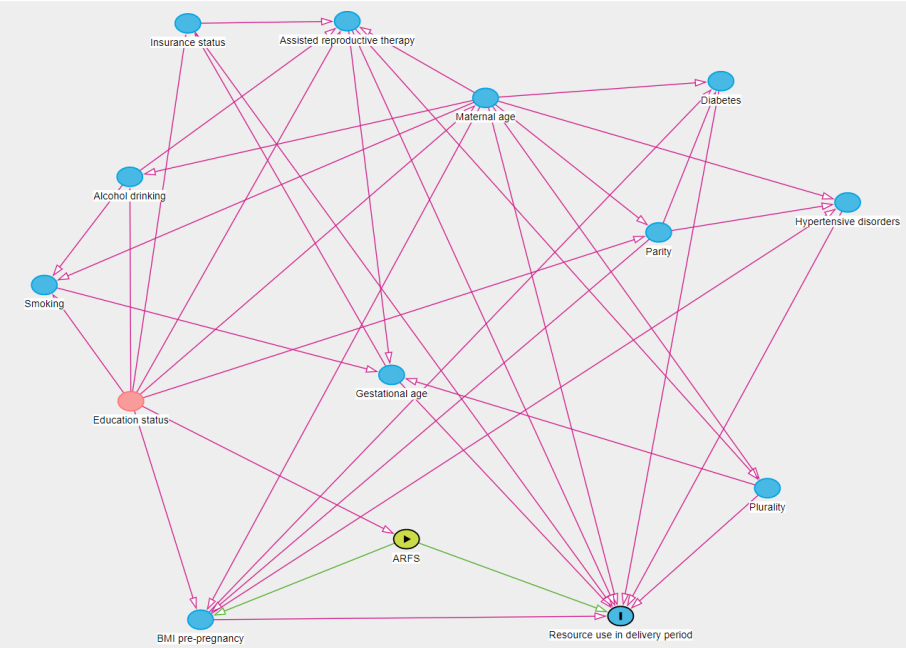

Figure 2. Directed acyclic graph developed for Aim (ii).
Each variable included in the DAG is listed in alphabetical order: 'Alcohol drinking indicates the participants alcohol consumption during this pregnancy; 'ARFS' indicates the participants diet quality; 'Assisted reproductive therapy' (ART) indicates the use for the current pregnancy; 'BMI pre-pregnancy' indicates the mothers BMI pre-pregnancy; 'Diabetes' indicates the participant's history of diabetes and diabetes status for the current pregnancy; 'Education status' indicates the mother's highest level of education attainment; 'Gestational age' indicates to the infants gestational age at birth; 'Hypertensive disorders' indicates the participant's history of hypertensive disorders and status for the current pregnancy; 'Insurance status' indicates a participant's insurance status for the birth admission (public or private patient); 'Maternal age' indicates the mothers age at delivery; 'Parity' indicates the number of pregnancies the participant has had; 'Resource use in the delivery period' indicates the participants resource use for the delivery admission; 'Smoking' indicates the participants smoking status during this pregnancy. Evidence to support the inclusion of each variable in this DAG is include in manuscript Appendix A. Table 5.

To generate the DAG in Figure 3. Launch DAGitty in your browser (http://www.dagitty.net/) and use the following model code:

```
dag {
bb="0,0,1,1"
"Alcohol drinking" [pos="0.179,0.309"]
"Assisted reproductive therapy" [pos="0.385,0.096"]
"BMI pre-pregnancy" [exposure,pos="0.280,0.912"]
```

```
"Education status" [pos="0.168,0.647"]
"Gestational age" [pos="0.427,0.580"]
"Hypertensive disorders" [pos="0.859,0.344"]
"Insurance status" [pos="0.234,0.099"]
"Maternal age" [pos="0.516,0.201"]
"Resource use in delivery period" [outcome,pos="0.644,0.910"]
ARFS [pos="0.452,0.782"]
Diabetes [pos="0.735,0.205"]
Parity [pos="0.680,0.385"]
Plurality [pos="0.783,0.735"]
Smoking [pos="0.098,0.457"]
"Alcohol drinking" -> "Assisted reproductive therapy"
"Alcohol drinking" -> Smoking
"Assisted reproductive therapy" -> "Gestational age"
"Assisted reproductive therapy" -> "Resource use in delivery period"
"Assisted reproductive therapy" -> Plurality
"BMI pre-pregnancy" -> "Hypertensive disorders"
"BMI pre-pregnancy" -> "Resource use in delivery period"
"BMI pre-pregnancy" -> Diabetes
"Education status" -> "Alcohol drinking"
"Education status" -> "Assisted reproductive therapy"
"Education status" -> "BMI pre-pregnancy"
"Education status" -> "Insurance status"
"Education status" -> "Maternal age"
"Education status" -> ARFS
"Education status" -> Parity
"Education status" -> Smoking
"Gestational age" -> "Insurance status"
"Gestational age" -> "Resource use in delivery period"
"Hypertensive disorders" -> "Resource use in delivery period"
"Insurance status" -> "Assisted reproductive therapy"
"Insurance status" -> "Resource use in delivery period"
"Maternal age" -> "Alcohol drinking"
"Maternal age" -> "Assisted reproductive therapy"
"Maternal age" -> "BMI pre-pregnancy"
"Maternal age" -> "Hypertensive disorders"
"Maternal age" -> "Resource use in delivery period"
"Maternal age" -> Diabetes
"Maternal age" -> Parity
"Maternal age" -> Plurality
"Maternal age" -> Smoking
ARFS -> "BMI pre-pregnancy"
ARFS -> "Resource use in delivery period"
```

Diabetes -> "Resource use in delivery period"
Parity -> "BMI pre-pregnancy"
Parity -> "Hypertensive disorders"
Parity -> Diabetes
Plurality -> "Gestational age"
Plurality -> "Resource use in delivery period"
Smoking -> "Gestational age"
}

Minimal sufficient adjustment sets for estimating the total effect of BMI pre-pregnancy on Resource use in delivery period:

- *ARFS, Assisted reproductive therapy, Diabetes, Gestational age, Hypertensive disorders, Insurance status, Maternal age, Plurality*
- *ARFS, Assisted reproductive therapy, Diabetes, Gestational age, Hypertensive disorders, Insurance status, Maternal age, Smoking*
- *ARFS, Diabetes, Education status, Hypertensive disorders, Maternal age*

Aim iii) Estimate the total unconfounded effect of maternal diet quality on resource use during the delivery admission

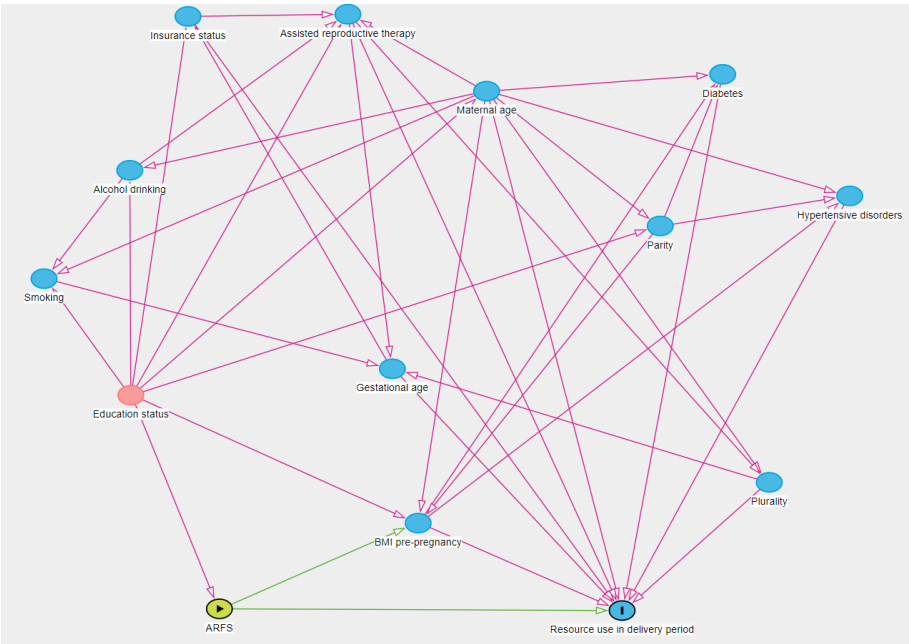

Figure 3. Directed acyclic graph developed for Aim (iii).
Each variable included in the DAG is listed in alphabetical order: 'Alcohol drinking indicates the participants alcohol consumption during this pregnancy; 'ARFS' indicates the participants diet quality; 'Assisted reproductive therapy' (ART) indicates the use for the current pregnancy; 'BMI pre-pregnancy' indicates the mothers BMI pre-pregnancy; 'Diabetes' indicates the participant's history of diabetes and diabetes status for the current pregnancy; 'Education status' indicates the mother's highest level of education attainment; 'Gestational age' indicates to the infants gestational age at birth; 'Hypertensive disorders' indicates the participant's history of hypertensive disorders and status for the current pregnancy; 'Insurance status' indicates a participant's insurance status for the birth admission (public or private patient); 'Maternal age' indicates the mothers age at delivery; 'Parity' indicates the number of pregnancies the participant has had; 'Resource use in the delivery period' indicates the participants resource use for the delivery admission; 'Smoking' indicates the participants smoking status during this pregnancy. Evidence to support the inclusion of each variable in this DAG is include in manuscript Appendix A. Table 5.

To generate the DAG in Figure 3. Launch DAGitty in your browser (http://www.dagitty.net/) and use the following model code:

```
dag {
bb="0,0,1,1"
"Alcohol drinking" [pos="0.179,0.309"]
"Assisted reproductive therapy" [pos="0.385,0.096"]
"BMI pre-pregnancy" [pos="0.451,0.791"]
```

"Education status" [pos="0.180,0.616"]
"Gestational age" [pos="0.427,0.580"]
"Hypertensive disorders" [pos="0.859,0.344"]
"Insurance status" [pos="0.234,0.099"]
"Maternal age" [pos="0.516,0.201"]
"Resource use in delivery period" [outcome,pos="0.644,0.910"]
ARFS [exposure,pos="0.264,0.908"]
Diabetes [pos="0.739,0.178"]
Parity [pos="0.680,0.385"]
Plurality [pos="0.783,0.735"]
Smoking [pos="0.098,0.457"]
"Alcohol drinking" -> "Assisted reproductive therapy"
"Alcohol drinking" -> Smoking
"Assisted reproductive therapy" -> "Gestational age"
"Assisted reproductive therapy" -> "Resource use in delivery period"
"Assisted reproductive therapy" -> Plurality
"BMI pre-pregnancy" -> "Hypertensive disorders"
"BMI pre-pregnancy" -> "Resource use in delivery period"
"BMI pre-pregnancy" -> Diabetes
"Education status" -> "Alcohol drinking"
"Education status" -> "Assisted reproductive therapy"
"Education status" -> "BMI pre-pregnancy"
"Education status" -> "Insurance status"
"Education status" -> "Maternal age"
"Education status" -> ARFS
"Education status" -> Parity
"Education status" -> Smoking
"Gestational age" -> "Insurance status"
"Gestational age" -> "Resource use in delivery period"
"Hypertensive disorders" -> "Resource use in delivery period"
"Insurance status" -> "Assisted reproductive therapy"
"Insurance status" -> "Resource use in delivery period"
"Maternal age" -> "Alcohol drinking"
"Maternal age" -> "Assisted reproductive therapy"
"Maternal age" -> "BMI pre-pregnancy"
"Maternal age" -> "Hypertensive disorders"
"Maternal age" -> "Resource use in delivery period"
"Maternal age" -> Diabetes
"Maternal age" -> Parity
"Maternal age" -> Plurality

"Maternal age" -> Smoking
ARFS -> "BMI pre-pregnancy"
ARFS -> "Resource use in delivery period"
Diabetes -> "Resource use in delivery period"
Parity -> "BMI pre-pregnancy"
Parity -> "Hypertensive disorders"
Parity -> Diabetes
Plurality -> "Gestational age"
Plurality -> "Resource use in delivery period"
Smoking -> "Gestational age"
}

Minimal sufficient adjustment sets for estimating the total effect of BMI pre-pregnancy on Resource use in delivery period:

- *Education status*

Aim iv) Estimate the direct unconfounded effect of maternal diet quality on resource use during the delivery admission

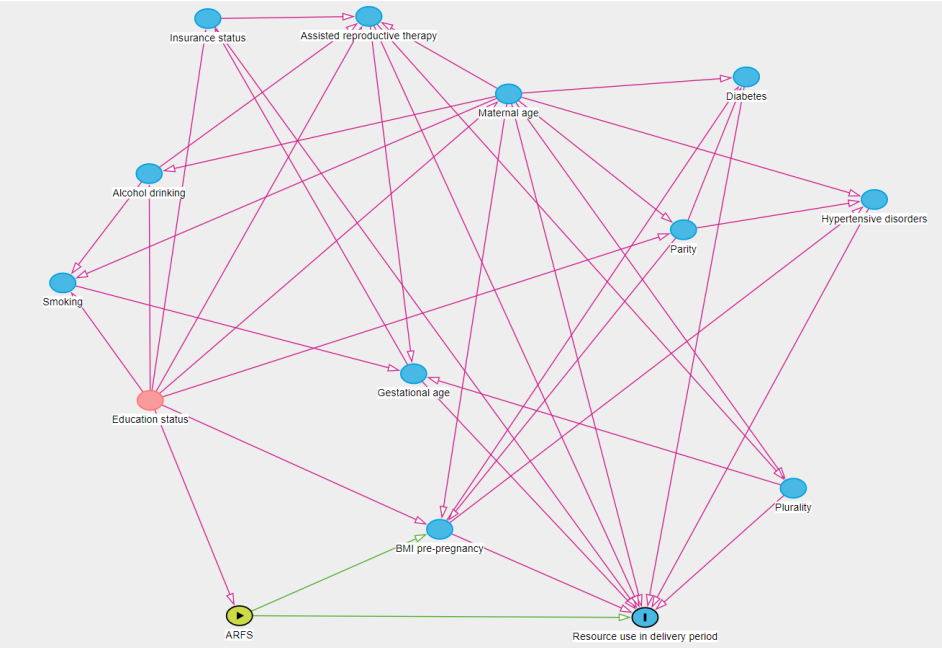

Figure 4. Directed acyclic graph developed for Aim (iv).
Each variable included in the DAG is listed in alphabetical order: 'Alcohol drinking indicates the participants alcohol consumption during this pregnancy; 'ARFS' indicates the participants diet quality; 'Assisted reproductive therapy' (ART) indicates the use for the current pregnancy; 'BMI pre-pregnancy' indicates the mothers BMI pre-pregnancy; 'Diabetes' indicates the participant's history of diabetes and diabetes status for the current pregnancy; 'Education status' indicates the mother's highest level of education attainment; 'Gestational age' indicates to the infants gestational age at birth; 'Hypertensive disorders' indicates the participant's history of hypertensive disorders and status for the current pregnancy; 'Insurance status' indicates a participant's insurance status for the birth admission (public or private patient); 'Maternal age' indicates the mothers age at delivery; 'Parity' indicates the number of pregnancies the participant has had; 'Resource use in the delivery period' indicates the participants resource use for the delivery admission; 'Smoking' indicates the participants smoking status during this pregnancy. Evidence to support the inclusion of each variable in this DAG is include in manuscript Appendix A. Table 5.

To generate the DAG in Figure 3. Launch DAGitty in your browser (http://www.dagitty.net/) and use the following model code:

```
dag {
bb="0,0,1,1"
"Alcohol drinking" [pos="0.179,0.309"]
"Assisted reproductive therapy" [pos="0.385,0.096"]
"BMI pre-pregnancy" [pos="0.451,0.791"]
```

```
"Education status" [pos="0.180,0.616"]
"Gestational age" [pos="0.427,0.580"]
"Hypertensive disorders" [pos="0.859,0.344"]
"Insurance status" [pos="0.234,0.099"]
"Maternal age" [pos="0.516,0.201"]
"Resource use in delivery period" [outcome,pos="0.644,0.910"]
ARFS [exposure,pos="0.264,0.908"]
Diabetes [pos="0.739,0.178"]
Parity [pos="0.680,0.385"]
Plurality [pos="0.783,0.735"]
Smoking [pos="0.098,0.457"]
"Alcohol drinking" -> "Assisted reproductive therapy"
"Alcohol drinking" -> Smoking
"Assisted reproductive therapy" -> "Gestational age"
"Assisted reproductive therapy" -> "Resource use in delivery period"
"Assisted reproductive therapy" -> Plurality
"BMI pre-pregnancy" -> "Hypertensive disorders"
"BMI pre-pregnancy" -> "Resource use in delivery period"
"BMI pre-pregnancy" -> Diabetes
"Education status" -> "Alcohol drinking"
"Education status" -> "Assisted reproductive therapy"
"Education status" -> "BMI pre-pregnancy"
"Education status" -> "Insurance status"
"Education status" -> "Maternal age"
"Education status" -> ARFS
"Education status" -> Parity
"Education status" -> Smoking
"Gestational age" -> "Insurance status"
"Gestational age" -> "Resource use in delivery period"
"Hypertensive disorders" -> "Resource use in delivery period"
"Insurance status" -> "Assisted reproductive therapy"
"Insurance status" -> "Resource use in delivery period"
"Maternal age" -> "Alcohol drinking"
"Maternal age" -> "Assisted reproductive therapy"
"Maternal age" -> "BMI pre-pregnancy"
"Maternal age" -> "Hypertensive disorders"
"Maternal age" -> "Resource use in delivery period"
"Maternal age" -> Diabetes
"Maternal age" -> Parity
"Maternal age" -> Plurality
```

"Maternal age" -> Smoking
ARFS -> "BMI pre-pregnancy"
ARFS -> "Resource use in delivery period"
Diabetes -> "Resource use in delivery period"
Parity -> "BMI pre-pregnancy"
Parity -> "Hypertensive disorders"
Parity -> Diabetes
Plurality -> "Gestational age"
Plurality -> "Resource use in delivery period"
Smoking -> "Gestational age"
}

Minimal sufficient adjustment sets for estimating the direct effect of ARFS on Resource use in delivery period:

- *Assisted reproductive therapy, BMI pre-pregnancy, Diabetes, Gestational age, Hypertensive disorders, Insurance status, Maternal age, Plurality*
- *Assisted reproductive therapy, BMI pre-pregnancy, Diabetes, Gestational age, Hypertensive disorders, Insurance status, Maternal age, Smoking*
- *Assisted reproductive therapy, BMI pre-pregnancy, Gestational age, Insurance status, Maternal age, Parity, Plurality*
- *Assisted reproductive therapy, BMI pre-pregnancy, Gestational age, Insurance status, Maternal age, Parity, Smoking*
- *BMI pre-pregnancy, Diabetes, Education status, Hypertensive disorders, Maternal age*
- *BMI pre-pregnancy, Education status, Maternal age, Parity*