

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

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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 period¹⁰ 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 al³⁶. 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) checklist⁴¹ 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}

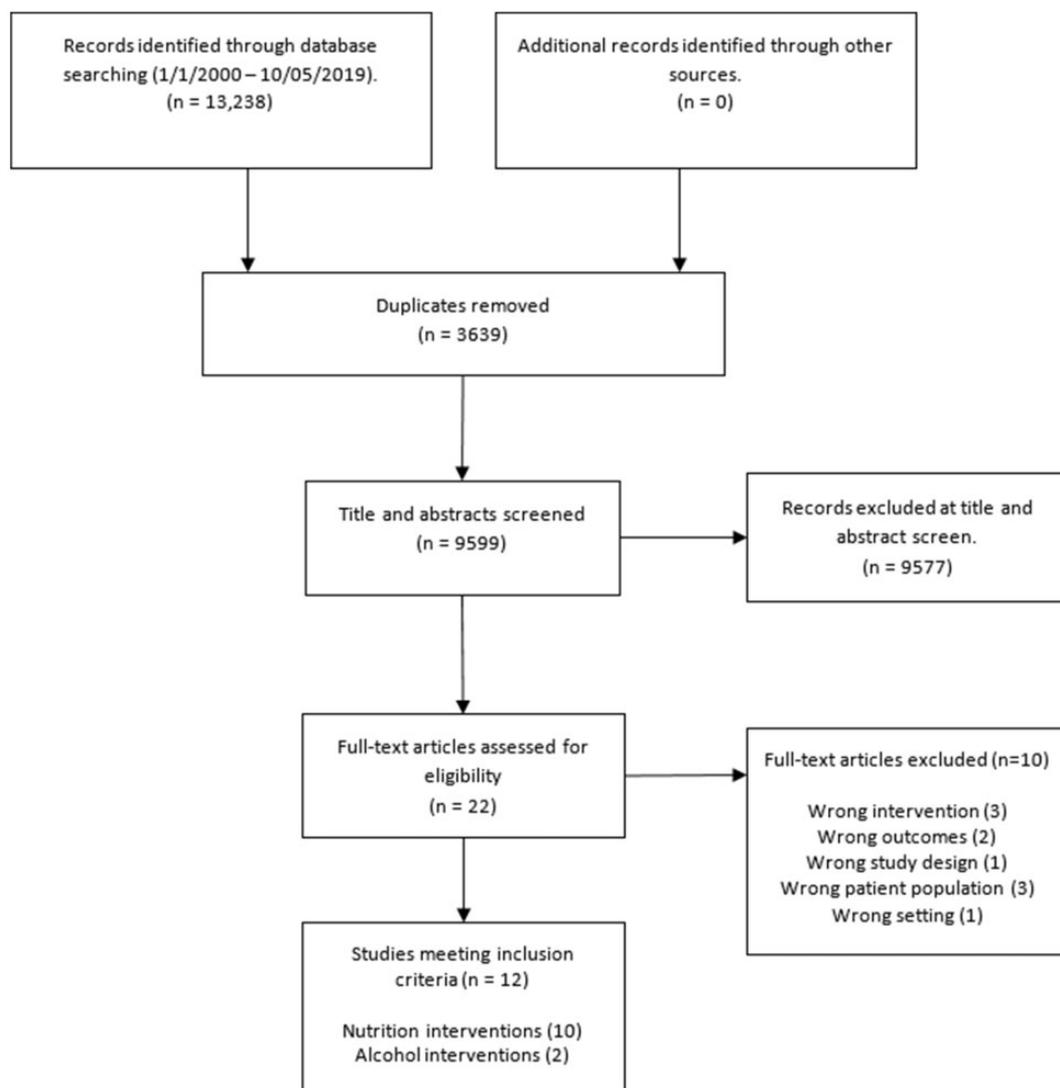


Figure 1 Flow diagram of the literature search process for review 1.

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

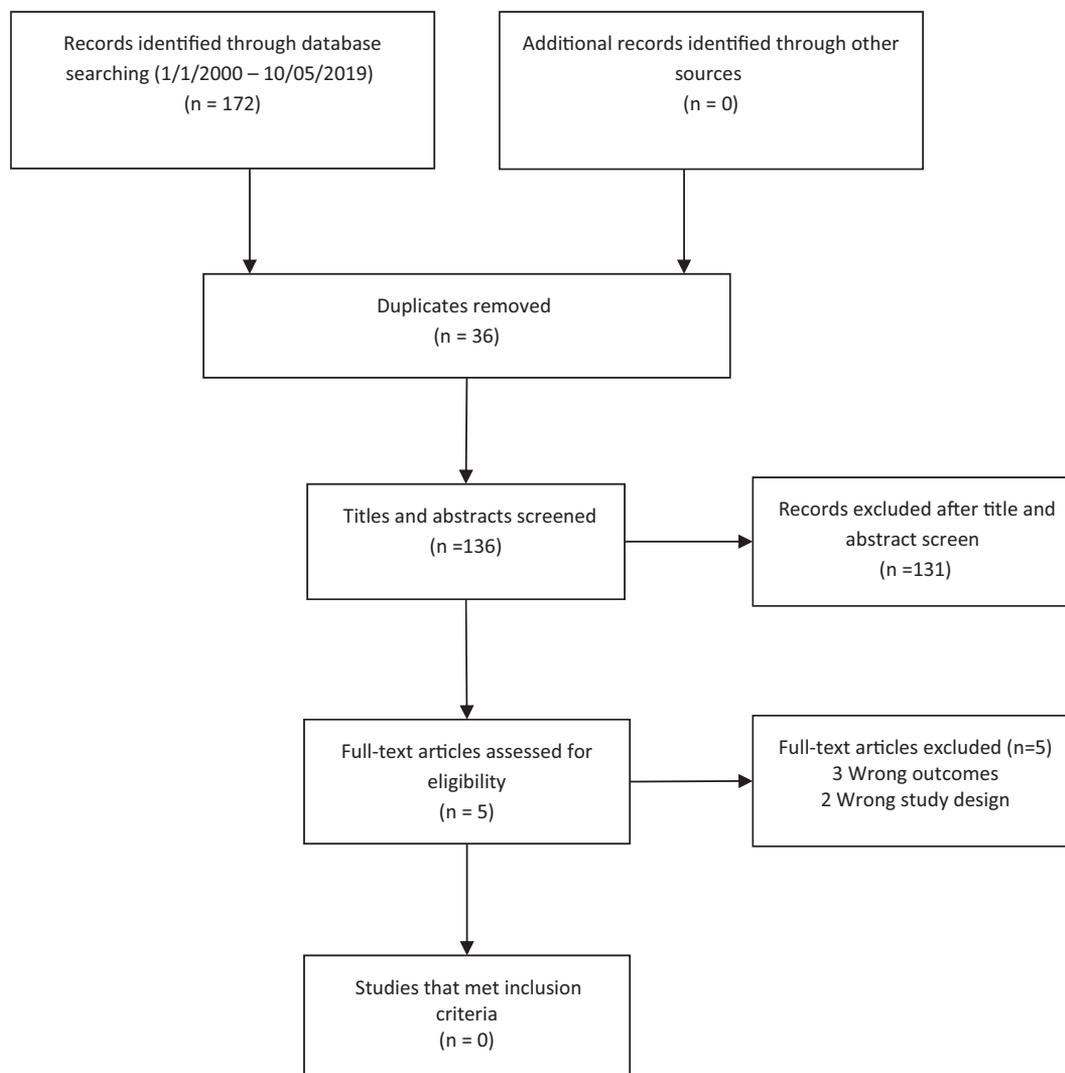


Figure 2 Flow diagram of the literature search process for review 2.

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) gained⁴⁹; life years gained per QALY^{44,47}; disability-adjusted life years avoided⁴⁴; life years gained and QALYs gained^{44,47,49}; intelligence quotient points gained⁵²; cases avoided⁴⁷; cost savings⁵¹; 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. 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
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	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
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	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
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	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
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	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	
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 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 pre-mature 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, 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
Broekhuizen et al (2018) ⁵⁵	Europe	Complications associated with GDM	Pregnant women at increased risk of GDM	Antenatal clinic or hospital	Decision-analytic model; 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	254 cases (13%) prevented; estimated net benefit €2,822,115 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 supplementation would reduce asthma-related childhood deaths, and save \$31,420,800 in societal costs at age >18 y per birth cohort.
Health Technology Analysis (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 years⁴⁴ 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

Parameter		Results of appraisal (n = 12 studies): parameter present/ not present/ unclear / not applicable							
		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		
Costing	Relevance of productivity impacts is discussed	11	92			1	8		
	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						
Modeling	Details of currency conversions or price adjustments are stated	12	100						
	Details of model are given	11	92	1	8				
Adjustments for timing of costs and benefits	Choice of model and key parameters are justified	10	83	1	8	1	8		
	Time horizon is stated	10	83	1	8			1	8
	Discount rate is stated if applicable	10	83					2	17
Allowance for uncertainty	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
	Details of statistical tests are given	7	58	2	17	3	25		
	Approach to sensitivity analysis is stated	7	58	2	17	3	25		
Presentation of results	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		
Conclusions	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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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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