



Global Systematic Review of the Cost-Effectiveness of Indigenous Health Interventions

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Abstract

Background: Indigenous populations around the world have consistently been shown to bear a greater burden of disease, death and disability than their non-Indigenous counterparts. Despite this, little is known about what constitutes cost-effective interventions in these groups. The objective of this paper was to assess the global cost-effectiveness literature in Indigenous health to identify characteristics of successful and unsuccessful interventions and highlight areas for further research.

Methods and Findings: A systematic review of the published literature was carried out. MEDLINE, PSYCINFO, ECONLIT, EMBASE and CINAHL were searched with terms to identify cost-effectiveness evaluations of interventions in Indigenous populations around the world. The WHO definition was followed in identifying Indigenous populations. 19 studies reporting on 27 interventions were included in the review. The majority of studies came from high-income nations with only two studies of interventions in low and middle-income nations. 22 of the 27 interventions included in the analysis were found to be cost-effective or cost-saving by the respective studies. There were only two studies that focused on Indigenous communities in urban areas, neither of which was found to be cost-effective. There was little attention paid to Indigenous conceptions of health in included studies. Of the 27 included studies, 23 were interventions that specifically targeted Indigenous populations. Outreach programs were shown to be consistently cost-effective.

Conclusion: The comprehensive review found only a small number of studies examining the cost-effectiveness of interventions into Indigenous communities around the world. Given the persistent disparities in health outcomes faced by these populations and commitments from governments around the world to improving these outcomes, it is an area where the health economics and public health fields can play an important role in improving the health of millions of people.

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Introduction

There are almost 400 million Indigenous people living in countries around the world [1]. The World Health Organisation (WHO) defines Indigenous populations as those that live in distinct geographical territories, identify themselves as belonging to a cultural group separate from mainstream society and are descendent from groups present in the area before modern states and borders were defined [2]. Indigenous populations have been repeatedly shown to bear a greater burden of death, disease and disability than their non-Indigenous counterparts [1,3–6]. Despite this, little is known about what constitutes cost-effective health interventions in these unique population groups and there is a lack of evidence as to the extent and nature of investment in programs to address the burden of ill-health in these populations [7,8].

Economic evaluation of health care programs has become an important area of applied economics over the last 30 years [8–10].

The field has had a significant impact on policy-making processes in countries around the world most prominently through high level policy initiatives such as the National Institute for Health and Care Excellence in the UK and the Pharmaceutical Benefits Advisory Committee in Australia. Economic evaluation analyses whether the additional benefits of an intervention is worth undertaking relative to another intervention or normal care [9]. Without a substantial evidence-base on the cost-effectiveness of policy options, policy-makers have little economic evidence to make resource allocation decisions in the field of Indigenous health.

The objective of this review is to systematically search the literature to pull together existing evaluations that estimate the cost-effectiveness of health interventions into Indigenous populations around the world. This review allows for an exploration of the type of interventions that have been shown to be effective in these unique population groups, the specific resource requirements needed to deliver programs to these populations and the aspects of

these programs that are deemed to be of value by the populations to whom they are targeted.

Suitability of the traditional health economic paradigm for the Indigenous health field

There is an increasing recognition of the shortcomings of traditional methods of measuring health benefits in economic evaluations of healthcare programs [8,10–12]. Indigenous populations have been shown to hold different conceptions of health to mainstream populations [1,8]. Specifically, family, community, connections to the land and cultural sensitivity have been shown to be qualitatively valued with regards to health by Indigenous populations [8]. While this has led some to argue that the traditional approaches of the health economic paradigm are inappropriate to measure the impact of interventions in these communities, it highlights the importance of further economic research into the field and suggests that valuation of outcomes within economic studies should ideally incorporate some form of patient or user-elicited valuation so that they reflect these broader conceptions of health.

To provide a basis for further evaluating these arguments, this review also highlights any explicit attempts by included studies to incorporate these concerns into cost-effectiveness evaluations.

Methods

A systematic review of the literature was conducted to find articles that provide an economic evaluation of interventions targeting or reporting on an Indigenous population. No protocol has been previously published for this review.

Inclusion Criteria

The inclusion criteria for this review specified three characteristics for studies. First, the studies had to examine interventions that were primarily aimed at improving the health of target populations. Second, included papers had to be economic-evaluations of an intervention that met the definition of one of the types outlined in Table 1. This depicts a broad spectrum of economic evaluation methodologies from cost-benefit analysis, generally considered the form of economic evaluation that is most comprehensive in scope, to the narrower forms of evaluation including simple cost-analyses. The search strategy was adapted from previously published systematic reviews of economic evaluations [13,14]. Studies were required to report on either the cost impacts of the intervention of interest or some measure of cost-benefit to be included in the study. Finally the papers had to either focus on or separately report on a population that is either wholly or partially Indigenous. The WHO definition of Indigenous mentioned above was used as a basis for identifying these populations in the literature [2]. The specific search strategy was adapted from a previously published systematic review of this population group and is designed to encompass Indigenous populations around the world in line with this definition [15].

Search strategy

A search was conducted of CINAHL, MEDLINE, EMBASE, PSYCINFO and ECONLIT (from inception to May 2014) using variations of the search string contained in Table 2. Reference lists of included studies were also searched for further applicable studies.

Data Extraction

Study review, selection and data extraction were independently undertaken by two authors (BA and JM). Abstracts, titles and

keywords of the studies returned from the search were screened for compatibility with the inclusion criteria. Once studies were identified for potential inclusion, full texts were reviewed. Data were extracted from the studies using a form developed for the review based on standard techniques used in the literature and included the following items: country of origin, methodology including type of evaluation, comparators used, outcome measures, settings and participants, results and evidence of inclusion of Indigenous conceptions of health [16]. The primary outcome measures were reported measures of cost-effectiveness.

Results

The search yielded 559 abstracts (see Figure 1). One further study was identified through a hand search of relevant journals. Once duplicates were removed, 458 unique abstracts were reviewed. Three published abstracts were found that appeared to meet the inclusion criteria. Relevant authors were contacted to identify if further publications resulted from these abstracts. The authors of one study did not respond [17], one was published as a short-report that included no additional information to the abstract [18] while one was being readied for submission and not yet available to other researchers [19]. Two of the abstracts were included as studies as they contained enough information to meet the data extraction requirements [17,18] while the other was excluded as there was insufficient information in the abstract to be included [19]. In total, nineteen studies reporting on 27 interventions met the criteria to be included in this review [7,11,17,18,20–34]. Tables 3 and 4 summarise the characteristics of included studies.

Country of Origin

Seven studies were conducted in Australia (covering eleven interventions) [7,11,20,21,25,27,33], four in Canada [22–24,31] and three each in New Zealand [26,28,29] and the USA (covering seven interventions) [30,32,34]. A published abstract was included from both Thailand [17] and Brazil [18].

Settings and Participants

Two studies evaluated interventions in urban areas, one looking at a midwifery program [11] and the other at palivizumab treatment for children [27]. Twelve studies focused solely on rural or remote locations [17,18,20–25,30–34] while the remaining five studies were based on wider populations encompassing rural, remote and urban Indigenous communities [7,26,28,29,31].

The majority of the studies focused on Indigenous populations with known health conditions including diabetes (six studies all conducted in rural or remote locations) [20,22–25,32], post-traumatic stress disorder [30], heart conditions [26], dental problems [21], drug addiction [29] and pregnancy [11,33]. The other intervention studies targeted population groups that were not based on the presence of some particular medical condition [7,17,18,27,28,31,34].

Of the 27 interventions included in the study, two were carried out in infants [27,31], one targeted school children [28], another in children more generally [17], one targeted young adults [34], two specified older patients [26,32] while the rest were not targeted at any specific age-groups [7,11,18,20–25,29,30,33,34].

Methodology

Studies were broadly grouped into two groups. The first included group included studies where authors collected effectiveness data within the study itself (twelve studies and sixteen interventions) [11,17,18,20–22,24,25,30,32–34]. The second

Table 1. Types of Economic Evaluation.

Cost Analysis	A partial form of economic analysis where only the costs of an intervention are compared to another potential intervention.
Cost-Effectiveness Analysis	Provide a measure of the effectiveness of an intervention using natural units such as life-years gained relative to the cost incurred to obtain that outcome.
Cost-Utility Analysis	A particular form of Cost-Effectiveness Analysis that measures effectiveness using a measure of utility such as Quality Adjusted Life Years or Disability Adjusted Life Years.
Cost-Benefit Analysis	An economic evaluation that sees both the costs and benefits of a particular intervention valued in monetary terms.

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group included studies that used previous findings in the literature to model the impact of potential interventions on these populations (seven studies looking at eleven interventions) [7,23,26–29,31].

The types of economic evaluation are outlined in Table 1. Only one study met the criteria of a cost-benefit analysis, generally considered the most comprehensive form of health economic evaluation [34]. Eight studies met the criteria of cost-analyses, the least complex of the four categories [11,17,20,22,24,25,30,33]. There were three cost-effectiveness analyses [21,27,29] and seven cost-utility analyses [7,18,23,28,29,31,32].

Outcome Measures

Costs were the primary outcome measure reported in eight of the studies [11,17,20,22,24,25,30,33]. One study reported cost-benefit ratios for five injury-prevention interventions [34]. The study of a remote dental service in Western Australia attempted to use published valuations of equivalent government services as an estimate for the value of services provided and reported on the cost-benefit ratio in this regard [21]. Five studies reported costs per quality adjusted life years gained [23,26,31,32] and two reported on cost per disability life years gained [7,18]. Costs per life years saved were reported by Sheerin et al. in their study on Hepatitis C treatment for injecting drug users in New Zealand [29], while cost per avoided hospitalisation was the focus of the study of Reeve et al. on palivizumab injections for high risk infants [27].

Each included paper made some judgment as to the cost-effectiveness or cost-impact of the interventions being studied. In total, only five of the 27 interventions were deemed to be strictly not cost-effective or cost-saving [7,11,27,32]. Of the eight cost-analysis studies, six found interventions would be cost-saving over time relative to the comparison [17,20,22,24,25,30]. The study of the group midwifery program in the Top End of Australia found no significant cost differences between the provided intervention and usual care [33], while the urban midwifery program was deemed not cost-saving although qualitative results demonstrated that patients valued the service [11]. The cost-benefit analyses carried out all found the injury prevention interventions to be cost-

beneficial in that they had benefit-cost ratios above one [34]. Two of the three cost-effectiveness studies found their interventions to be cost-effective [21,29]. Three interventions analysed using cost-utility analysis were found to cost-ineffective [7,32]. Table 5 depicts included interventions by cost-effectiveness.

Comparators Used

The choice of comparator against which the cost-effectiveness of the intervention is assessed plays a large part in determining whether a particular intervention is cost-effective or not. Included studies could be grouped into two main categories in this regard. Fourteen of the studies assessed the cost-effectiveness of their intervention against so-called ‘business as usual’ cases where they were compared to a situation with no intervention, either through the use of a control group [11,28,30,32], projecting historical trends [7,17,20,25,26,29,31,33,34] or in one case actual hospital records with the impact of the intervention being retrospectively assessed [27]. The remaining five studies compared the cost-effectiveness of the intervention to a hypothetical or alternatively modelled scenario where participants would be forced to obtain the intervention through alternative service providers [18,21–24].

Wider conceptions of health

Only one study that met the inclusion criteria explicitly set out to capture wider benefits of culturally appropriate service provision [11]. This was done through broader qualitative evaluation of the value of the provided midwifery service and the use of a cost-consequence approach designed to incorporate broader values than narrowly defined health outcomes. Another included study also included qualitative results from patient interviews to document the appropriateness of the service to the Indigenous community [22]. The work of the ACE prevention project in Australia modelled the different impact of delivering interventions via Aboriginal Medical Services and mainstream general-practitioners, suggesting that health benefits to Indigenous communities would be higher from those services delivered through Aboriginal Medical Services as a result of increased

Table 2. Search Strategy.

Database/s	Search terms
Cinahl, Medline, EMBASE and PsycINFO	(1) The following terms as words within the title, abstracts or texts of papers: aborigin* or american indian* or eskimo* or Ethnic Group* or first nation* or greenlandic or indigenous or inuit* or inupiat* or inuvialuit* or kalaallit* or maori or maoris or mapuche* or native american* or native people* or native population* or native siberian* or navaho* or nunangat* or sami* or skolt* or taiga* or tribe or tribal or yuit or yupik or zuni (2) “cost-effectiveness” or “economic evaluation” or “cost impact” as words within the title, abstracts or texts of papers or containing a subject heading under “cost analysis”
Econlit	(3) Econlit was also searched with “Health” as a subject

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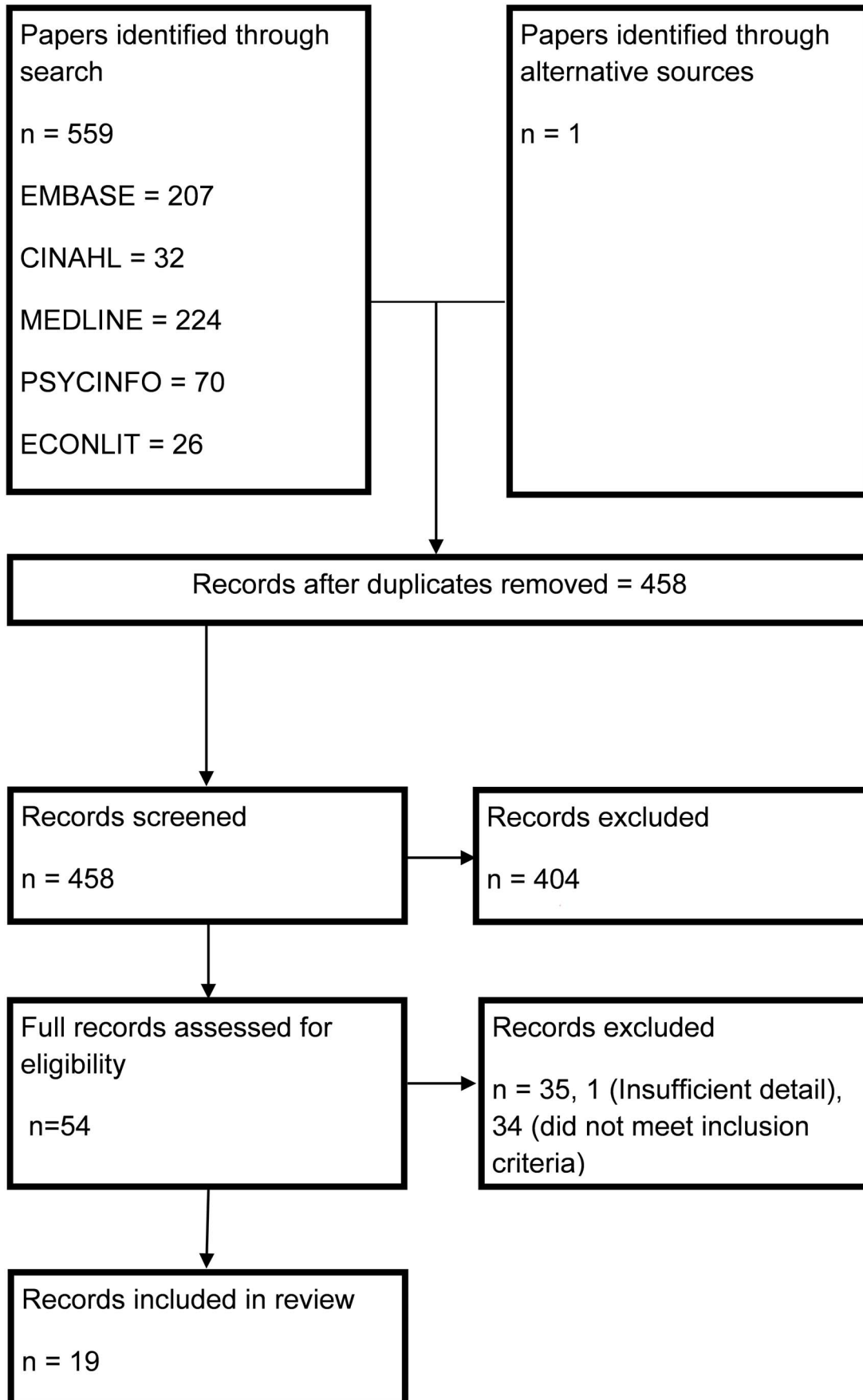


Figure 1. PRISMA Flowchart.
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Table 3. Primary intervention Studies.

Study	Country	Setting	Intervention	Population	Comparator	Type of economic evaluation	Finding
McDermott and Segal (2006)	Australia	Remote primary care centres and hospitals	Primary health care – visiting specialist service on top of improved training for local staff, preparation of registers, care plans and recall systems for patients with diabetes and an information system that can report on care quality.	Remote Indigenous Islander population with diabetes	Business as usual – increases based on historical trends	Cost-analysis	Cost-saving – Net Present Value cost saving with a 5% discount rate over 9 years.
Dyson, Kruger and Tennant (2012)	Australia	Rural and remote dental health services	Dental health care (outreach) One-week clinics of a visiting dentist assisted by an Aboriginal Health Worker. Transport was provided as needed by local health services and all services provided were free of charge to the patient	Remote communities presenting with dental problems	Cost-Benefit ratios compared to unpublished estimates of WA government services as well as weightings published by New South Wales.	Cost-effectiveness	Cost-Effective – Cost benefit ratios ranged from between 1.22 and 2.05 for different clinics.
Jin, Martin et al. (2004)	Canada	Remote communities, mobile clinic	Primary health care (outreach): Outreach services comprising of a diabetes nurse educator and an ophthalmic technician offering recommended services within Aboriginal reserves	Diabetic residents of remote areas	Costs associated with accessing similar services in the absence of the mobile clinic	Cost-analysis	Cost-Saving – Over the first year of operation the mean cost per client was found to be \$1231 (CDN) VS \$1437 if these services had been obtained elsewhere. Qualitative findings showed the service to be highly valued by the local population.
Zaloshnja et al. (2003)	USA	Rural and remote Native American Reserves	Prevention regulatory: Enforcement of law requiring automobile drivers and passengers to wear safety belts including promotion of the law and benefits of safety belt use.	Remote Indigenous residents	Business as usual rates of injuries based on historical trends	Cost Benefit Analysis	Cost-Effective – benefit cost ratio (BCR) = 256
Zaloshnja et al. (2003)	USA	Rural and remote Native American Reserves	Prevention (built environment): Installation of streetlights along a dark section of highway designed to reduce pedestrian injuries.	Remote Indigenous residents	Business as usual rates of injuries based on historical trends	Cost Benefit Analysis	Cost-Effective – BCR = 10
Zaloshnja et al. (2003)	USA	Rural and remote Native American Reserves	Prevention (regulatory): Authority given to impound free-roaming livestock on reservation roads.	Remote Indigenous residents	Business as usual rates of injuries based on historical trends	Cost Benefit Analysis	Cost-Effective – BCR = 1.67

Table 3. Cont.

Study	Country	Setting	Intervention	Population	Comparator	Type of economic evaluation	Finding
Zaloshnja et al. (2003)	USA	Rural and remote Native American Reserves	Prevention: Swimming and water survival courses as well as summer-weight coats that served a secondary function as floatation devices.	Remote Indigenous residents	Business as usual rates of injuries based on historical trends	Cost Benefit Analysis	Cost-Effective – BCR = 2592
Zaloshnja et al. (2003)	USA	Rural and remote Native American Reserves	Prevention: Employment of a social worker who spent 80% of her time on suicide prevention supplemented by a school-based program which trained youth leaders to recognise warning signs of suicidal ideation.	Remote Indigenous residents	Business as usual rates of injuries based on historical trends	Cost Benefit Analysis	Cost-Effective – BCR = 43
Wilson et al. (2010)	USA	Regional Primary Medical centres	Primary health care (prescribing): Aggressive targets of LDL-C and systolic blood pressure versus standard targets.	American Indians over the age of 40 with type two diabetes and no prior cardio vascular events	Control group receiving usual care	Cost-Utility	Cost-Ineffective – Cost per QALY = \$82,589
Shore et al. (2007)	USA	Remote native American communities	Telehealth – psychiatric interviews for American Indian Veterans conducted using telehealth, digital network equipment.	American Indian Veterans living in remote communities	Non-intervention sites receiving in person interviews (usual care)	Cost Analysis	Cost-Effective – Telehealth cost \$6,000 more in 2003 but \$8,000 less in 2005 for clinics that had to be set up. For clinics already set up telehealth interviews in 2003 telehealth cost \$1,700 more but in 2005 they cost \$12,000 less.
Baker et al. (2005)	Australia	Remote Primary Care	Primary health care (prescribing): Perindopril along with other medication as necessary and education	Aboriginal adults with hypertension, diabetes with microalbuminuria or overt albuminuria and overt albuminuria living in remote communities	Business as usual increases in costs and cases based on historical trends	Cost analysis	Cost-saving – \$1 M net saving after 3 years and \$3.4 M at 4.6 years
Jan et al. (2004)	Australia	Urban primary care	Primary health care (midwifery): Aboriginal community controlled midwifery service	Aboriginal pregnant women	Aboriginal women not in the program receiving usual care	Cost analysis	Not Cost-Saving - Net cost to health sector estimated to be \$1200 per client over normal care. Qualitative evaluation found service to be highly valued by recipients.
Fergusson et al. (2011)	Thailand	Remote primary care	Primary health care (screening). Serologic screening prior to hepatitis B vaccines in remote tribes	Akha tribal children in Northern Thailand	Usual care where all children receive the vaccine	Cost analysis	Cost-Saving – over two years \$1104 and \$1556 (USD) were avoided as a result of screening

Table 3. Cont.

Study	Country	Setting	Intervention	Population	Comparator	Type of economic evaluation	Finding
Martin and Yidegilligne (1998)	Canada	Remote Primary Care	Primary health care (screening): Travelling retinal photography screening team to see remote patients	Aboriginal Canadians living on remote reserves	Costs associated with accessing similar services in the absence of the mobile clinic	Cost Analysis	Cost-Saving – seeing diabetic patients with the traveling team would cost \$103,000 (Canadian) less than if these patients had to travel to obtain the services
Gao et al. (2014)	Australia	Remote Primary Care	Primary health care (midwifery): Midwifery group practice where a group of midwives offer continuity of care throughout the pre and post pregnancy period.	Regional Aboriginal pregnant women.	Business as usual increases in costs, presentations and complications based on historical trends	Cost analysis	Non-significant cost-savings of \$703 found to result from the program
Carvalho et al. (2011)	Brazil	Remote Primary Care	Primary health care screening and treatment): Universal rapid syphilis testing and treatment.	Remote Amazonian population – pregnant women and the sexually active population.	Argue that intervention is cost-effective relative to costs associated with accessing similar services in the absence of the mobile clinic	Cost-Utility Analysis	Cost-Effective – Cost per DALY saved \$484 (USD)

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engagement of the target population [7]. The remaining studies did not explicitly attempt to measure any wider or Indigenous-specific conceptions of health. It is important to note, though, that of the 27 interventions included in the analyses, only four were not targeted specifically at Indigenous populations [26–29]. Of the modelled studies, six of the eleven interventions examined were based on estimates of intervention effectiveness that had been obtained from studies carried out in Indigenous populations [7,26–29,31]. The other five were based on effectiveness estimates emanating from the general non-Indigenous literature and applied to Indigenous populations.

Discussion

This systematic review has found that very few cost-effectiveness studies are available in the published global Indigenous health literature. This has implications for generating investment into Indigenous health programs since the lack of such evidence limits our ability to assess the investment-case of interventions based on the criteria of cost-effectiveness, rather than solely for equity reasons or broader policy objectives. This is concerning given the significant disparities in health and access to health care that exist between Indigenous and non-Indigenous populations worldwide. Nonetheless, the evidence-base that does exist in the literature provides some isolated insights into the potential cost-effectiveness of specific types of interventions. There is potential for further work to both increase the use of economic evaluation in this area and methodological work to ensure that health economic methodologies are relevant to Indigenous populations.

Limited Economic Research in the Field of Indigenous Health

A total of nineteen studies met the inclusion criteria for this review. Given the broad scope of the research question and search strategy, this depicts a very limited evidence-base from which to draw insights on the potential cost-effectiveness of interventions into Indigenous populations. This finding implies that investment into the area is largely being undertaken blind, based on assumptions rather than evidence of the cost and effectiveness of particular policies and interventions.

Three main reasons are offered here as potential factors explaining the lack of research in the field. First, there is a general lack of effectiveness studies in the field of Indigenous health, with the majority of research carried out in the field being observational rather than interventional in nature [35]. The findings of this review build upon previous literature that has emphasised the need to focus further research on finding effective interventions to improving the health of these unique groups. Second, the lack of studies could be a reflection on the attitudes of policy-makers and service providers in the area of Indigenous health that due to the severe inequalities faced by Indigenous population groups, interventions are justified purely on equity grounds rather than cost-effectiveness considerations. Such an argument overlooks the role that economic research could play in not only highlighting the relative importance of investing in Indigenous health, but providing guidance as to the best use of resources within the sector to maximise their impact. Third, as a result of the unique conceptions of health held by Indigenous populations, traditional economic evaluation methodologies may be inappropriate for the field of Indigenous health [8]. Specifically, it has been argued that traditional economic evaluation methods have failed to adequately accommodate the values, knowledge and beliefs of Indigenous populations such as those set out in the United Nations Declaration on the Rights of Indigenous People [8,36]. Health

Table 4. Modelled Intervention Studies.

Study	Country	Setting	Intervention	Population	Comparator	Type of economic evaluation	Finding
Sheerin (2004)	New Zealand	Primary Care	Primary health care (vaccination?) Hepatitis C virus anti-viral therapy for injecting drug users on methadone maintenance therapy as opposed to MMT on its own.	Modelled cohort of 1000 injecting drug users including Maoris.	No treatment	Cost Effectiveness – Markov model was used with a lifetime follow up to model cost-effectiveness.	Cost-Effective – cost per life-year saved for Maori men ranged between \$8,000 and \$35,000NZD while for Maori women these numbers were \$7,000-\$23,000
Maberly et al. (2003)	Canada	Remote primary care	Primary health care (outreach, screening) Retinopathy screening by travelling retina specialists versus retinal photography with a portable digital camera	Isolated First Nations Cohort with diabetes	Usual care where a specialist visits the regional centre and remote patients are flown in for assessment.	Cost Utility Analysis – Markov models were used to model the implementation of services over 5 years with a total timeframe of 10 years for the analysis.	Cost-Effective – Portable retinal camera (\$15,000 per QALY gained) found to be a more cost-effective means of screening for diabetic retinopathy than a retina specialist (\$37,000 per QALY gained)
Ong et al. (2012)	Australia	Primary care	1. Broad community based intervention involving: regular health promotion activities, physical activity groups, smoking restrictions in public buildings and improved nutritional value of food at local store. 2. Statins	Indigenous population of Australia aged 35 and above	Interventions were modelled against a situation of usual care	Cost Utility Analysis – a decision analytic Markov model was used with a lifetime follow-up (or until individuals reached 85 years).	Cost-Ineffective – the intervention is modelled to cost \$210,000AUD per DALY which was deemed cost-ineffective using a \$50,000 cost per DALY threshold.
Ong et al. (2012)	Australia	Primary care	2. Statins	Indigenous population of Australia aged 35 and above	Interventions were modelled against a situation of usual care	Cost Utility Analysis – a decision analytic Markov model was used with a lifetime follow-up (or until individuals reached 85 years).	Cost-Ineffective – \$80,000AUD per DALY when delivered through Aboriginal Controlled Community Health Services (ACCHSs) and \$59,000 when delivered through mainstream GPs
Ong et al. (2012)	Australia	Primary care	3. Low dose diuretics	Indigenous population of Australia aged 35 and above	Interventions were modelled against a situation of usual care	Cost Utility Analysis – a decision analytic Markov model was used with a lifetime follow-up (or until individuals reached 85 years).	Cost-Effective – \$31,000AUD per DALY through ACCHSs or \$11,000AUD through mainstream GPs
Ong et al. (2012)	Australia	Primary care	4. ACE inhibitors	Indigenous population of Australia aged 35 and above	Interventions were modelled against a situation of usual care	Cost Utility Analysis – a decision analytic Markov model was used with a lifetime follow-up (or until individuals reached 85 years).	Cost-Effective – \$50,000AUD per DALY when delivered through ACCHSs and \$31,000AUD through mainstream GPs
Ong et al. (2012)	Australia	Primary care	5. Polypill	Indigenous population of Australia aged 35 and above	Interventions were modelled against a situation of usual care	Cost Utility Analysis – a decision analytic Markov model was used with a lifetime follow-up (or until individuals reached 85 years).	Cost-Effective – \$21,000AUD per DALY when delivered from ACCHSs (\$13,000AUD from mainstream GPs)

Table 4. Cont.

Study	Country	Setting	Intervention	Population	Comparator	Type of economic evaluation	Finding
Panattoni et al. (2012)	New Zealand	Hospital	Treating all Acute Coronary Syndromes patients across New Zealand with generic clopidogrel and using genetic testing	Entire ACS population in New Zealand public hospitals	Non-genetically guided treatment	Cost-Utility Analysis – used a decision tree model to project clinical effectiveness data over a lifetime follow up.	Cost-Effective – The genetically guided strategy was particularly cost effective for Maoris (\$NZ7312/QALY)
Reeve (2006)	Australia	Hospital	Palivizumab immunoprophylaxis for infants at risk	‘High-risk’ infants including those with low-birth weight and mothers who were multiparous babies born in an urban hospital.	Actual treatment costs (cases were retrospectively identified for the analysis)	Cost-effectiveness Analysis – calculated the costs and projected outcomes if these groups of infants had been treated rather than receiving actual care.	Cost-ineffective – cost (only drug costs) per prevented admission ranged from \$69,861 to \$88,547AUD.
Rush (2014)	New Zealand	Schools	A nutrition and physical activity program designed to help reduce excess weight gain and risk of chronic disease	All New Zealand school students up until grade 8.	Other students not participating in program	Cost-Utility Analysis – applied a previously used Markov model with a lifetime follow-up to determine effectiveness	Cost-Effective – Cost per QALY gained in Maori population was given by – \$28,241 for the younger group and older \$22,151
Tam et al. (2009)	Canada	Hospital	Palivizumab injections for infants (<1 year)	Indigenous Inuit communities in either a regional centre or remote area.	No prophylaxis or usual care.	Cost-Utility Analysis – used a decision analytical model with lifetime follow-up used in the analysis	Cost-Effective – For all infants the ICER was \$39,435/QALY. Looking only at rural areas there was an associated ICER of \$24,750/QALY. Prophylaxis was a dominant strategy (cost saving) for rural infants under 6 months of age.

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Table 5. Included Interventions by cost-effectiveness.

<i>Cost-Effective Interventions</i>
Palivizumab in Indigenous infants
Multicomponent physical activity and nutrition program
Genetic testing for CYP2C19 Variants to guide thienopyridine treatment
Low dose diuretics for the prevention of cardiovascular disease
ACE Inhibitors for the prevention of cardiovascular disease
Polypill for the prevention of cardiovascular disease
Screening for diabetic retinopathy
Rapid syphilis testing
Hepatitis C treatment for injecting drug users on methadone maintenance programs
Safety-belt program
Installation of streetlights on remote highways to prevent crashes
Livestock control measures to prevent crashes
Drowning prevention program
Suicide prevention program
Outreach dental services
<i>Cost-Saving Interventions</i>
Screening for diabetic retinopathy
Screening for hepatitis B prior to vaccination
Perindopril for diabetes patients along with other medication as necessary and education
Telehealth for psychiatric interviews
Outreach diabetes services
Better training of local diabetes staff and visiting specialist
<i>Interventions with Non-Significant Cost Savings</i>
Midwifery group practice
<i>Cost-Ineffective Interventions</i>
Palivizumab for high-risk infants
Broadbased healthy living program to prevent cardiovascular disease
Statins to prevent cardiovascular disease
Lower targets for blood pressure and LDL cholesterol in diabetics
<i>Interventions that were not cost-saving</i>
Community-based midwifery service

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benefits have generally been measured using individualistic and Westernised constructs of health, which have been shown, at least in the Australian context, to be distinctly different from the communitarian values of Indigenous culture [8]. This has potentially led to missed opportunities to improve indigenous health and wellbeing as the full range of benefits, costs and cost-savings that potentially arise from indigenous health interventions may not be captured. There is room for further refinement of economic methodologies to incorporate these concerns and particularly in the assessment of the applicability of existing health utility instruments, and potentially the development of new ones that may be more sensitive to Indigenous conceptions of health.

While the evidence-base identified in this review demonstrates that traditional health economic approaches can ostensibly be used to show the cost-effectiveness (or otherwise) of interventions aimed at improving Indigenous health, there has rarely been much attempt to incorporate Indigenous valuations of the potential gains from such programs.

Examples do exist in the literature of attempts to incorporate these values into economic evaluations of health interventions.

The study of the Daruk-controlled midwifery service included above attempted to do so by taking a broader cost-consequence approach rather than restricting the analysis to narrowly defined health outcomes [11]. This involved a strong qualitative component to the study, which is an approach also taken by Jin et al. in their included study above [22]. Cost-consequences analyses or 'the basket of goods approach' has been viewed with some disdain in the health economic literature because of the potential for data mining and its inability to generate a clear decision rule [37]. It has been suggested however that this can be to some extent addressed by pre-specification of a conceptual framework in which the link between the multiple outcomes are linked to the intervention [38]. Further research into the suitability of existing health economic techniques used to elicit preferences from target populations to Indigenous groups could provide a means to incorporate these values in a meaningful and rigorous way.

Characteristics of Included Studies

While there was a limited amount of cost-effectiveness research of interventions to improve the health of Indigenous population

groups, a number of conclusions can be drawn from the studies that were identified.

First, this review highlights that interventions into Indigenous populations, in particular rural and remote Indigenous communities, can be cost-effective, a broad but important finding given the often isolated and small populations of these groups when compared to non-Indigenous populations. Of the 27 interventions examined by included studies, 21 were deemed to be cost-effective or cost-saving while of the twelve interventions targeted solely to rural and remote populations, ten were found to be cost-effective or cost-saving by the respective studies. Being able to point to a body of evidence highlighting the cost-effectiveness of such interventions is important to justify widespread implementation of such programs on more than solely equity grounds and ensure that domestic debates on service provision are informed and based on the best available evidence.

The evidence-base drawn together by this review provides insights into particular interventions. Outreach programs were shown to be consistently cost-effective or cost-saving in all six interventions studied. These interventions were assessed relative to populations obtaining the services from alternative service providers. Thus they were found to be cost-saving or cost-effective despite often representing relatively high-costs for the health gains that occurred. They may be prohibitively costly in low-income environments outside of donor provision and it is also unclear how sustainable or community appropriate such models of service provision are. Explicit decisions need to be made by policy-makers in assessing the appropriateness of these services to local conditions.

The four injury prevention interventions were all found to be cost-effective as was the study of telehealth. Conversely, neither of two midwifery programs studied was found to be strictly cost-effective (one found non-significant cost-savings). Nor were the two studies focused solely on interventions in urban areas, highlighting the need for further work in this area. The majority of the interventions were targeted specifically at Indigenous groups (twenty-three interventions) and most were delivered through culturally specific medical providers, such as Aboriginal Medical Services in Australia and Canada. This is in line with findings from the literature that culturally specific services are more effective in reaching these populations [39].

Limitations of this Review and included studies

While the strength of the review lies in the broad search strategy and research question, the heterogeneity of included studies limited the policy implications that could be drawn from the identified literature. The studies were of varied scope and included different notions of what constituted a cost-effective intervention. There are inherent difficulties in comparing the outcome of the studies when the notion of what constituted a cost-effective intervention varied so greatly between them.

References

1. Gracey M, King M (2009) Indigenous health part 1: determinants and disease patterns. *Lancet* 374(9683): 65–75.
2. World Health Organization (2014) indigenous Populations. Available: http://www.who.int/topics/health_services_indigenous/en/. Accessed 30 April 2014.
3. Stephens C, Porter J, Nettleton C, Willis R (2006) indigenous Health 4: Disappearing, displaced, and undervalued: a call to action for Indigenous health worldwide. *The Lancet* 367(9527): 2019.
4. Anderson I, Crengle S, Kamaka ML, Chen TH, Palafox N, et al. (2006) Indigenous Health 1: Indigenous health in Australia, New Zealand, and the Pacific. *The Lancet* 367(9524): 1775.
5. Ohenja N, Willis R, Jackson D, Nettleton C, Good K, et al. (2006) Indigenous Health 3: Health of Indigenous people in Africa. *The Lancet* 367(9526): 1937.
6. Montenegro RA, Stephens C (2006) Indigenous Health 2: Indigenous health in Latin America and the Caribbean. *The Lancet* 367(9525): 1859.
7. Ong KS, Carter R, Vos T, Kelaher M, Anderson I (2013) Cost-effectiveness of Interventions to Prevent Cardiovascular Disease in Australia's Indigenous Population. *Heart Lung and Circulation*.
8. Mooney GH. (2009) *Challenging health economics*. New York: Oxford Univ. Press. 1–250 p.
9. Drummond M (2005) *Methods for the economic evaluation of health care programmes*. Oxford: Oxford University Press.
10. Goddard M, K Hauck, PC Smith. (2006) Priority setting in health - a political economy perspective. *Health economics, policy, and law* 1(Pt 1): 79–90.
11. Jan S, Conaty S, Hecker R, Bartlett M, Delaney S, Capon T (2004) An holistic economic evaluation of an Aboriginal community-controlled midwifery

The studies identified were largely drawn from high-income nations and focused at a primary-care level in rural or remote populations. There is a large gap in the literature for Indigenous populations of low and middle-income nations. Similarly, urban Indigenous communities have been largely overlooked in the literature despite these communities often representing the bulk of Indigenous populations within countries. In Australia, for example, it is estimated that the 60% of the 'gap' in health outcomes between the Indigenous and non-Indigenous populations is a result of the health of urban Indigenous communities [40]. The results of this review are consistent with previous studies that have pointed to a lack of studies in the area of urban Indigenous health relative to remote and rural communities [41]. Indigenous conceptions of health were rarely explicitly acknowledged in the cost-effectiveness literature. While the finding that the majority of included interventions were Indigenous-specific suggests that these factors may be implicitly be worked into most of the studies (at least to the extent that interventions are appropriately designed for these cultural groups), there is room to better include these ideas into general economic methodologies.

Conclusion

Despite global commitments to reducing Indigenous health disadvantage, relatively little is known about what constitutes cost-effective investments into Indigenous populations around the world. Furthermore, the evidence that exists has often relied on pivotal evidence extrapolated from non-Indigenous settings and been based on methods that have not allowed for the values that such communities place on health to be included. Nevertheless, in light of the limited available evidence, this review suggests that interventions into these often hard to reach populations can be cost-effective. Further economic research has the potential to provide much needed guidance to policy-makers on resource allocation decisions and help improve the health of Indigenous people around the world but it needs to be based on the development of methods that incorporate values specific to the communities in question.

Supporting Information

Checklist S1 PRISMA checklist.
(DOC)

Author Contributions

Conceived and designed the experiments: BA SJ. Performed the experiments: BA JM. Analyzed the data: BA JM. Contributed reagents/materials/analysis tools: MI SE. Contributed to the writing of the manuscript: BA SJ.

- programme in Western Sydney. *Journal of Health Services & Research Policy* 9(1): 14–21.
12. Jan S (1998) A holistic approach to the economic evaluation of health programs using institutionalist methodology. *Social science & medicine* (1982) 47(10): 1565–1572.
 13. Taylor CB, Stevenson M, Jan S, Middleton PM, Fitzharris M, et al. (2010) A systematic review of the costs and benefits of helicopter emergency medical services. *Injury* 41(1): 10–20.
 14. Ziolkowski NI, Voineskos SH, Ignacy TA, Thoma A (2013) Systematic review of economic evaluations in plastic surgery. *Plastic and reconstructive surgery* 132(1): 191–203.
 15. Arnold M, Moore SP, Hassler S, Ellison-Loschmann L, Forman D, et al. (2014) The burden of stomach cancer in indigenous populations: a systematic review and global assessment. *Gut* 63(1): 64–71.
 16. Drummond MF, et al. (1997) Users' Guides to the Medical Literature: XIII. How to Use an Article on Economic Analysis of Clinical Practice A. Are the Results of the Study Valid? *JAMA: The Journal of the American Medical Association* 277(19): 1552.
 17. Ferguson KL, et al. (2011) Cost effectiveness of serologic screening for hepatitis b prior to vaccination in hill tribes of northern Thailand. *Annals of Emergency Medicine* 58(4): S214.
 18. Carvalho CH, Custodio H, Rathore M, Salahuddin AN, Mirza A (2011) Cost-effectiveness of introducing rapid syphilis testing in the amazon region, Brazil. *Sexually Transmitted Infections* 87: A333.
 19. Magnus A, Moodie ML, Ferguson M, Cobiac LJ, Liberato SC, et al. (2013) Economic evaluation of potential fiscal strategies to improve Indigenous nutrition and health in remote communities of Australia. *Obesity Research and Clinical Practice* 7: e46–e47.
 20. Baker PR, Hoy WE, Thomas RE, (2005) Cost-effectiveness analysis of a kidney and cardiovascular disease treatment program in an Australian Aboriginal population. *Advances in Chronic Kidney Disease* 12(1): 23–31.
 21. Dyson K, Kruger E, Tennant M (2012) Networked remote area dental services: a viable, sustainable approach to oral health care in challenging environments. *The Australian Journal of Rural Health* 20(6): 334–338.
 22. Jin AJ, Martin D, Maberley D, Dawson KG, Seccombe DW, et al. (2004) Evaluation of a mobile diabetes care telemedicine clinic serving Aboriginal communities in Northern British Columbia, Canada. *International Journal of Circumpolar Health* 63 Suppl 2: 124–8.
 23. Maberley D, Walker H, Koushik A, Cruess A (2003) Screening for diabetic retinopathy in James Bay, Ontario: A cost-effectiveness analysis. *Canadian Medical Association Journal* 168(2): 160–164.
 24. Martin JD, Yidegiligne HM, (1998) The cost-effectiveness of a retinal photography screening program for preventing diabetic retinopathy in the First Nations diabetic population in British Columbia, Canada. *International Journal of Circumpolar Health* 57 Suppl 1: 379–82.
 25. McDermott R, Segal L (2006) Cost impact of improved primary level diabetes care in remote Australian indigenous communities. *Australian Journal of Primary Health* 12(2): 124–130.
 26. Panattoni L, Brown PM, Te Ao B, Webster M, Gladding P (2012) The cost effectiveness of genetic testing for CYP2C19 variants to guide thienopyridine treatment in patients with acute coronary syndromes: a New Zealand evaluation. *Pharmacoeconomics* 30(11): 1067–84.
 27. Reeve CA, Whitehall JS, Buettner PG, Norton R, Reeve DM, et al. (2006) Cost-effectiveness of respiratory syncytial virus prophylaxis with palivizumab. *Journal of Paediatrics and Child Health* 42(5): 253–258.
 28. Rush E, Obolonkin V, McLennan S, Graham D, Harris JD, et al. (2013) Lifetime cost effectiveness of a through-school nutrition and physical programme: Project Energize. *Obesity Research and Clinical Practice*.
 29. Sheerin IG, Green FT, Sellman JD (2004) What is the cost-effectiveness of hepatitis C treatment for injecting drug users on methadone maintenance in New Zealand? *Drug and Alcohol Review* 23(3): 261–272.
 30. Shore JH, Brooks E, Savin DM, Manson SM, Libby AM (2007) An economic evaluation of telehealth data collection with rural populations. *Psychiatric Services* 58(6): 830–835.
 31. Tam DY, Banerji A, Paes BA, Hui C, Tarride JE, et al. (2009) The cost effectiveness of palivizumab in term Inuit infants in the Eastern Canadian Arctic. *Journal of Medical Economics* 12(4): 361–370.
 32. Wilson C, Huang CC, Shara N, Howard BV, Fleg JL, et al. (2010) Cost-effectiveness of lower targets for blood pressure and low-density lipoprotein cholesterol in diabetes: The Stop Atherosclerosis in Native Diabetics Study (SANDS). *Journal of Clinical Lipidology* 4(3): 165–172.
 33. Gao Y, Gold L, Josif C, Bar-Zeev S, Steenkamp M, et al. (2014) A cost-consequences analysis of a Midwifery Group Practice for Aboriginal mothers and infants in the Top End of the Northern Territory, Australia. *Midwifery* 30(4): 447–455.
 34. Zaloshnja E, Miller TR, Galbraith MS, Lawrence BA, DeBruyn LM, et al. (2003) Reducing injuries among Native Americans: Five cost-outcome analyses. *Accident Analysis and Prevention* 35(5): 631–639.
 35. Sanson-Fisher RW, Campbell EM, Perkins JJ, Blunden SV, Davis BB (2006) Indigenous health research: a critical review of outputs over time. *The Medical journal of Australia* 184(10): 502.
 36. United Nations, United Nations Declaration on the Rights of Indigenous Peoples. *Human Rights Quarterly*, 2011. 33(3): 909–921.
 37. Brazier JE, McCabe C, Edlin R, (2004) Health economics and cost consequences analysis: a step back in time. *BMJ* 329: 1233.
 38. Jan S, Pronyk P, Kim J, (2008) Accounting for institutional change in health economic evaluation: a program to tackle HIV/AIDS and gender violence in Southern Africa. *Social science & medicine* (1982) 66(4): 922–932.
 39. Ong KS, Carter R, Kelaher M, Anderson I (2012) Differences in primary health care delivery to Australia's Indigenous population: a template for use in economic evaluations. *BMC health services research* 12(1): 307–307.
 40. Vos T, Barker B, Begg S, Stanley L, Lopez AD (2009) Burden of disease and injury in Aboriginal and Torres Strait Islander Peoples: the Indigenous health gap. *International journal of epidemiology* 38(2): 470–477.
 41. Eades SJ, Taylor B, Bailey S, Williamson AB, Craig JC, et al. (2010) The health of urban Aboriginal people: insufficient data to close the gap. *The Medical journal of Australia* 193(9): 521.