Title

Understanding the economic value of interventions that address perinatal mental health problems: Literature review and methodological considerations

Abstract

Objective

Economic evaluations of mental health problems typically only include short-term measures from an individual healthcare perspective. In perinatal mental illness which spans generations, this is likely to lead to underestimation of interventions' potential benefits. We sought to understand the spectrum of outcomes of perinatal mental health problems that have economic consequences and how they are captured in economic evaluations.

Methods

We conducted a systematic search of the peer-reviewed literature to identify two types of evidence: (i) synthesised evidence (i.e., systematic reviews, meta-analyses) or recent cohort studies that measured the outcomes of perinatal mental health problems, (ii) economic evaluations of interventions. After presenting the evidence narratively, we derive an overview of different types of outcomes to include in economic evaluations.

Results

Evidence on the many, wide-ranging adverse outcomes with short- and long-term economic consequences is rich, ranging from those measured during the perinatal period (e.g., mother's employment), those that require a longer-term follow-up period (e.g., children's mental health service use) and those that can be used as predictors in modelling studies (e.g., birth weight). Only a small subset of economic consequences, and their predictors (e.g., child maltreatment, poor attachment), are currently measured in economic evaluations. We make some

recommendations for how more and new types of economic evaluations might start addressing the gap in knowledge.

Conclusions

To inform decisions about reducing the costs of perinatal mental health problems, economic evaluations that provide knowledge of how interventions can reduce the short- and long-term economic consequences are urgently needed.

Key words

Economic evaluation; perinatal mental health problems; child outcomes; parenting

Highlights

Lack of evidence of how interventions address the short- and long-term economic consequences of perinatal mental health problems prevents informed resource allocation.

By identifying the many economic consequences, and categorising those by how they might be captured in economic evaluation, this study highlights the need for more and different designs of economic evaluations.

Those funding and conducting economic evaluations should consider adopting a long-term, societal perspective in economic evaluation, including benefits for families and society.

Introduction

Mental ill-health during the perinatal period, defined as the period from conception to up to 2 years after birth, affects at least one in five women [1,2]. We showed in our previous research [3] that there are high costs to governments, individuals, and society. These costs relate to the economic consequences linked to short- or long-term adverse effects of perinatal mental health problems for those giving birth and children. Examples of adverse outcomes for children include low birth weight, child health and development problems, which, for some children, might be directly linked to short-term costs (e.g., hospital care costs) or might predict future costs linked to healthcare, education, criminal justice and losses in productivity and earnings [3]. The pathways from untreated perinatal mental health problems to adverse child outcomes are increasingly well-established and include genetic, physiological, and biological mechanisms in pregnancy [4] as well as postnatal mechanisms, such as reduced caregivers' abilities to care for and nurture their infants [5].

Evidence from systematic reviews of economic evaluations [6-9], covering different types of interventions during ante- and postnatal periods, find that identifying and treating common maternal mental health problems, such as depression, during the perinatal period is likely to be cost-effective. Such findings are based on the short-term quality-of-life improvements for mothers that have been found for many psychosocial interventions, such as cognitive behaviour therapy. The scaling of those interventions has therefore been recommended in national and international guidelines [10,11] and is increasingly incorporated into countries' policies.

However, on their own, those interventions might not address all adverse consequences, including long-term ones, on women giving birth and children, which are more likely to occur when other risk factors such as poverty, violence, substance abuse or low levels of

support are present [12-14]. Parenting and parent-infant interventions have been developed that specifically seek to reduce the potential adverse consequences of perinatal mental health problems on children at risk, but so far not enough evidence is available to confirm their cost-effectiveness [15]. Systematic reviews of intervention trials have highlighted that most studies do not include long-term outcomes for children, therefore underestimating the benefits of interventions in this area [9].

Governments might be persuaded by evidence showing that interventions improve long-term outcomes for mothers and children, particularly those known to be linked to long-term costs. Economic evaluations, including through the use of decision-analytic or simulation modelling, can provide decision-makers with information about the likely short- and long-term economic consequences of preventing or reducing adverse effects in both mothers or other birthing people and children. A first step is to understand which outcomes with economic consequences might need to be considered when deciding how to design an economic evaluation in this field.

The main aim of this study was to identify and summarise evidence on the adverse short- and long-term outcomes of perinatal mental health problems, and their potential economic consequences, and show how (if at all) those are currently being addressed in economic evaluations in the field. The study also sought to explore the role of social determinants or correlates of perinatal mental health problems in influencing adverse outcomes and economic consequences. Ultimately, we wanted to contribute to a growing evidence base that can inform resource allocation decisions and also inform future economic evaluation.

Method

We reviewed the evidence on the outcomes with (likely) economic consequences of untreated perinatal mental health problems, on their correlates and on interventions that seek to address those consequences. The information was gathered and narratively synthesised with the aim to develop an overview of the many adverse short- and long-term outcomes with economic consequences of perinatal mental health problems, as well as to understand how those are currently reflected in economic evaluation designs.

By 'economic consequences' we refer to the adverse effects (= outcomes) of perinatal mental health problems that can be expressed in monetary terms. We therefore applied the following principles when including and reporting papers: We were interested in outcomes that can be almost immediately converted into economic consequences by applying a unit cost (e.g., frequency and duration of hospital services used) as well as in outcomes that can be converted into economic consequences with additional calculations (e.g., modelling). The latter is typically done using data on well-established relationships between an outcome that happened during the perinatal period (e.g., child born pre-term) and one or several long-term outcomes that are more likely to occur when the earlier adverse outcome happened (e.g., additional risk of children born pre-term developing cognitive impairment), whereby the long-term outcome is associated with costs (e.g., additional school support). For the decision whether an outcome can be expressed in monetary terms, we took a broader societal perspective in line with the World Health Organization [16], which means that values are assigned not just to service use but also to quality-of-life losses (linked to mental or physical health conditions), life-years lost (linked to mortality, including suicide), and productivity losses (including loss in earnings).

We conducted one large search of the literature, focusing on evidence from high-income countries relevant to the context of the United Kingdom, namely Australia, New Zealand, Canada, Europe, and United States of America. First, we searched databases (EMBASE,

Medline, PsycINFO, CINAHL, Cochrane) for peer-reviewed studies that measured the consequences of maternal mental health problems on mothers and children. We then identified systematic reviews and meta-analyses as well as large cohort or cross-sectional studies measuring the associations between perinatal mental health problems and adverse consequences, including social determinants and correlates of perinatal mental health problems. Whilst fathers and other non-gestational parents are also affected, there is not yet enough evidence to systematically search for it.

Next, using the same databases as before, we identified economic evaluations (and, where available, reviews of economic evaluations), i.e., studies that evaluated the (cost-) effectiveness of interventions that sought to prevent or reduce the consequences of perinatal mental health problems on children, by focusing on parenting or parent-infant relationships. Whilst we were interested in economic evaluations, we also wanted to be able to place those in the context of robust effectiveness evidence as an important source of evidence to inform economic modelling, and we therefore also included effectiveness studies. Due to similarities in how economic consequences might be addressed in relevant studies, we included economic evaluations of parenting interventions addressing parental substance misuse during the perinatal period. The systematic search was complemented with additional pragmatic hand-searches to identify evidence of potential longer-term economic consequences of some of the outcomes that interventions have effectively addressed in this area. Here, we only focus on children. This included evidence from the 'early years field' more generally - showing long-term trajectories of problems during early childhood into later childhood and adulthood, and the costs associated with those long-term trajectories.

Our inclusion criteria are shown in Table 1. Of the total of 1,588 studies screened, we identified N=41 consequences studies and N=15 intervention studies that met inclusion

criteria. The search terms, flow diagram, and data extraction tables can be found in the Supplement.

--- Table 1 about here ---

Results

We first present the findings of the studies measuring adverse outcomes of perinatal mental health problems with economic consequences summarised in Graph 1. Then, we present findings from the intervention studies and synthesise knowledge on outcomes with economic consequences currently considered in economic evaluation. Where helpful, we present the findings in the context of additional economic evidence known to us, for example to reflect on knowledge gaps or to provide information on the likely importance of an economic consequence.

Outcomes with economic consequences occurring during the perinatal period for mothers

Consequences that occur immediately during the perinatal period for mothers include*, morbidity and mortality, health-related quality-of-life losses, healthcare use and productivity losses..*

Morbidity and mortality. A large cohort study [17] found that postpartum depression is linked to an increased risk that women subsequently develop physical health conditions or die from natural or unnatural causes. Severity of mental illness further elevates the risk. Whilst it is established that suicide is the leading cause of death during the perinatal period, the links between depression or anxiety and suicide are more difficult to establish due to reporting challenges but have been suggested in small studies that analyse death record data [18].

Health-related quality-of-life losses. One systematic review of 37 studies [19] found that depression, anxiety, and stress all negatively affected the health-related quality-of-life of pregnant women. Factors such as educational attainment, employment, financial support, social support from family and friends, and a good relationship with the father have protective effects. Being poor, Black American and having a son were risk factors in certain country contexts [20,21].

Healthcare use. Evidence from three large or very large cohort or cross-sectional studies [22-24], showed that perinatal mental health problems are linked to substantially higher healthcare use by mothers, particularly in the early postpartum period. Women from a lower socio-economic background account for the largest proportion of psychiatric admissions, whilst women from a higher socio-economic group are more likely to access privately paid care, including specialist mental health services.

Productivity losses. Surprisingly, we did not identify evidence that would allow quantifying how mental health affects the employment or productivity of women giving birth even though substantial evidence exists for the general population [25]. The economic consequences have been considered in evaluations of perinatal mental health interventions in resource-poor settings, suggesting the importance of considering them [26]. The only peer-reviewed study we identified on the topic [27] found that mothers with unintended pregnancies were more likely to return to work because of financial pressures rather than because they wanted to return, in turn increasing the risk of mental health problems.

Outcomes with economic consequences occurring <u>during</u> the perinatal period for children

Consequences of perinatal mental health problems that can affect children during the perinatal period include *birth outcomes* (*pre-term birth, low-birth weight) and healthcare use*.

Birth outcomes. Findings from a meta-analysis of 23 studies [28] suggest that antenatal depression increases the risk of pre-term birth (i.e., child born before 37 weeks of gestation) as well as low birth weight. The effect on pre-term birth has been also confirmed by a large cohort study published later [29]. The effects were exacerbated when depression was severe and intimate partner violence or race other than White co-existed [30]. Pre-term birth and low birth weight are clinical outcomes that have been directly linked to quantifiable short-and long-term economic consequences in the form of healthcare costs for delivery and neonatal care [31,32], early intervention, special education, and lost productivity in adulthood [33].

Healthcare use. A meta-analysis of six studies by Jacques et al. [34] showed that infants of mothers with postnatal depression are at greater risk of being hospitalised and of death in their first year of life compared to children of unaffected mothers. A large cohort study found increased health service use and total healthcare costs in children under the age of two [35]. The latter refers to outpatient specialist visits, emergency room visits, early-intervention screenings for developmental delays.

Outcomes with economic consequences occurring <u>after</u> the perinatal period for mothers

We were unable to identify reviews of studies on the adverse long-term outcomes of perinatal mental health problems on mothers after the perinatal period.

Outcomes with economic consequences occurring <u>after</u> the perinatal period for children

With regards to consequences that occur after the perinatal period, we only identified evidence relating to children. Those consequences include *immunisation uptake, wheezing*, *child maltreatment, mental health, healthcare use, suicide, cognition, special education and school performance*.

Immunisation uptake. Findings from one cohort study [37] suggest that perinatal mental illness (of any type) negatively impact the completion rate of childhood immunisation

measured from birth to age 5 years. Maternal alcohol and substance misuse disorders had the strongest consequences on this adverse outcome. Although their economic value is difficult to quantify, childhood vaccinations are considered one of the most cost-effective interventions that contribute to healthcare system efficiency, prevention of childhood mortality, increased health-related quality-of-life and productivity gains [36].

Wheezing. Evidence from cohort studies [39,40] show an association between mother's psychological distress during pregnancy or postnatal depression on wheezing in children aged one to four years. Primary care and prescriptions costs for children with wheezing problem are sizeable in high-income countries; for example, an older study estimated those exceed 50 million Great Britain Pounds (GBP) in the United Kingdom [38].

Child maltreatment. According to a meta-analysis of 17 studies [44], perinatal depression and post-traumatic stress disorder are associated with maltreatment of children at ages up to 11 years. Severity of mental illness, intimate partner violence and relationship conflict all increase the risk and severity of this outcome [45,46]. Childhood maltreatment has many short-term and long-term economic consequences. The costs of (mental) health and social care, special education, and criminal justice linked to childhood maltreatment have been estimated at GBP 44,800 in 2013 prices [41]. If costs to wider society (i.e., productivity loss, health-related quality-of-life loss and life-years lost) are included costs are rated at GBP 630,000 [42] and are highest for children who do not survive [43].

Mental health, healthcare use and suicide. The costs of mental health problems in children are well established [47]. There is strong evidence from two meta-analyses, summarising evidence from many studies [48,49], that perinatal depression, combined with anxiety and on its own, has adverse effects on the socio-emotional development of children, at ages up to 18 years. Evidence from cohort studies [50-54] suggests a possible association between maternal

depression in both antenatal and postnatal periods and behaviour problems in children under 18 years. Correlates include maternal sleep disorder, persistence of maternal mental health problems, intimate partner violence, poverty, and child gender. A large cohort study found that maternal anxiety significantly increased the odds of neuropsychiatric-related hospitalisation in children under age 18 years [55]. Findings from one large cohort study suggest that children exposed to perinatal and ongoing maternal depression are more likely to have suicidal thoughts or attempt suicide, assessed at ages 11 to 25 years [56].

Cognition, special education, and school performance. For cognitive and related development problems, findings from three meta-analyses [57-59] suggest that maternal depression during the early postpartum period is adversely affecting children's cognitive and related development (various ages up to 18 years), and there is some evidence that this is also the case for depression during pregnancy. Evidence as to whether this association differs between boys and girls is mixed, with some recent evidence suggesting that the consequences only relate to boys.

Children with cognitive problems are much less likely to leave school with qualifications and have much lower earnings prospects [60]. From older evidence, we know that children exposed to perinatal depression are more likely to require special education [3], and findings from one very large and one large cohort study show that perinatal depression adversely affects children's readiness for school and school performance, with studies suggesting effects are strongest when mother's depression persists beyond the perinatal period [53, 61].

-- Graph 1 about here --

Short and long-term cost-effectiveness of interventions

Several interventions exist that might reduce or prevent some of the economic consequences. Understanding the costs of delivering those interventions is an important first step in economic evaluation. Evidence from a systematic review [62] shows that delivering universally provided psychological or psychosocial interventions costs less than GBP 100 per woman, whilst interventions targeting women considered at-risk because of their socio-economic circumstances cost between GBP 70 and GBP 495, and interventions targeting women with raised scores on mental health screening tools cost between GBP 500 and GBP 1,850 (all in 2013 prices). Mean total costs of psychoeducation have been estimated at GBP 266 per woman in 2013 prices [6,63]. Cost of delivering parent-infant interventions ranges from GBP 60 to GBP 437 in 2014 prices [64-67]. The cost of peer-support strongly varies depending on how the scheme is delivered and for how long women receive support, ranging between GBP 350 and GBP 2,900 in 2011 prices [68,69]. It is important to note that costs are only those of immediate resource inputs such as time spent by practitioners on delivering the intervention, or participating in training and supervision, and do not include the resources required for introducing a new intervention into an existing system.

A second step in understanding the potential cost-effectiveness of interventions is to identify whether costs might be offset by an intervention's economic consequences. (Of course, costs might also increase, thus reducing the likely cost-effectiveness of interventions.) Findings from an evaluation of a universally provided psychosocial intervention suggest that costs can be offset in the short-term through efficiency in how trained health professionals spend their time, leading to overall reduction in healthcare use and costs [70]. Peer-support evaluated in two randomised controlled trials [68,69] has been found to reduce healthcare expenditure (GBP 801 in intervention group versus GBP 1,538 in control group, in 2011 prices), although it is unclear whether those are large enough to offset costs of the intervention in the short-term. Studies also report narrative evidence on the long-term effects of peer-support on a

reduction in healthcare use. Total mean health and social care costs, including both cost of the intervention and economic consequences, were lower in the group using a sleep intervention compared to the group receiving standard care (GBP 97 versus GBP 117; price year not reported) [65,71]. The opposite was the case for a parenting programme addressing substance abuse and mental health (GBP 18,031 versus GBP16,451, in 2016 prices) [72].

We only identified one economic evaluation [73] which included long-term economic consequences by modelling the reduction in a single outcome (child maltreatment) to potential long-term economic savings. This was a parent intervention for methadone-maintained parents: it estimated a potential net saving of GBP 1.7 million for every 100 families treated (in 2013 prices). This was based on a single outcome showing that 20 cases of child maltreatment per 100 families could be prevented [73], and savings include costs incurred by health and social care, school, and criminal justice sectors.

A third step is to compare the net costs (i.e. costs of delivering the intervention minus cost consequences) with outcomes, such as quality-adjusted life-years (QALYs). Since many psychological and psychosocial interventions have strong significant and clinically meaningful effects on mother's mental health symptoms and health-related quality-of-life [74], most interventions have been found to be cost-effective based on this one outcome (i.e., QALYs gained) alone [6,7,75,76]. For example, guided-self-help has been found to be highly cost-effective for women with mild to moderate perinatal mental health problems with cost per QALY of GBP 7,200 in 2013 prices [76], which falls well below the threshold range of GBP20,000 to GBP 30,000 commonly applied by the English health technology assessment agency, the National Institute for Health and Care Excellence. Intensive cognitive behavioural therapy provided in mothers' homes can be cost-effective for women with low income [75].

In addition to or instead of establishing cost per QALY, we identified a few economic evaluations that sought to establish cost-effectiveness based on other effects on children as found for some of the above psychological and psychosocial interventions [13, 14, 77, 78] as well as, and perhaps more consistently for, parent-interventions [15, 79, 80]. If those outcomes are considered, interventions might be cost-effective based on their ability to achieve a unit improvement in certain child-related outcomes, such as reduction in child abuse potential, improvement in maternal sensitivity or infant cooperativeness [81,82]. For example, Barlow *et al*. [81] find a 51.8% probability that a parent-infant intervention is cost-effective if decision-makers were willing to pay GBP 1,000 (in 2016 prices) for a unit improvement in a measure of child abuse potential. The probability increased to 98% if decision-makers were willing to pay GBP 20,000 per unit improvement for this outcome. And McIntosh *et al.* [82] find that the mean cost per unit improvement in maternal sensitivity and infant cooperativeness was GBP 3,246 per woman (in 2004 prices). Outcomes with economic consequences include parent-infant attachment [79], child maltreatment [79], and infant sleep [80,86].

Overview of outcomes to be included in economic evaluations

Table 2 provides an overview of outcomes that might be included in economic evaluation because, based on our findings from the literature review, they seem to be consistently linked to economic consequences. This will need to be updated as new evidence emerges, such as consistent evidence on the long-term impact on mothers. We included child abuse potential as a measure of the outcome 'child maltreatment' and maternity sensitivity or infant cooperativeness as a measure of the outcome 'parent-infant attachment', which have been found to be linked to economic consequences [83-85].

We distinguish between: mothers' and children's outcomes; outcomes that can be measured during the perinatal period (e.g., maternal mortality) versus those that require longer-term follow up (e.g., children's mental health service use); outcomes that have immediate economic consequences (e.g., neonatal hospital care) versus those that do not (e.g., infant sleep); outcomes that might be useful *indicators* for short- or long-term economic consequences (e.g., immunisation uptake) versus those that are less useful as indicators (e.g., children's mental health service).

Discussion

We have summarised evidence that can inform the design of economic evaluations of interventions that seek to prevent or reduce the consequences of perinatal mental health problems on mothers and children. We identified many potential short- and long-term outcomes with economic consequences. This was a pragmatically conducted review, but it nevertheless highlights the need for more and new types of economic evaluation in the field of perinatal mental health. Previous modelling work of the costs of perinatal mental health problems have suggested the sizeable nature of the many economic consequences [3, 87]. Only a small subset of outcomes with short- and long-term economic consequences are currently measured in the few available economic evaluations, leaving a knowledge gap about how to avert those potentially sizeable impacts.

So, what needs to change? First, we argue for a broader range of outcomes, with economic consequences to be included. It is common for standard economic evaluations to be conducted alongside clinical trials and compare changes in healthcare expenditure against changes in health-related quality-of-life. As we have shown, this kind of analysis neglects a range of important outcomes with economic consequences, some of which can be collected in

the short term and others requiring longer follow-up. For example, economic evaluations in this field have not measured mother's employment situation, productivity, and income, even though those outcomes can be relatively easily measured, and are likely to have substantial economic consequences [25] that can be positively affected by interventions in this area [26].

Second, we argue that, as already done in the early child intervention field [88], future economic evaluations in the perinatal mental health field should employ more modelling alongside trials to link outcomes to longer-term economic consequences. This might be done using threshold analysis to generate knowledge about the amount by which a predictor of a negative economic consequences needs to change to offset the cost of the intervention or to be considered cost-effective. This might include establishing the costs of changing child-related outcomes (e.g., parent-infant attachment) from above to below the cut-off point of a 'case' (e.g., poor attachment) and compare those against the long-term economic consequences linked to the 'case' to establish the potential return on investment [83-85,89]. This kind of knowledge can be powerfully presented alongside a wider range of outcomes and economic consequences to persuade those that are mainly interested in changing the trajectory of a common, highly costly outcome.

Third, we need a better theoretical understanding of how interventions work for different subpopulations, and how the context in which interventions are implemented affect costs, outcomes and economic consequences [90]. We need to develop and test clearer hypotheses about what resources are required for which population to achieve different outcomes and reduce economic consequences. Participatory economic evaluation approaches, developed with relevant stakeholders, might provide a new way of identifying the most important economic consequences and predictors, and ultimately contribute to better resource allocation decisions [91].

Conclusion

The rich evidence of multiple, long-term economic consequences of perinatal mental health problems that we have identified demands that cost-effectiveness research is designed to measure such consequences. Those funding and conducting economic evaluations should give higher priority to long-term economic evaluations, conducted from a societal perspective so as to include the benefits for individuals, families and society.

Economic analyses are essential for informing the implementation that translates these potential benefits of research findings into real impacts. Economic evaluation approaches that are theory-informed and differentiate between populations and contexts, would provide valuable insights that could further improve the targeting of interventions, future adaptations and refinements.

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