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Prevention and Treatment of Externalizing Behaviour Problems in Children through Parenting Interventions

An Application of Health Economic Methods

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Abstract

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The early onset of externalizing behaviour problems (EBP) is associated with negative outcomes later in life, such as poor mental health, substance use, crime, and unemployment. Some children also develop conduct disorder (CD), entailing a high disease and economic burden for both individuals and society.

Most studies on the effectiveness and cost-effectiveness of parenting interventions targeting EBP among children have evaluated selective or indicated preventive interventions, or treatment strategies. Evidence on the effectiveness of universally delivered parenting programmes is controversial, partly due to methodological difficulties.

The overall aim of this thesis was to 1) address the methodological challenges of evaluating universal parenting programmes, and to 2) employ different health economic methods to evaluate parenting interventions for EBP and CD in children.

Study I indicated that offering low intensity levels of Triple P universally, with limited intervention attendance, does not result in improved outcomes, and may not be a worthwhile use of public resources. Study II showed that using the distribution of an outcome variable makes it possible to estimate the impact of public health interventions at the population level. Study III supports offering bibliotherapy to initially target CP in children, whereas Comet could be offered to achieve greater effects based on decision-makers' willingness to make larger investments. Cope could be offered when targeting symptom improvement, rather than clinical caseness. The economic decision model in Study IV demonstrated that Triple P for the treatment of CD appears to represent good value for money, when delivered in a Group format, but less likely, when delivered in an Individual format.

To reduce the burden of mental health problems in childhood, cost-effective and evidence-based interventions should be provided on a continuum from prevention through early intervention to treatment. We believe our results can assist decision-makers in resource allocation to this field.

Keywords: parenting interventions, externalizing behaviour problems, conduct problems, conduct disorder, health economics, cost-effectiveness, prevention, treatment

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"We never will have all we need.
Expectation will always exceed
capacity..."

Aneuryn Bevin, 1948
Welsh Minister of Health 1945-1951

List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I **Sampaio, F.,** Sarkadi, A., Salari, R., Zethraeus, N., Feldman, I. (2015) Cost and effects of a universal parenting programme delivered to parents of preschoolers. *European Journal of Public Health*, 25(6): 1035-42.

II Sarkadi, A., **Sampaio, F.,** Kelly, M.P., Feldman, I. (2014) A novel approach used outcome distribution curves to estimate the population-level impact of a public health intervention. *Journal of Clinical Epidemiology*. 67(7): 785-92.

III **Sampaio, F.,** Enebrink, P., Mihalopoulos, C., Feldman, I. Cost-effectiveness of four parenting programs and bibliotherapy for parents of children with conduct problems: a multicentre randomized controlled trial. *Under review at the Journal of Mental Health Policy and Economics.*

IV **Sampaio, F.**, Barendregt, J., Feldman, I., Mihalopoulos, C. Population cost-effectiveness of the Triple P parenting programme for the treatment of Conduct Disorder: an economic modelling study. *Manuscript*

Contents

Abbreviations

ACE	Assessing cost-effectiveness
CBA	Cost-benefit analysis
CD	Conduct disorder
CEA	Cost-effectiveness analysis
CP	Conduct problems
CUA	Cost-utility analysis
DALY	Disability adjusted life year
DASS	Depression Anxiety Stress Scales
DW	Disability weight
EBP	Externalizing behaviour problems
ECBI	Eyberg child behaviour inventory
GBD	Global burden of disease
GP	General practitioner
ICER	Incremental cost-effectiveness ratio
IY	Incredible Years
MAUI	Multi-attribute utility instrument
MBS	Medical benefits schedule
QALY	Quality adjusted life year
RCT	Randomized controlled trial
RR	Relative risk
SD	Standard deviation
UI	Uncertainty interval
WTP	Willingness-to-pay
YLD	Years lived with disability
YLL	Years of life lost

1. Introduction

Externalizing behaviour problems (EBP), including conduct problems (CP), hyperactivity and oppositional behaviour, are one of the most frequent reasons for referral to child and adolescent mental health services in Western countries (1). For some children these problems are a stage of development that eventually resolve themselves, but for a considerable proportion the early onset of problems entails a poor prognosis and is associated with a range of negative outcomes later in life, such as poor mental health, substance use, crime (2), poor academic achievement, unemployment, and lower earnings (3, 4). Some children are also given a diagnosis of conduct disorder (CD) (5). CD entails a high disease (6) and economic burden for individuals, families and society (7, 8).

Parenting interventions are effective in the prevention and treatment of EBP (9-11) and are the recommended approach in targeting these problems amongst children and adolescents (12). A variety of parenting interventions are available in many countries, including in Sweden. The recognition of the importance of the parent-child relationship in the mental and physical health of children has prompted the Swedish government to invest 140 million SEK to finance parenting interventions in 2009-2013 (13). In 2012, approximately 41% of the counties and 87% of the municipalities in Sweden were offering parenting interventions to target EBP (14). Unfortunately no economic evaluation of these interventions was conducted prior to their implementation to ensure that these interventions are an appropriate and worthwhile use of scarce Swedish resources. There is thus, a need to investigate the cost-effectiveness of parenting interventions within a Swedish context to inform decision-making on whether they are truly value for money.

Only a handful of studies have looked at the short-term cost-effectiveness of parenting interventions for EBP (9, 15, 16), and even fewer have assessed their long-term cost-effectiveness (17, 18). Notably, only one has recently been undertaken within a Swedish context (16). Further, a majority of the studies on the effectiveness and cost-effectiveness of parenting interventions targeting EBP among children and adolescents are of either selective or indicated preventive interventions, or treatment strategies (9, 15, 17, 18). Evidence on the effectiveness of universally delivered parenting programmes is controversial, partly due to methodological challenges (19, 20). Importantly,

there is only one economic evaluation of a universal preventive parenting intervention for EBP (16). A mental health and social care service system should provide evidence-based interventions in different areas, on a continuum from prevention and early intervention to treatment (21).

To support decision-making and the optimal allocation of public resources, there is a need to have high quality information of the effectiveness and cost-effectiveness of alternative interventions available. Economic evaluations provide the platform necessary to make such decisions. This thesis aimed to: 1) address the methodological challenges of evaluating universal parenting interventions, and 2) evaluate parenting interventions for the prevention and treatment of EBP in children, using different health economic methods, thus contributing to narrowing the knowledge gap in regard to their costs and effects. The use of different health economic methods, and of different analytical frameworks in the studies upon which this thesis is based provides information relevant to different stakeholders, and constitutes a piece in the process of decision-making about the allocation of resources to the prevention and treatment of EBP in children and adolescents.

2. Background

2.1. Mental health among children

Mental disorders are highly prevalent and account for 7.4% of the total disease burden worldwide, as measured by disability-adjusted life years (DALYs) (22), and the leading cause of disability worldwide, as measured by years lived with disability (YLDs). Childhood behavioural disorders per se account for 3.4% of the total burden (DALYs), caused by mental and substance use disorders. The total burden varies by age and sex, with the highest burden occurring in people aged 10-29 years (22). Research shows that most adulthood mental disorders begin in childhood and adolescence, with behavioural disorders, including attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD) and conduct disorder (CD) having the earliest age of onset (23). A review of the literature on the epidemiology of child psychiatric disorders shows that approximately one fourth of youth has experienced a mental disorder during the past year, and about one third across their lifetimes (24). The most frequent conditions in children are anxiety disorders, followed by behavioural disorders, mood disorders, and substance use disorders. Fewer than half of youth, in the US and UK, with current mental disorders receive mental health specialty treatment. However, those with the most severe disorders tend to receive mental health services (24).

2.2. Externalizing behaviour problems among children

Behaviour problems in children can be divided into two major classes: internalizing and externalizing. Internalizing behaviours are reflected in social withdrawal, fearfulness, unhappiness and anxiety. Externalizing behaviours are expressed outward against others or have an impact on the child´s environment. These consist of disruptive, hyperactive and aggressive behaviours (25) and may include impulsivity, tantrums, fighting, destructive behaviour, disobedience, hitting, biting, bullying, lying and stealing (26). Thus, the externalizing construct includes three types of problems: conduct problems, hyperactivity and oppositional behaviour. Depending on the intensity and frequency of these behaviours, they can be linked to a different diagnosis of CD, ADHD and ODD, respectively (5). This thesis will focus on externaliz-

ing behaviour problems (EBP) and conduct problems (CP), as the main target of the parenting interventions evaluated in the papers included.

Within the externalizing behaviours construct, CP can be seen as occurring on a continuous scale with different intensity levels. Some children display a more repetitive and persistent pattern of CP that is not considered age appropriate, and can be warranted a diagnosis of CD. CD is manifested by a persistent pattern (12 months or more) of hostile and defiant behaviour. To obtain a DSM-V diagnosis a child needs to fulfil at least three criteria out of 15, e.g. destruction of property and aggression toward humans or animals (5). A CD diagnosis is normally given to children aged between five and 18 years. Figure 1 depicts the dimensions of the constructs EBP, CP and CD.

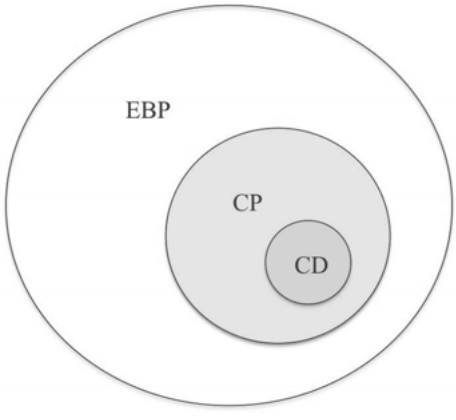


Figure 1. Relation between the constructs of externalizing behaviour problems, conduct problems, and conduct disorder.

CD can be sub-classified into childhood or adolescent onset, depending on whether symptoms appeared before or after age ten. An early age of onset has been shown to predict a life-course persistent pattern of CP, whereas an adolescence onset predicts a temporary period of CP with discontinuation after adolescence (27). The prevalence of CD is estimated to range between 0%-10% worldwide (28), with approximately 7.5% of girls and 8.2% of boys aged 7-15 years having life-course persistent CP, and 17.4% of girls and 12.3% of boys having adolescent onset CP (29). For some children CP is a stage of development that eventually remits, with studies showing probabilities of remission lying between 33% and 56% (30-34). For children whose problems do not remit, the early onset of CP increases the risk of negative outcomes later in life, including poor educational outcomes, antisocial and criminal behaviour, alcohol and drug abuse, mental health problems including depression (2, 4), and unemployment (3). In sum, a high propor-

tion of children and adolescents with CP and diagnosed CD grow up to be antisocial adults with poor and destructive lifestyles (2, 3), and a significant minority will develop antisocial personality disorder (35).

The aetiology of CP is multifactorial, with numerous studies over the years having identified a multitude of risk factors that are thought to be involved in the emergence and development of CP, depending on their age of onset (27). Some of the factors thought to predict CP include impulsivity (36), cognitive deficits (37), genetic heritability (38), parental history of CP (39), harsh and inconsistent parental practices (40, 41), child physical abuse (42), parental conflict (43), large family size (44), low family income (45), aggressive peers, and peer rejection (46). However, for many risk factors, it is not known whether they have causal effects (47). What is clear, however, is that many children with CP find themselves in a vicious cycle of high baseline environmental and relational risks, norm-breaking and impulsive behaviour. This leads to more conflict and coercive reactions from parents and school, thus to increased environmental (low school attainment) and relational (antisocial peers) risks, contributing to further norm-breaking behaviours.

2.2.1. Disease and economic burden of conduct disorders

According to the most recent burden of disease study, CD is the 72nd leading contributor overall, and among the 15 leading causes of the global disease burden among children aged 5-19 years. Together with ADHD, CD accounted for 0.8% of the total global disability (morbidity) (6). CD and its related consequences also place a high financial burden on the individual, families and society. A study by Romeo and colleagues in 2006 has estimated the mean annual cost of a child aged 3-8 in the UK with CD is £5960 including health care, educational and voluntary sector service use, with the greatest cost burden being borne by the family (8). In the UK another longitudinal study of children aged 10 found that the costs of children with CD at age 28 were ten times higher than those of children with no conduct problems and three times higher than those of children with conduct problems (but not a diagnosis of CD) (7).

In summary, CD in childhood and adolescence is becoming more frequent in Western countries, and places a high disease and economic burden on individuals, families and society. There is substantial health sector and non-health sector costs, involving different sectors of the economy (e.g. health and social care services, family, schools, police and criminal justice agencies), which means that any interventions, which can either prevent or appropriately treat CD, should be considered for routine implementation. However, the evidence of the value for money credentials of such interventions

also needs to be considered in climates of increasing competition of use of scarce health sector resources.

2.2.2. Management of conduct problems

To reduce the prevalence and thus the large burden caused by CD, both treatment interventions targeting children with existing problems, and interventions to prevent problems from occurring or worsening must be implemented and made available. Prevention and treatment are necessary and complementary components of a comprehensive approach to the mental, emotional, and behavioural health of young people.

Within the mental health intervention spectrum (48), prevention can be classified according to the population they target (See Figure 2). Universal interventions target the whole population. They target high-risk populations, rather than high-risk individuals within a population; it is the population, and not the individual within the population, that may carry the risk, which is generally relatively low (49). Examples are programmes offered to all parents to provide them with skills to communicate with their children, and build positive relationships. Selective interventions target at-risk population groups, and examples are programmes offered to children or parents exposed to risk factors, such as high-risk or low SES neighbourhoods, and parental mental illness, to reduce the risk of adverse mental, emotional, or behavioural outcomes. Indicated interventions target high-risk groups with signs or symptoms of disorders, but who do not meet the full criteria for a diagnosis. Examples are programmes for children or parents of children with CP.

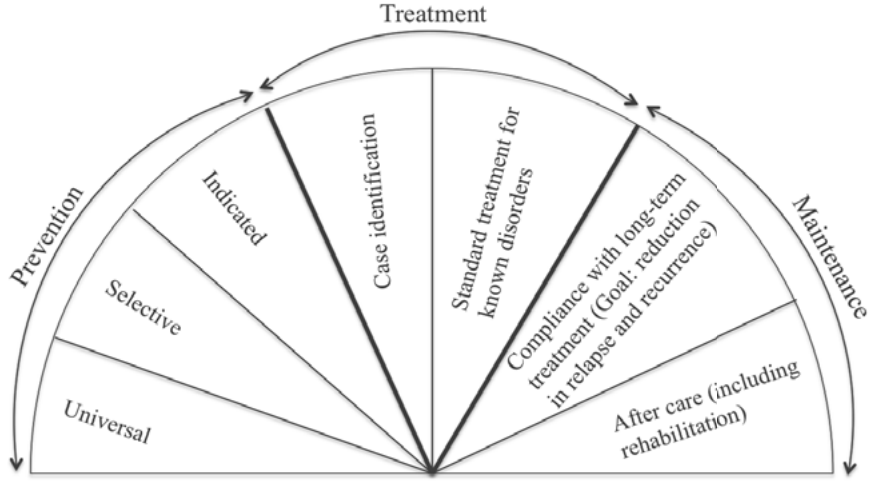


Figure 2. The mental health intervention spectrum for mental disorders (Mrazek and Haggerty, 1994)

CD offers good opportunities for prevention because it can be detected early reasonably well. Early intervention offers a way to tackle symptomatology early, and prevent problems from becoming deep-rooted (50). Psychological interventions for CP have been developed across a wide spectrum, from those focused on the psychological wellbeing of the child to those targeting familial and social domains. The interventions available can be child-, parent-, or family-focused, and may involve teachers and the community. They can be based on different theoretical backgrounds, ranging from those based on social learning theory to more individually conceptualized cognitive behavioural therapy approaches, systemic approaches and psychodynamic approaches (12).

Treatment of CD can involve psychological interventions, pharmacotherapy or a combination of both. Currently, psychological interventions are recommended as the first line treatment for CD (12). Psychological interventions are preferred over pharmacotherapy because of the lack of approved pharmacological interventions for CD alone. The best-studied pharmacological interventions for children and adolescents with CD are medicines used for ADHD comorbid with CD, where there is evidence that reduction in hyperactivity and impulsivity also results in reduced conduct problems. Furthermore, there are also concerns regarding medication side effects, as well as concerns regarding lifetime treatment since those medications do not target related risk factors, but temporarily alter CD symptomatology (12).

2.3. Parenting interventions and their effectiveness

Parenting interventions are based on the assumption that parenting practices are involved in the emergence, progress, and maintenance of child EBP (51). Thus, a variety of parenting interventions have been developed to teach parents strategies to deal with problematic behaviour in their children. These interventions have the major aim of improving parenting styles and parent-child relationships through the reduction of harsh and inconsistent parenting practices, and the focus on positive incentives and enhanced parental communication with the child (52).

These interventions can have different delivery formats including: face-to-face; in groups; individually; and or self-directed, using written materials such as books, CDs or DVDs, or multimedia, such as the Internet. They can also have different theoretical underpinnings, with a common distinction being made between behavioural and non-behavioural interventions. Behavioural parenting interventions are based on social learning theory, and their goal is to change negatively reinforced interactions within families by providing parents with strategies to respond to the child's misbehaviour.

Non-behavioural programmes can be very diverse but commonly have their base in psychotherapy and attachment theory. They aim to improve the parent-child relationship by encouraging parents to reflect on their own feelings and expectations about their children (53). Parenting interventions tend to be intensive and short-term, commonly lasting between 1-2h weekly for about 8 to 10 weeks. They can be held in a variety of settings including clinics, preschools, schools, and community facilities. Further, they can be delivered by a variety of practitioners including psychologists, nurses, social workers, or community workers.

Parenting programmes have been shown to be effective in the treatment of CP in children (9, 10, 12) and are related to positive changes in parenting skills and parental mental wellbeing, when delivered at high intensity levels (9-11). The impacts of parenting programmes have been shown to remain for up to 12- to 18-months, while other studies show a decline of impact at one-year follow-up (9, 54).

In terms of preventing mental health problems in children, various studies on selective and targeted parenting interventions have shown promising results, and the potential of such interventions to reduce child CP (11, 55). Additionally, self-help parenting interventions, employing multimedia and written materials, have also shown effectiveness in reducing child CP in the short-term, compared to control groups (56-58). The evidence on universal parenting interventions shows conflicting results, with some studies showing effective results (often small effect sizes) in the reduction of child problem behaviour (19), and others showing no effects (20, 59, 60). A meta-analysis, conducted by the Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU) (61), concluded that the existent international studies on parenting interventions for the prevention of mental ill-health amongst children have shown limited scientific evidence. In general, studies on parenting programmes offered universally have had difficulties showing effects. This is probably due to limited power in relation to the prevalence of problems in the targeted population, limited coverage due to self-selection into the intervention, and clinical instead of promotive outcome measures employed (20).

2.4. Decision-making in health care

Economic considerations have assumed an increasingly central role in the planning, management and evaluation of health systems. This is due to the scarcity of resources relative to the increasing health needs and demands of the population, and the large number of available interventions (62). There-

fore, there is a need for informed decision-making that can help to allocate heath resources, and to set priorities in health and health care.

Health economic evaluations have become a popular tool used to guide decision-making and inform health policy (63, 64). Economic evaluations can be defined as the comparative analysis of the benefits (consequences) and costs of alternative interventions targeting a certain health event (65). It is thus, normative in nature, concerned with how benefits are measured and valued, and with making judgments on alternative ways of allocating resources. It differs from 'positive economics', which is descriptive and predictive in nature, and where the focus is on describing trends in economic variables and predicting future trends (66).

Importantly, one of the principles underpinning economics and economic evaluations is the concept of opportunity cost. It pertains to the understanding that the real cost of any intervention is the benefit foregone by not allocating the resources to the next best alternative intervention (65). Normative economics underpins the principles and practice of economic evaluation, as it aims to value and compare different uses of resources to inform decision-making and policy (67). In normative economics, the notion of cost is in relation to the value of other opportunities foregone.

Normative economic approaches

There are three main normative economic approaches that are evident in the practice of economic evaluations in health care: welfarism; extra-welfarism; and the decision-making school (68). Welfarism (or welfare economics*)* aims to maximize societal welfare given a societal budget constraint. It is based on the assumption that social welfare depends only on the wellbeing of the individuals, where they are assumed to be the best judges of their own wellbeing or utility. Welfare economics utilizes the principle of Pareto optimality, where no person can be made better off without making someone else worse off (69). What happens is that, in public health, interventions often make some people better off and others worse off. This economic approach deals with this by applying a potential Pareto criterion such as the Kaldor-Hicks criterion (also called the compensation principle) (69), where the person who becomes better off can compensate the person who becomes worse off, and still be better off than before. Such compensation does not need to be paid (in practice, it is only theoretical), and is thus used to estimate the willingness-to-pay (WTP) estimate of societal benefits. If the societal benefits exceed the costs, welfare is increased. In welfare economics, welfare is considered as the sum of all individual utilities. Because utility per se is difficult to measure, this approach assumes that individuals can express their value for something by their preferences, which are signalled by their WTP for goods and services in the market place. However it does not take

into account the distribution of outcomes in the population. The applicability of this approach to health care has been questioned by notable economists including Anthony Culyer (1989) (67), since health may be considered an important dimension, which contributes to social welfare separately than other goods or services, i.e. sits outside of the Paretian welfarist function. Due to such thinking regarding the value of health, the "extra-welfarism" school of economic thought came into prominence in the late 1980s and early 1990s.

Briefly, the extra-welfarist school of economic thought includes other aspects of social welfare in the social welfare function, such as happiness, pain, and quality of relationships (67). Much of Culyer's thoughts were influenced by Amartya Sen (70). Sen argued that the focus of social welfare should be on individual "functionings" and "capabilities", rather than preferences or utilities. Functionings are defined as ranging from elementary (such as being adequately nourished) to more complex (such as being able to have self-respect). Capabilities are defined as the different combinations of functionings a person can achieve. Such functionings and capabilities may be considered essential for people to engage in utility maximizing choices. Extra-welfarist economics aims to maximize health effects, encapsulated by "functionings" and "capabilities", which may reflect both individual and societal preferences. Therefore, Culyer argued that the maximand in health economics should be "health", rather than the more traditional "utility". Extra-welfarism allows the use of outcomes other than utilities, for example health, and allows the use of sources of valuation other than individual preferences (i.e. decision-makers or general public). However, similar to welfarism, permits the weighting of outcomes according to principles based on preferences (e.g. ethical principles); and allows for comparisons of wellbeing through different dimensions (71).

Another economic approach to economic evaluation, which has arisen from the need to capture the broad range of issues that are relevant to decision-makers, is the *decision-making school (68).* This approach states that whatever is useful to decision-makers should be considered in economic evaluation, including health, equity, acceptability, and feasibility, or even utility of interventions. Carter (2001) proposes that this approach has two distinctive features: 1) it is the responsibility of the analysts to ensure all relevant objectives of decision-makers are captured in the welfare function (it does not exclude the welfarist or the extra-welfarist approach, but rather seeks to capture all objectives and values of decision-makers); 2) equity should be considered and balanced against economic efficiency, given that equity is of importance to decision-makers in the financing of health care systems (68).

Forms of economic evaluations

The three schools of economic thought, briefly discussed above, mean that the format of economic evaluation can change. There are three main forms of full economic evaluation techniques: cost-benefit analysis (CBA), cost-effectiveness analysis (CEA), and cost-utility analysis (CUA) (65). All three differ in terms of the theoretical school of thought upon which they are based, and the method used to measure and value the benefits of the interventions being compared. CBA stems from welfare economics, where both the costs and benefits of alternative courses of action are valued in monetary terms, based on individuals' willingness to pay. In this way, the economic evaluation resembles a standard market transaction whereby the "value" of a good is expressed in terms of the willingness to pay for that good. What goes into this valuation is up to each individual, and relies on the individual knowing what the attributes and/or benefits of the good (or intervention) are. Results are usually expressed as either a ratio of costs to benefits, or as the net benefits of one intervention over the other. Both CEA and CUA have arisen from the extra-welfarist approach, where outcomes are measured in health related terms/physical units, with results expressed as incremental cost-effectiveness ratios (ICER). CEA measures benefits with symptomatic or diagnostic indicators that are meaningful to clinicians, e.g. clinical cases averted, or number of symptom-free days. However, this impedes cross-therapy patient comparisons, limiting comparisons to studies with the same outcome measures. In a CUA benefits are measured, which combine mortality and morbidity into one single measures (65), with the quality adjusted life years (QALYs) gained or disability adjusted life years (DALYs) averted. Both outcome measures allow for the comparison of study results across different therapies and clinical areas.

Other common forms of economic evaluations include cost-minimization analysis (where costs of alternative interventions that have equal outcomes are compared), and cost-consequence analysis (where costs and outcomes are presented separately, leaving the decision regarding the relative importance of different outcomes to the reader). Partial economic evaluations, comparing either costs or effects only, are also possible. Any of the existing economic evaluation techniques can be used under the decision-making school approach, depending on the objectives of the decision-maker. Which type of evaluation is the most appropriate is a matter of debate, and depends on the context, and on who makes the decision about which interventions to use. For example, CBA are broader in scope, and can be used to inform resource allocation decisions, both within and between sectors of the economy, not limited to comparing programmes within health care. CBA are particularly used in two areas of the public sector, the transport and environmental sector (65). Within health economics, several studies have been performed within the willingness-to-pay approach, e.g. studies on the WTP for antihy-

pertensive therapy (72), or for in vitro fertilization (73). CEA and CUA are the predominant forms of economic evaluation within the health sector. CEA is good for technical efficiency decisions ("Technical efficiency is achieved when production is organized to minimize the inputs required to produce a given output." (69)) within a single disease area, where a single clinical outcome is meaningful. For example, when a decision needs to be made about interventions that affect the same outcome, e.g. two interventions to increase depression screening, using the outcome number of cases detected. When the objective is to make decisions about allocative efficiency ("…allocative efficiency is achieved when resources are produced and allocated so as to produce the "optimal" level of each output and to distribute the outputs in line with the value consumers place on them." (69)), or interventions that affect different health programmes targeting different outcomes, for example, depression screening and prevention of externalizing behaviour problems in children, a CUA is the most appropriate. It allows to compare interventions across different clinical areas, and to include benefits that affect different aspects of health.

Cost-utility analysis

In CUA benefits are commonly measured using QALYs (other measures are also used such as DALYs or healthy years equivalent (HYE) (65)) as briefly mentioned in the sub-section above. These measures take into account morbidity and mortality, and allow for comparisons to be made across different diseases. A QALY is calculated as the length of time spent in a particular health state multiplied by a "weight", sometimes also called a utility, denoting a preference for that health state. The weights usually sit on a continuum ranging from 0 (denoting death) to 1 (denoting perfect health). Less than perfect states of health are assigned different weights along this continuum. There are a number of ways to obtain weights, which should be preference-based. According to Drummond et al. (2005) (65) preferences can be value-based or utility-based, where "values" denote decisions made under conditions of certainty, and "utilities" denote decisions made under conditions of uncertainty. A decision made under conditions of certainty would be a situation where an individual would be asked to compare two or more outcomes, and to choose between them, or scale them. In a decision made under conditions of uncertainty, an individual would be asked to compare two alternatives, where at least one of the alternatives contained uncertainty or probabilities (62, 65). Measuring preferences for health outcomes through direct elicitation from the population, with first hand experience from the health condition being assessed, can be a very time consuming and expensive task. Therefore, pre-scored multi-attribute utility instruments (MAUIs) have been developed to obtain weights for different health states from the general population. These MAUIs have scoring formulas that allow deriving quality of life weights for different health states (65).

DALYs are a descriptive measure of overall disease burden, and are the metric used in the Global Burden of Disease (GBD) studies (6). DALYs combine years of life lost due to premature mortality (YLL) and years of life lived with a disability (YLD) (determined by multiplying the duration of illness by a disability weight (DW) associated with that particular health state) into one metric (65). DALYs are much like QALYs in reverse. DALYs measure years of healthy life lost, whereas QALYs measure years of healthy life gained. Thus, a weight of 0 denotes no disability, and a weight of 1 denotes death. DALYs are often based on a series of universal weights, based on expert valuations of the level of wellbeing associated with various conditions, rather than based on the reported experience of people who have a disability. DALYs were used in study IV, as the context of the study was the latest GBD study (28), used as a source of the DW and epidemiological parameters.

CUA are the most commonly used framework for formal decision-making, as the ICERs have inherent value for money criteria, in contrary to CEA. Thus, CUA are the recommended framework for most international decision-making authorities, such as The National Institute for Health and Care Excellence in the UK, and the Pharmaceutical Benefits Advisory Committee in Australia (74). There are no fixed value for money thresholds, and different international decision-making authorities suggest different cut-offs. In the UK a threshold of £30,000/QALY gained is suggested (63), whereas in Australia a threshold of $50,000/QALY gained is commonly used (75). In Sweden, the Swedish National Board of Health and Welfare suggests a cut-off of SEK 500,000 (76). Any intervention whose ICER falls below this criterion is denoted good value for money and worthy of financing. Such thresholds are largely value judgements and not reflective of a "gold standard" of value for money.

The societal perspective in economic evaluation

In economic evaluations, a clear specification of the research question and the study perspective provides the foundation for identifying and measuring the costs and consequences to be included in the analysis. It can be confined to a specific payer, i.e. the health care system, the municipality, or include broader societal costs (societal perspective). The societal perspective provides the broadest description of the consequences of choices, and considers costs incurring to all sectors of the economy, including patients, informal care provided by family members and carers, voluntary sector, justice, education, and productivity losses from morbidity or premature death. This perspective is recommended by the Swedish Pharmaceutical Benefits Board (77). In the UK, the perspective of the health sector is recommended for clinical decisions, and the perspective of the public sector is recommended for public health programmes (63).

In economic evaluations in child health, the inclusion of the broad spectrum of societal costs are important, as large costs often incur in sectors other than the health care (7, 8). For example, as previously mentioned in section 2.2.1, the costs of a child with CD accrue to different sectors of the society, including health care, educational and voluntary sector, as well as costs to the family (7, 8). If all relevant costs and outcomes of the alternatives being compared can be collected, they can be averaged across all patients in the groups being compared to obtain a mean cost and a mean effect for each group. This allows for the estimation of the cost-effectiveness of the intervention compared to the alternative being assessed: the ICER. The ICER is the difference in costs divided by the difference in effects of both alternatives (65).

Analytical frameworks for economic evaluations

Economic evaluations can be based on data from studies such as Randomised Controlled Trials (RCTs), or based on decision analytic models, or can incorporate both. RCTs are commonly used as the vehicle for economic evaluations of health care interventions. RCTs have long been used to provide the source of data on resource use, baseline event rates, health outcome values and relative treatment effects. If designed adequately they: 1) allow relevant representative samples of the patient population who would use the therapy/programme to be enrolled in the study; 2) adopt sufficient follow-up periods to allow for assessment of all relevant costs and benefits; 3) measure a wide range of effectiveness endpoints, including quality of life, resource use, feasibility; 4) enrol a sufficient number of participants to ensure adequate study power; 5) allow proper randomization of participants to minimize bias; 6) allow for the intervention to be compared with a well-accepted therapeutic comparator; and 7) collect data on a broad set of resource use (78). However RCT-based evaluations have limitations. These include: 1) failure to compare all relevant options – often RCTs compare only few of the options, which are relevant for the process of decision-making in a specific clinical area; 2) limited time horizons – in many trial based evaluations the follow-up periods are shorter than the appropriate time frame needed to capture all benefits and costs relevant for decision-making (however, for some studies the time horizon can suffice if a longer follow-up period would only confirm the results, and thus the decision-adopted); 3) restricted generalizability to different settings – estimates of costs and benefits, collected via evaluations conducted in specific countries or settings, may reflect great variability in patients and routine clinical practice; 4) failure to incorporate all evidence – trials may fail to collect all relevant data necessary for cost-effectiveness analysis, such as data on resource use and health-related quality of life; and 5) inadequate quantification of decision-uncertainty, which is only limited to the evidence in the trial (79). Trial-based evidence can be sufficient for the adoption of a decision on whether it is "worth" investing in

a new intervention, but in many cases it will not suffice (78). Ideally, a combination of trial and model-based evidence is necessary, where evidence from RCTs can be used as inputs to decision-analysis.

Economic decision-modelling has been defined as a systematic approach to decision-making under uncertainty (80). It compares the expected costs and consequences of decision options by synthetizing information from multiple sources, and applying mathematical techniques (81). The use of decision-modelling provides a framework that has the potential to meet all the requirements for economic evaluation for decision-making (80). Some of the more notable advantages of modelling include the ability to use the epidemiological literature to extrapolate shorter-term outcomes (which might come from an RCT) to a longer-term time horizon (therefore capturing all important costs and consequences), as well as model the population cost-effectiveness of interventions (not just limiting this to the trial participants). Modelling can also test the impact of varying assumptions in the model (e.g. around adherence rates) to determine the impact on the ICER. Of course, information from RCTs using regression techniques can also provide information on such variables (e.g. impact of adherence rates, or of initial disease severity on the ICER). Notably, another key advantage of modelling is that it allows for the creation of an appropriate structure of the disease at hand, reflecting the prognosis that the patients may be experiencing, and the impact of the interventions evaluated on these prognoses. Other advantages of modelling include that all relevant intervention options can considered, by bringing together all available evidence on the matter from different sources. Finally, economic decision modelling allows for the assessment of uncertainty around the evaluation related to the parameters and model structure, and makes it possible to identify the value and need for additional research (65, 79).

2.5. Economic evaluations of parenting interventions

As noted above in section 2.3, parenting interventions are the current recommended approach in targeting CP among children and adolescents (9, 12). With the increasing availability of parenting interventions in a variety of countries, and the vast literature on their effectiveness (9-11), there is a need to investigate their cost-effectiveness to inform decision-making as to whether they are value for money. Most existing economic evaluations of parenting programmes are of preventive indicated and targeted interventions. Only a handful of studies have looked into the short-term cost-effectiveness of parenting interventions (9, 15, 16). Two studies, one by Edwards and colleagues, 2007 (82), and one by O´Neill and colleagues, 2011 (83) have investigated the cost-effectiveness of the Incredible Years (IY) parenting pro-

gramme, and found it to be cost-effective in the short-term (6 months follow-up), with an ICER of £73 (€109, $142) (82) and €87 (83) per reduced point on the intensity scale of the Eyberg Child Behaviour Inventory (ECBI). However, as argued above, while the authors stated this is cost-effective, it is not immediately clear whether £73/point reduction in the ECBI is actually cost-effective, since there is no established threshold value for society's WTP for such outcome. Both studies based their evaluations on data from RCTs, with participants (children) who at baseline had scored over the clinical cut-off point on a symptom-based rating scale. O'Neill and colleagues (83) also conducted a long-term cost-benefit analysis, with the assumption of long-run benefits of the intervention, and suggested that the IY had the potential to generate favourable long-term economic returns, in relation to reduction in crime, unemployment and improvement in education (83). Both studies adopted a public sector perspective, including health, social and special education services.

Other studies have used modelling techniques to assess the longer-term cost-effectiveness of parenting interventions pertaining to the reduction of the prevalence of CD (17, 18). Mihalopoulos and colleagues, 2007 (18) found that another programme, Triple P, had a high likelihood of being cost saving when a longer-term time horizon is considered. Mihalopoulos used Australian population level data to model if Triple P could be a worthwhile use of public resources, and compared programme costs with the cost savings associated with the projected reduction in population prevalence of CD. The study by Bonin and colleagues, 2011, modelled, in a scenario analysis, the costs and longer-term savings of a range of programmes likely to be implemented in the UK, associated with the reduction of the probability of persistent CD among children in the UK, and found them to be cost saving.

As regards universal preventive interventions, Ulfsdotter and colleagues, 2015 (16) investigated the cost-effectiveness of a universal parenting programme, All Children In Focus, in Sweden, and found it to be cost-effective in the short-term with an ICER of €47 290 per gained QALY, below the Swedish WTP threshold value of 500,000 SEK (€55,000), but with a low probability of cost-effectiveness. The evaluation was conducted alongside an RCT, from a limited societal perspective, including parents' time and travel costs.

The evidence on whether parenting interventions are value for money is still scarce. The wide use of these interventions in different contexts and countries, their potential to improve child outcomes, in particular child behaviour, and the high costs associated with CP, highlight the need to conduct economic evaluations that can support decision-making. There is also a need to broaden the spectrum of the economic evaluations targeting all types of pro-

grammes from the mental health intervention spectrum (48), and help set priorities, so that resources can be allocated in an optimal manner, and gains in total population health can be achieved.

2.5.1. Challenges in economic evaluations of parenting interventions

Applying the standard methods of economic evaluation to child health, and in particular to parenting interventions, can be challenging (84). A major limitation is the scarcity of validated child-specific outcome measures. Most existing economic evaluations of parenting programmes use disease specific symptom-based rating scales to measure outcomes, such as the Eyberg Child Behaviour Inventory (ECBI) (measures externalizing behaviour problems) (85), the Child Behaviour Checklist (measures internalizing and externalizing behaviour problems) (86), or the Strengths and Difficulties Questionnaire (measures emotional problems, peer relations, ADHD and conduct problems) (87). The inclusion of these measures poses limitations. First, these measures are not immediately comparable; second these are clinical measures, which means they miss improvements that may be relevant to everyday life, self-efficacy and general wellbeing; third, there is no established threshold value for society's WTP for such outcomes, thus the comparison of cost-effectiveness results is limited to other studies with the same outcome measures (84).

To tackle these limitations, the use indirect preference-based utility measures, i.e. multi-attribute utility instruments (MAUIs) is advocated (84). MAUIs make it possible to obtain quality of life weights for different health states (65), thus generating QALYs, and allowing for pragmatic value for money estimations to be made. Measuring preferences for health outcomes through direct elicitation from children (or even from adults) is difficult due to conceptual challenges (time consuming and expensive), and the inability of children to grasp the concept of time, which would allow them to trade risks against time spent in various health states (84). Importantly, there is no MAUI applicable for children at preschool age.

Another limitation is that economic evaluations of parenting interventions often use parent proxies to report health status and resource use in young children (84). However, due to difficulties in measuring outcomes in young children, the proxy use may be the only viable option to measure such outcomes. Moreover, existing economic evaluations of RCTs of parenting interventions are largely short-term cross-over trials, as commonly control groups quickly cross-over to the intervention group, so the longer term impacts are not known (88). Therefore, economic evaluations of parenting in-

terventions often have difficulty in capturing the full span of consequences and costs, as most of these occur way into the future, and it is very difficult and expensive to run such long-term trials (84). This is an important matter, as in the case of CD, such condition often results in the excessive use of resources in different sectors of the society, such as health care, education and justice services (7).

2.6. Evaluating parenting programmes as public health interventions

A majority of the studies on the efficacy and effectiveness of parenting interventions are of selective, indicated or treatment strategies. Few studies assess the effectiveness of universal parenting interventions, which stems from the fact that RCTs of universal interventions are harder to implement and evaluate, and often require very large sample sizes to show a significant reduction of the problem measured. Trials of parenting programmes, especially those using universal approaches often report small effect sizes with low or no significance levels (59). This tendency to focus on determining effect size and significance levels at an individual rather than population level (89, 90) is one of the unintended consequences of the application of the principles of evidence-based medicine to public health. However, small effects in population-based studies could be of importance from a population health point of view because they may be comparable to larger effect sizes from studies on clinical populations.

Geoffrey Rose introduced the population health approach, in 1985 (91). The goal was to obtain overall population change rather than individual outcomes. The population health approach has the potential to reach population benefits by controlling the determinants of incidence, lowering the mean level of risk factors, thus shift the whole distribution of the exposure variable of interest toward healthier levels. This is simply the goal of public health interventions. These benefits, however, cannot always be estimated by using standard analytical methods of evidence-based medicine, which only focus on analysing differences in mean values as a consequence of an intervention. These benefits may be estimated by taking into account the shape and the changes in the main parameters of the distribution of the variable of interest. For example, as a result of a targeted intervention that has successfully addressed the need of a population at risk for a studied outcome, the standard deviation (SD) may have decreased, while the population mean is unchanged. This approach is used in paper II, where we demonstrate how we can use the distribution curve to estimate the population-level impact of a universal parenting programme.

3. Rationale for this dissertation

Many studies and government documents have drawn attention to the importance of tackling mental health problems among children and adolescents for optimal psychological and social functioning, and wellbeing. Externalizing behaviour problems are of particular relevance due to their high prevalence, associated negative outcomes down the line, and consequently high disease and economic burden for the individuals, families and societies.

Poor parenting practices are involved in the emergence, progress, and maintenance of child EBP. Thus, parenting interventions have been developed to teach parents strategies to deal with problematic behaviour in their children. Several studies on the effectiveness of parenting interventions have demonstrated they can result in positive changes in child behaviour and parental wellbeing.

A majority of the studies on the effectiveness of parenting interventions targeting EBP among children and adolescents are of either selective or indicated preventive interventions, or treatment strategies. Evidence on the effectiveness of universally delivered parenting programmes is controversial, partly due to methodological challenges.

In addition, although the number of studies on the cost-effectiveness of parenting interventions is increasing, there is still insufficient evidence on whether they are a good use of public spending. Furthermore, these studies have been variably undertaken, making it difficult to compare their results to each other. This thesis aimed to: 1) address the methodological challenges of evaluating universal parenting interventions, and 2) evaluate parenting interventions for the prevention and treatment of EBP in children, using different health economic methods, thus contributing to narrowing the knowledge gap in regard to their costs and effects.

4. Overall and specific aims

The overall aim of this thesis was to 1) address the methodological challenges of evaluating universal parenting interventions, and 2) evaluate parenting interventions for the prevention and treatment of EBP in children, using different health economic methods, thus contributing to narrowing the knowledge gap in regard to their costs and effects.

The specific aims of the studies included in this thesis were to:

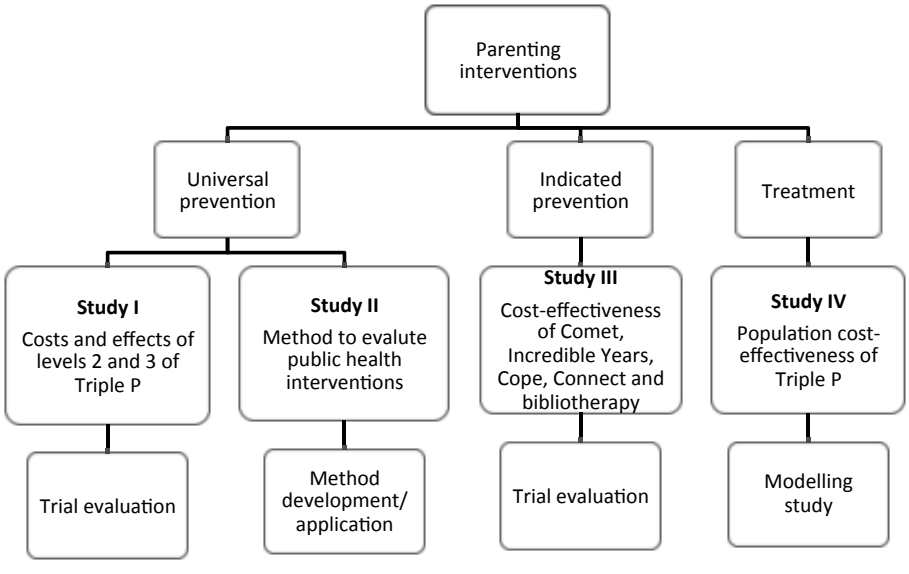
1. Assess the intervention costs and the effects of levels 2 and 3 of the Triple P programme, delivered universally, to parents of preschoolers, on child externalizing behaviour problems and parental mental health, compared to a waitlist control

2. Propose an analytical framework within which public health interventions can be evaluated, present its mathematical proof, and demonstrate its use using trial data from study I

3. Determine the cost-effectiveness of four indicated group-based parenting programmes: Comet, Incredible Years, Cope, and Connect, along with bibliotherapy compared to a waitlist control, targeting CP in children

4. Determine the cost-effectiveness of Triple P for the treatment of CD in children, from a health sector perspective, using the Australian population as an example, through the use of economic modelling techniques

5. Schematic summary of the studies included in this dissertation



5.1. Study I: Cost and effects of a universal parenting programme delivered to parents of preschoolers

5.1.1. Aim

To assess the intervention costs and the effects of levels 2 and 3 of the Triple P programme, delivered universally, in Sweden, to parents of preschoolers aged 2-5 years, on child EBP and parental mental health, compared to a waitlist control, at 18-months follow-up.

5.1.2. Methods

Study design

This study is based on data from a cluster randomized controlled trial (RCT), conducted in 2009-2011, in Uppsala municipality, Sweden. The trial comprises the intervention condition (the Triple P programme offered universally, and allowing for self-selection of participants, thus a real-world scenario was created) and a waitlist control condition (no intervention).

Randomization and study participants

Twenty-two preschools expressed interest to participate. These were matched into pairs by size and socioeconomic status, and randomized to the intervention (12) or to the control group (10). After randomization, one preschool dropped out from the control condition. Preschool teachers invited both parents of all eligible 830 children (502 in the intervention and 328 in the control group), aged 2-5 years, to participate in the study.

Of the 502 children in the intervention group, 312 (62.2%) children had baseline data, corresponding to 488 parents: 286 mothers and 202 fathers. Of the 328 children in the control group, 176 (53.7%) children had baseline data corresponding to 271 parents: 160 mothers and 111 fathers. The parental outcome analyses are based on this sample with baseline data.

For the child outcome analyses, we excluded parents of children younger than 3 years, to whom the child behaviour problem instrument did not apply. Ratings for only one parent per child were included. For children with both parents participating, mothers were selected, as mothers had a higher participation rate, and more often provided ratings of child outcomes (10). This resulted in a final sample of 355 children: 234 children in the intervention (213 mothers and 21 fathers), and 121 in the control (111 mothers and 10 fathers). Parents completed questionnaires at baseline, 6-, 12-, and 18-months follow-up, where information on socio-demographic variables, child and parental health outcomes was collected. Parents from the control group

had to wait 18 months before they were offered the intervention. All preschools in both conditions had access to care-as-usual.

The intervention

The Triple P – Positive Parenting Programme, developed at the University of Queensland, Australia, is a multilevel system of parenting support that has its origins in social learning theory and the principles of behaviour, cognitive and affective change. Its aims to prevent and treat social, emotional, and behavioural problems in children, from birth to 16 years, by enhancing the knowledge, skills, and confidence of parents. It has five levels of increasing strength, from universal parenting information strategies (Level 1), to an intensive intervention for families facing multiple sources of distress (Level 5) (92).

In this study, only levels 2 and 3 were offered to parents in the intervention preschools, who could self-select into the intervention. Level 2 consists of a series of three stand-alone 90-min group seminars. It provides developmental guidance to parents of children with no or mild behaviour difficulties. Level 3 includes up to four 15-20-min individual sessions targeted towards parents of children with mild to moderate behaviour difficulties. It involves active skills training for parents (92). The intervention was delivered continuously and unevenly throughout the study period.

Health outcomes

The primary outcome is *child externalizing behaviour problems* measured by an abbreviated version of the Eyberg Child Behaviour Inventory (ECBI-22), validated in a Swedish sample (93). The ECBI is a commonly used parent-report measure of EBP in children aged 2-16 years. Parents rate the frequency of externalizing behaviours on a 7-point Likert scale measuring the intensity of the problem. The ECBI total score ranges from 22 to 154, and is an aggregation of all items. Higher scores mean higher level of problems. Scores above the 95th percentile were considered clinical.

A secondary measure was *parental mental health* measured by the Depression Anxiety and Stress Scales (DASS-21) (94), which provides mean scores for each subscale and cut-off points, to indicate risk of depression (score > 9), anxiety (score > 7), and stress (score > 14).

Identification, measurement and valuation of intervention costs

Intervention costs were collected from a municipality payer´s perspective, and based on 312 children, aged 2-5 years, and 488 parents with baseline data, in the intervention preschools. Costs at 12- (accrued within 1 year) and 18-months follow-up (length of programme delivery) are presented in 2014

prices in Swedish krona (SEK), and converted into Euros (€). Cost data, obtained from project documentation, included investment costs and running costs. Investment costs included marketing and practitioner training costs. Running costs included course material, rent of the venue, and time for practitioners preparing and running the intervention. Other resources potentially impacted by the intervention (such as general practitioner (GP) costs, etc) were not measured in this study.

Analysis strategy

Preschool intracluster correlation coefficients at baseline were found negligible, thus clustering effects were ignored. Linear Mixed Models (LMM) for repeated measures analyses, using an intention-to-treat principle (all families irrespective of intervention uptake were included), were used to assess the impact of Triple P on the outcome variables. LMM is suitable for longitudinal designs, where missing data are present.

5.1.3. Results

Over 12 months, 30% of the mothers and 16% of the fathers self-selected into the intervention. Sixty-seven (app. 29%) of the parents of the 234 children in the intervention group attended at least one session; 86.9% between baseline and 6-month follow-up, 13.1% between 6- and 12-month follow-up, and 19.7% between 12- and 18-month follow-up. The numbers add up to more than 100% because the attendance was spread over time for some parents, with some participating in multiple modules of Triple P. There were no significant ($p > .05$) baseline differences between conditions, however, children in the intervention group had higher problem scores than children in the control group ($p < .05$).

Our intention-to-treat analysis showed that, compared to the waitlist control, Triple P showed no significant improvement in child EBP, or parental mental health at either of the follow-up points ($p > .05$) (Table 1).

The annual costs of running Triple P were 227 SEK (€24) per child, or 145 SEK (€16) per parent. Including investment costs, Triple P cost 3007 SEK (€323) per child, or 1922 SEK (€207) per parent. Most costs accrued within 1 year.

Table 1. Effects of time and intervention on child EBP and parental mental health

		Intervention	Control	Pairwise Condition*Time Interaction			
		M (SE)	M (SE)	t	p	95% CI	Effect size*
Child behaviour	n	229	120				
Baseline		57.53 (0.87)	53.70 (1.21)	-	-	-	-
6m FU		54.85 (0.92)	53.14 (1.25)	-1.719	0.086	[-4.64, 0.31]	0.18
12m FU		54.50 (0.97)	52.78 (1.30)	-1.688	0.092	[-4.58, 0.34]	0.21
18m FU		53.75 (0.97)	52.08 (1.30)	-1.805	0.072	[-4.42, 0.19]	0.15
Parental mental health							
Depression	n	475	259				
Baseline		4.13 (0.27)	4.67 (0.37)	-	-	-	-
6m FU		3.85 (0.30)	4.26 (0.40)	1.044	0.296	[-0.48, 1.58]	0.00
12m FU		3.54 (0.33)	4.09 (0.42)	-0.032	0.974	[-1.04, 1.01]	0.03
18m FU		3.70 (0.33)	3.68 (0.43)	0.252	0.801	[-0.82, 1.07]	0.13
Anxiety	n	476	262				
Baseline		1.79 (0.18)	2.30 (0.24)	-	-	-	-
6m FU		1.68 (0.20)	2.16 (0.26)	1.279	0.201	[-0.26, 1.21]	0.02
12m FU		1.58 (0.22)	1.97 (0.28)	0.299	0.765	[-0.61, 0.84]	0.01
18m FU		1.94 (0.22)	1.97 (0.29)	0.102	0.919	[-0.63, 0.70]	0.14
Stress	n	476	270				
Baseline		8.29 (0.31)	8.53 (0.42)	-	-	-	-
6m FU		7.55 (0.34)	8.08 (0.45)	0.081	0.935	[-1.11, 1.20]	0.02
12m FU		7.19 (0.38)	8.11 (0.48)	-1.176	0.240	[-1.83, 0.46]	0.10
18m FU		7.14 (0.37)	7.33 (0.49)	-0.542	0.588	[-1.34, 0.76]	0.08

SE = Standard error; CI = Confidence interval
*Effect size formula used = difference between two mean changes (baseline – follow-up) between conditions, divided by the pooled standard deviation of both conditions at baseline

5.1.4. Conclusions

Offering low levels of Triple P universally, with 29% intervention attendance, may not be a reasonable use of public resources, as it provided no evidence of improvement in child EBP, or in parental mental health. As the cost per child is very low, further studies, with a greater number of participants to detect small effect sizes, are needed to specify the intensity and attendance rate needed to produce sustainable effects, and infer cost-effectiveness.

5.2. Study II: A novel approach used outcome distribution curves to estimate the population-level impact of a public health intervention

5.2.1. Aim

To propose an analytical framework within which public health interventions can be evaluated, present its mathematical proof, and demonstrate its use using real trial data.

5.2.2. Methods

In study I, we applied standard inferential statistical methods to assess the impact of levels 2 and 3 of Triple P, offered universally, on child EBP. When using traditional analytical methods designed for clinical trials we could not detect a programme effect. This was in line with other trials of universal preventing interventions that often report small effect sizes with low or no significance levels, when using conventional statistical analyses (20, 59). However, small effects in a single study could be of importance from a population health point of view. In public health the goal is to ”shift the curve”, i.e. move the population distribution curve of the targeted outcome or risk factor toward healthier levels, and to decrease the distribution of the outcome, implying higher proportions of the population being within the healthier intervals (95).

With this in mind, we tested another way to analyze our trial data with a population health approach in mind, looking at the outcomes through a population lens, rather than considering the effects of the parenting programme on the individual level. In this study, we present and discuss the use of the distribution curve to estimate the impact of levels 2 and 3 of Triple P, delivered universally, and allowing for self-selection of participants into the intervention, on child EBP, using 12-months follow-up trial data.

Using the distribution curve to analyse outcomes

Many of the measures used widely in population health research can be described by a distribution. Mathematically, the shape of the curve depends on two parameters, namely a mean (μ) and an SD (σ), representing the dispersion of a certain variable from its mean level in that population. This dispersion variable can be used to describe the probability density for that health variable, creating what is called a normal distribution function.

When trying to use the normal (Gaussian) distribution curve as a measure of effect of an intervention, account should be taken of the distribution curve of

the outcome of interest at baseline (φ1) and at follow-up (φ2). The intervention is successful if there is a shift of the baseline distribution curve in the desirable (healthier) direction. The same approach can be used for other types of distribution. The area between the two overlapping distribution curves at baseline and follow-up (non-overlapping area) represents the impact of the intervention, that is, the proportion of the target population that benefited from the intervention.

5.2.3. Results

Child EBP, in our sample, followed a normal distribution. The distribution of total ECBI intensity scores at baseline and 12-months follow-up, for both the intervention and control groups, are presented in Figure 3A and B, respectively. The grey area between the two curves (non-overlapping area) represents the health gains between baseline and follow-up.

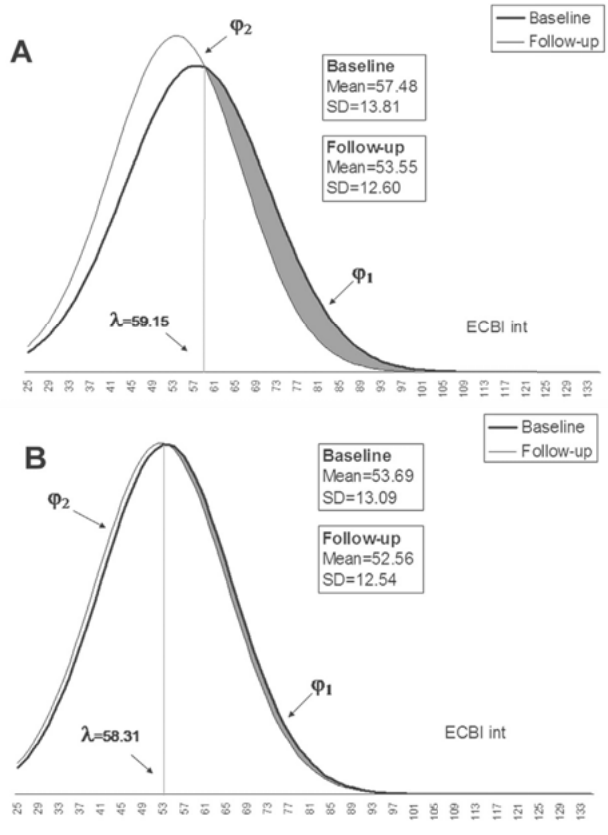


Figure 3A and B. Using the normal distribution curve to demonstrate the distribution of ECBI intensity scores in the target population. φ1 (F1) represents the distribution function of the outcome at baseline, and φ2 (F2) represents the distribution function at follow-up. λ is the intersection between the two curves φ1 and φ2.

The size of the overlapping area between the two curves can be calculated for both the intervention and the control group by using the equation:

$f(\mu 1,\sigma 1, \mu 2,\sigma 2,) = F2 - F1$

Approximately 12% [95% CI 9%-17%] of the children in the intervention group improved health outcomes, compared to 3% [95% CI 1%-7%] in the control group. The absolute health gain after the intervention was 9% (estimated difference between the health gains in both groups). This difference was considered significant because the 95% confidence intervals for both groups did not overlap.

The same approach was used to estimate the impact of Triple P on child EBP, based on parents' educational level. We estimated that 15% [95% CI 6%-25%] of the children with parents with lower educational level improved health outcomes, compared to 6% [95% CI 4%-16%] for those with higher educational level. This difference was not significant, but serves for demonstration purposes. The method requires knowing the distribution function of the outcome of interest a priori.

5.2.4. Conclusions

In Study II, we proposed a new model for evaluating public health interventions, where the focus is on population level and not individual change. We demonstrated that it is possible to calculate the impact of public health interventions by using the distribution of an outcome variable. This requires knowing the distribution function. The method can be used to evaluate the differential impact of population health measures on different segments of the population, with diverse risk profiles, and their potential to improve health inequities.

5.3. Study III: Cost-effectiveness of four parenting programmes and bibliotherapy for parents of children with conduct problems: a multicentre randomized controlled trial

5.3.1. Aim

To determine the cost-effectiveness of four parenting programmes: Comet, Incredible Years (IY), Cope, and Connect, along with bibliotherapy, compared to a waitlist control, targeting conduct problems in children, aged 3-12 years.

5.3.2. Methods

Study design and participants

This study is based on data from a multicentre RCT, conducted in Sweden, in community-based services, The National Effectiveness Trial of Parenting Programmes. This RCT evaluated four group-based face-to-face programmes: Comet, IY, Cope and Connect, compared to a waitlist control (55). In addition to these conditions, in our study, bibliotherapy is included. Parents of 1104 children were randomized to one of the programmes, bibliotherapy, or the waitlist control. Randomization was done according to the child's age, thus parents of children aged 3-8 years were randomized to the age-relevant versions of Cope, IY and Comet, and parents of children aged 9-12 years were randomized to the programmes developed for older children, Cope, Comet and Connect. Bibliotherapy was offered to all parents, irrespective of the child's age.

Of the 1104 randomized families, 802 started a programme, or read part of the book (Comet=172, Connect=196, IY=92, Cope=175, bibliotherapy=167), and 159 remained in the waitlist control, thus constituting our study's sample (n=961). 765 families (95.4%) in the intervention conditions, and 148 (93%) in the waitlist control, completed post-test data. The parent who attended most of the sessions was the primary reporter (mother=86.6%). If attendance was equal, the mother was selected.

Interventions evaluated

The four parenting programmes evaluated in this study share common features (they are all manual-based and practitioner-led on a group face-to-face basis), and they also differ on some key aspects. Comet (56), IY (50), and Cope (96) are based on behavioural techniques, teaching parents to use positive reinforcement, and to be consistent about rules. Connect (97) is based on

attachment theory, and emphasizes the importance of strengthening the parent-child relationship through, e.g., parents' self-reflection and understanding of the child's need for autonomy. The number and length of sessions varies across programmes, with Comet comprising 11 sessions, 2.5 hours long; IY 12 sessions, 2.5 hours long; Cope 10 sessions, 2 hours long; and Connect 10 sessions, 1 hour long. Bibliotherapy consists of the book "Five times more love" (98), a self-guided parent management tool, in Swedish, that aims to help parents develop positive parenting strategies. It builds on behavioural theories, and all chapters are based on different themes about common problems experienced by parents, and combine advice with practical exercises and examples, supported by practice and research.

Economic evaluation

This study is a within trial comparative cost analysis, followed by a cost-effectiveness analysis (CEA), undertaken from a limited health sector perspective. Parents' time costs have also been included as a separate analysis. The time horizon is 4 months, which mirrors the last follow-up of the RCT upon which the study is based. Costs were collected in 2009 prices, adjusted for inflation, and presented in 2014 US dollars (US$).

Health outcomes

Child conduct problems (CP) were measured with the Eyberg Child Behaviour Inventory with 36 items (85). In this study, we adopt a way of measuring outcomes that combines improvement and recovery, the *reliable clinical change index* (CS/RCI) (99), based on the changes in the total ECBI total intensity scores. The CS/RCI allows the creation of categories: recovered, improved, unchanged, and deteriorated. Effectiveness was expressed as the proportion of "recovered cases" of conduct problems.

Identification, measurement and valuation of costs

Only the *costs of delivering the interventions* were included in this analysis, as the RCT did not measure in detail other health services, which children may also be using. The cost analysis was based on all parents of the 802 children in the intervention group, and is presented on a group level. Intervention costs include training and operating costs. Training costs include training fees, allowance for training time, and travel cost per practitioner. Operating costs include salaried time for two group practitioners preparing and running the interventions, rent of the venue, cost of the books, and programme yearly license cost. Total intervention costs include only 20% of the total training cost, to represent the spread of the costs over a five-year period before reaccreditation.

Other costs impacted by the interventions include parents' time for attending programme sessions, homework, and reading the book. Parents' time was

estimated based on the opportunity cost of foregone leisure time, as all group meetings took place after working hours.

Analysis strategy

The analyses included all parents who participated at least once in a programme, or read part of the book. A logistic regression was used to predict the likelihood of a child being recovered, at post-test, based on condition, i.e. based on the different groups. Chi-squares were used to compare the proportion of recovered cases between conditions. Data on parents' participation in the interventions were linked to group costs to estimate individual level costs. Differences between conditions were evaluated with a non-parametric Kruskal-Wallis test for overall comparisons, and Mann-Whitney tests for pairwise comparisons.

A comparative cost analysis was performed for interventions whose outcomes differed significantly from the waitlist control, and later a CEA for all interventions whose outcomes differed significantly from both the waitlist control and each other. Interventions that did not show significant differences from the waitlist control were excluded from further consideration in both analyses. Cost and effect data for the interventions that showed differences in the CEA were combined and rank ordered in ascending order of outcomes following the principle of extended dominance (78). Later, an incremental cost-effectiveness ratio (ICER) was calculated. The proportion of recovered cases at post-test, and the total intervention costs including parents' time costs were used in the primary CEA. Non-parametric bootstrapping was used to obtain 95% confidence intervals around the ICER (100). Secondary analyses were performed to study the robustness of the results: "improved+recovered" cases, intervention completers, exclusion of parents' time costs, exclusion of training costs.

5.3.3. Results

All interventions apart from Connect significantly reduced child conduct problems compared to the waitlist control ($p < .05$). Of the other interventions, Comet resulted in a significantly higher proportion of recovered cases compared to bibliotherapy (29.7% vs 17.4%; $p < .05$).

Table 2 shows the intervention costs on a group level, and the average costs per child, with inclusion and exclusion of parents' time costs, for all the interventions. On a group level*, excluding parents' time costs,* Comet had the highest total intervention cost, US$162,240 (operating costs were the major cost driver), and the IY had the highest total operating cost, US$125,324 (practitioners' time preparing sessions were the major cost driver). The average cost per child, for total intervention costs, varied between US$14 per

child for bibliotherapy, and US$1457 per child for IY. The average cost per child, for total operating costs, varied between US$14 per child for bibliotherapy, and US$1362 per child for IY. *Including parents' time costs*, Comet yielded the highest total intervention cost, US$207,040, and bibliotherapy the lowest, US$23,402. The IY had the highest average cost per child both for total intervention and operating costs, US$1765, US$1670, respectively. Bibliotherapy had the lowest average cost per child for both total cost estimations, US$140. Cope had the highest parent time costs, US$53,869, whereas bibliotherapy had the lowest, US$21,090.

Table 2. Group intervention costs and group average cost per child, with inclusion and exclusion of parents' time costs, 2014 US$ prices

Total intervention costs (group level)	**Comet**	**Connect**	**IY**	**Cope**	**Bibliotherapy**
Number of children	172	196	92	175	167
Total intervention cost (with parents' time)*	**207,040**	**102,133**	**162,391**	**129,994**	**23,402**
Average total cost/child	1204	521	1765	743	140
Total intervention cost (without parents' time)	**162,240**	**71,193**	**134,071**	**76,125**	**2312**
Average total cost/child	943	363	1457	435	14
Total operating cost (with parents' time)	**162,266**	**80,288**	**153,644**	**118,273**	**23,402**
Average operating cost/child	943	410	1670	676	140
Total operating cost (without parents' time)	**117,466**	**49,348**	**125,324**	**64,404**	**2312**
Average operating cost/child	683	252	1362	368	14

*Costs used in the primary and secondary analyses

As regards individual level intervention costs, bibliotherapy had the lowest average cost per child, US$83.95, followed by Connect, US$469.82, Cope, US$495.77, Comet, US$1109.30 and the IY, US$1685.28. There were significant differences in average costs per child between the interventions (total intervention costs including parents' time used in the analysis) (all pairwise comparisons $p < .001$) (Table 2).

In the primary analyses, a comparative analysis was performed on the interventions whose outcomes differed significantly from the waitlist control, namely bibliotherapy, Cope, Comet and IY. Subsequently, we estimated the cost-effectiveness of the interventions whose outcomes differed from the waitlist control, and from each other, namely bibliotherapy and Comet. Connect was excluded from further analyses, as its outcomes did not differ from the waitlist. A comparative cost analysis rendered an average cost per recov-

ered case for bibliotherapy of US$483, for Cope US$1972, for Comet US$3741, and for IY US$6668. When we used our stricter definition of outcome, Comet showed significantly better outcomes than bibliotherapy, with an incremental effect of 0.122 recovered cases (proportion) of CP and higher costs, with an incremental cost of US$1056, thus rendering an incremental cost-effectiveness ratio (ICER) of US$8375 (95% CI US$5087 to US$24,054) per recovered case of CP, compared to bibliotherapy.

Secondary analysis of "recovered and improved", and of intervention completers showed that bibliotherapy was no longer effective compared to the waitlist. No differences were found between the programmes, with Cope being the cheapest alternative. Excluding parents' time costs and training costs did not change the cost-effectiveness results of the primary analysis, with Comet entailing higher incremental costs and effects than bibliotherapy.

5.3.4. Conclusions

All interventions apart from Connect significantly reduced child CP, compared to the waitlist control. Of the other interventions, Comet resulted in a significantly higher proportion of recovered cases, compared to bibliotherapy. Comet had an ICER of US$8375 per recovered case of CP compared to bibliotherapy. Secondary analysis of "recovered and improved", and of intervention completers held Cope as the cheapest alternative. The results suggest the delivery of different programmes according to budget constraints and problem severity. In the absence of a willingness-to-pay threshold, bibliotherapy could be a cheap and effective option to initially target CP, within a limited budget, whereas Comet could be offered to achieve greater effects based on decision-makers willingness to make larger investments. Cope could be offered to target broader outcomes, other than clinical caseness. The results should be interpreted with caution when considering decision-making about value for money, as the time horizon is very short, the study has a limited costing perspective, and there is no inclusion of a multi-attribute utility instrument sensitive to domains of quality of life impacted by CP in children.

5.4. Study IV: Population cost-effectiveness of the Triple P parenting programme for the treatment of Conduct Disorder: an economic modelling study

5.4.1. Aim

To determine the cost-effectiveness of the Triple P programme for the treatment of CD in children, using the Australian population as an example. Through the use of modelling techniques this study aimed to determine if Triple P is good value for money, and thus assist priority setting of health care resources in Australia.

5.4.2. Methods

Economic evaluation framework

This study is part of a series of economic evaluations undertaken as part of the programme of research at the Centre for Research Excellence in Mental Health Systems Improvement in Australia (http://mhsystems.org.au). The programme is funded by the National Health and Medical Research Council, and has the overarching goal to design a model mental health service system for Australia, that could optimally reduce the burden of mental disorders.

While the studies undertaken in this centre are broad in scope, a significant proportion of the work is dedicated to assessing the cost-effectiveness of interventions across a range of mental disorders. All studies use a standardized economic evaluation modelling framework to avoid methodological confounding, ensure comparability of results, and provide transparency for stakeholders and potential users of the research results. The framework is based on the technical methods, which have been developed for use in the ACE studies, particularly the ACE-Prevention study (75, 101). Importantly, the cost-effectiveness of CD interventions have never been modelled using this type of modelling approach before, therefore this study is quite unique in that respect.

Briefly, the following principles underpin the analyses: (1) the economic perspective is the health sector, with the focus on government as a third-party payer; (2) costs are divided into costs accruing to the government and private costs, although time and travel costs are included and reported separately; (3) data on intervention effectiveness is sourced from published literature; (4) a cost-utility analysis is performed with DALYs averted as the main outcome (this is because the starting context of the study is the burden of disease as measured by DALYs (22)); (5) a "partial null" comparator is chosen to represent the theoretical level of disease that could be present if

the interventions under evaluation were not in place; (6) costs are measured in Australian dollars, and expressed in values for the reference year of 2013 (to best match the latest 2010 GBD study; (7) an annual discount rate of 3% is applied to both costs and outcomes.

Literature search and intervention effectiveness

Given that the context of our study is to estimate the avertable disease burden (as measured by the most recent GBD studies (6, 28)), we had to focus on diagnosed disorder. We excluded studies measuring changes in CD symptoms, which was due to difficulties in determining how changes in a mean and a SD score, on a symptom rating scale, translate into actual cases of CD.

While many parenting interventions exist for the treatment of CD, one of the most widely researched and internationally disseminated programmes is the Triple P programme (92), thus Triple P was used in this study for model testing. To find evidence on the effectiveness of Triple P, we performed a literature search of existing reviews in international databases, and a complementary search of empirical studies that may not have been included in the latest review of Triple P studies, published in 2014 (11). From all studies, we selected those that fulfilled the following inclusion criteria: RCT's and quasi-experimental designs; interventions for the treatment of CD (targeting children with a diagnosis of CD); and studies reporting diagnostic clinical outcomes (reported as number of prevalent cases) at follow-up, measured using structural clinical interviews, or disease-specific symptom scales with good predictive value of CD.

Most studies from the four reviews (9, 11, 102, 103), found through the literature search, were on the effectiveness of Triple P level 4 (n=101), thus we opted to model the cost-effectiveness of level 4 Triple P. Six studies satisfied our inclusion criteria (104-109). All six studies used the ECBI (85) as the main outcome instrument. The ECBI has good predictive value of CD, and discriminates between clinical and non-clinical conditions. A cut-off score is recommended to indicate the need for treatment. One intervention was delivered in group face-to-face format, one individual face-to-face (Standard), three self-directed, two self-directed plus telephone assisted, and one Internet self-directed.

The project's CD Technical Advisory Panel was consulted (composed of clinical experts and researchers in the field) to assess how sound the interventions are in the real world setting of the Australian mental health services. The self-directed formats of Triple P were excluded, as neither being relevant nor currently used for treatment of CD. Thus the Group (106) and the Standard individual (108) face-to-face versions were selected for economic evaluation.

Martin & Sanders, 2003 (106) assessed the effectiveness of Group Triple P, targeting a cohort of 2-9 year olds, and Sanders et al., 2000 (108), assessed the effectiveness of Standard individual Triple P, targeting a cohort of 3 year olds. We calculated an effect size for each intervention, at post-test, expressed as a relative risk (RR): RR = 0.054 [95% CI 0.003-0.875] for the Group version, and RR = 0.655 [95% CI 0.484-0.887] for the Standard version. Both estimates were based on studies with parents who completed the intervention, thus parents who dropped out prior to programme completion accrued costs but no benefits.

Study population and intervention pathway

This study models the delivery of Group and Standard Triple P, targeting children aged 5-9 years in the Australian 2013 population, receiving treatment for CD. The selected age group reflects the ages included in the two trials that provided the efficacy estimates. A lower limit of 5 years was applied, corresponding to the age a diagnosis of CD can be set in clinical practice. Although the trial on Standard Triple P targeted younger children (3 year olds), the model targets the same cohort of children aged 5-9 years, for both Group and Standard Triple P, for comparison purposes.

We developed an intervention pathway that is representative of the routine Australian mental health services. Children with conduct problems are first referred to a GP, who performs an assessment of the child and makes a referral to a psychologist. Here, we assumed parents are offered either the Group or the Standard variant of Triple P. Group Triple P includes four 2-hour group sessions, followed by four individual telephone consultations lasting in average 30 minutes. Parents are also given a workbook. Standard Triple P includes 10 individual 60-90 minute sessions. Upon completion of the course of treatment, the child is called for at least one GP follow-up visit. The following steps are considered, when selecting the final eligible population to participate in the interventions: a) proportion of children with a diagnosis of CD; b) proportion attending a first GP visit, and offered the intervention; c) proportion taking up the intervention; d) proportion dropping out; e) proportion completing intervention. The population modelled was separated by age and sex.

Model structure

A population-based multiple cohort Markov model, with 1-year cycles, was developed to simulate the disease dynamics with and without the delivery of the interventions. The disease model is based on Dismod II (110), which simulates the flow of a life table, where a population cohort moves between three health states over time: healthy, diseased, and dead (110). This model structure is considered appropriate, since there is only one DW for CD in the

GBD study (28). In the current scenario, a cohort of children considered healthy (without the diagnosis of CD) is subject to an incidence hazard, and may become diseased (prevalent cases of CD). When diseased, the children may be subject to a hazard of recovery from the disease (remission), or to a hazard of dying from the disease (case fatality). In the model, children were followed through to 18 years.

CD was modelled along the lines of a chronic rather than an episodic disorder, and attributed one single weight (as per the GBD study (28)), as children can either have the disorder, or be free from it. Comorbidities and longer-term consequences related to CD were not included in the model. The model estimates the impact of the intervention on the prevalence of CD in the Australian population, thus the impact on morbidity, reflected by the total number of years lived with disability. The current model produced incremental cost-effectiveness ratios (ICERs), reported in net cost per DALY averted. The patient flow chart, and an illustration of the model are depicted in Figure 4.

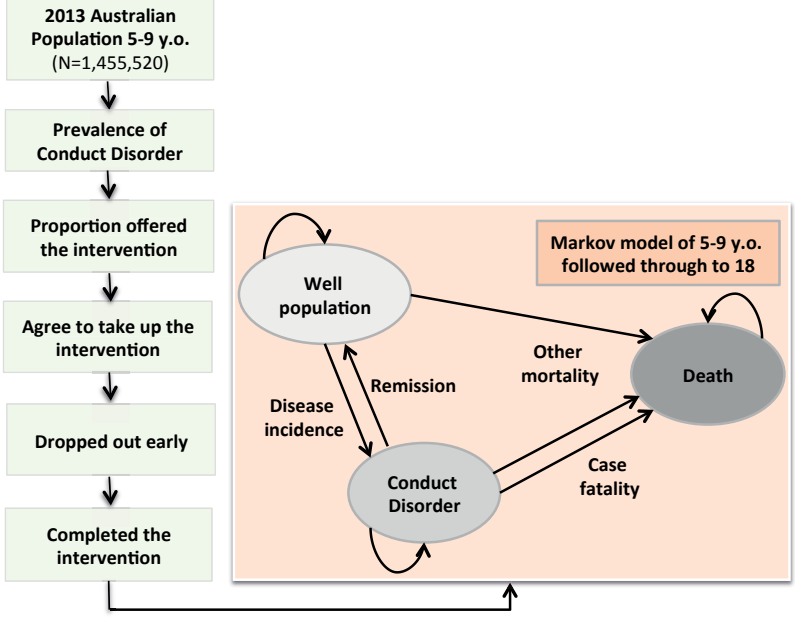


Figure 4. Patient flowchart and model representation

Epidemiological inputs

Data on prevalence, remission, and case fatality of CD were sourced from the 2010 GBD study (28). Single-age all-cause mortality rates, obtained from life tables constructed with 2010 Australian population data, and mortality data were sourced from the Australian Bureau of Statistics (111). Epidemiological data on prevalence, remission, case fatality, and all-cause mortality were entered into DisMod II, to reproduce the complete epidemiology of CD, and to obtain gender- and age-specific incidence rates. The study outcomes are expressed as DALYs, using the DW for CD (0.236) from the GBD study (28). Since case fatality was considered zero (this is because no estimate of excess mortality due to CD was found in the literature), DALYs were equivalent to YLDs. We assumed the intervention effects at post-test to be maintained at 1-year follow-up, and a decay rate of 50% in effect after year 1 for the intervention, supported by the literature (9, 11).

Costing analysis

We estimated the *costs to deliver the interventions* including: costs of assessment by GP, costs of psychologists to run the interventions, and the costs of workbooks distributed to parents. We assumed that the interventions would be delivered through the public sector, thus unit costs were sourced from the Medical Benefits Schedule (MBS) (112). The MBS details the national public payment fees for all non-hospital medical (including doctors, pathology, diagnostic, and some allied health services) services paid for by the Commonwealth of Australia. However, patients can also be charged out-of-pocket costs, depending on the type of service and the provider. Time and travel costs accruing to parents were excluded from the base-case analysis, but included in the sensitivity analysis, and reported separately.

Cost offsets, i.e. treatment costs avoided due to the reduction in the prevalence of CD, accruing to the health sector, were also included in the base-case analysis. Broader perspectives deemed relevant were included in the sensitivity analysis, as large costs associated with CD fall outside the health care sector. Cost-offsets were estimated from published international literature (7, 8, 82, 113), as there are currently no Australian estimates. These were divided into health care and other sector costs. Other sector costs included special education, social services, voluntary and private sector costs, foster and residential care, relationships, state benefits, and crime. Costs were converted into 2003-2004 Australian dollars, using purchasing power parities (http://eppi.ioe.ac.uk/costconversion/default.aspx), and inflated to 2012-2013 values, using the Australian health price deflators 2012-13 (http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=60129548869)
.

Base-case and sensitivity analyses

We calculated ICERs by dividing the estimated difference in costs, between Group/Standard Triple P and "no intervention", by the estimated difference in DALYs averted through the decrease in prevalence of CD. We used Ersatz, version 1.31, (http://www.epigear.com/index_files/ersatz.html) to perform a probabilistic uncertainty analysis, using Monte Carlo simulation modelling, to incorporate uncertainty around the cost and effect data. Results were displayed on a cost-effectiveness plane. The cost-effectiveness plane is a graphical representation of estimated cost differences plotted against estimated differences in DALYs averted between each intervention and "no intervention". The horizontal axis divides the plane according to incremental effect, and the vertical axis according to incremental cost, which divides the plane into four different quadrants. Each quadrant has a different implication for the cost-effectiveness decision. Iterations plotted in the north-east quadrant are those where the intervention is more effective and more costly than the comparator; those in the south-east quadrant are more effective and less costly; those in the south-west quadrant are less effective and less costly; and those in the north-west quadrant are more costly and less effective. The estimates around the ICER represent the uncertainty around the central cost-effectiveness estimate. To determine if the interventions were cost-effective, a threshold value of $50,000 per DALY averted was used (114). ICERs that fall below this threshold were considered cost-effective. To investigate the impact of specific input parameters and assumptions on the model outcomes, univariate sensitivity analyses were performed, and parameters were varied one by one.

5.4.3. Results

Group Triple P was cost-effective at a threshold of $50,000 per DALY averted, with an ICER of $9,856, and a probability of cost-effectiveness of 0.890. The Standard variant was not cost-effective, with an ICER of $54,535 per DALY averted, and a 0.480 probability of cost-effectiveness. Table 3 shows the cost-effectiveness results for the model. The uncertainty around the ICER of the Group variant is quite large, as can be seen by the wide 95% uncertainty interval (UI). The uncertainty iterations span from the north-east quadrant of the cost-effectiveness plane (where Group Triple P is more effective and more costly than the comparator), to the north-west quadrant of the plane, indicating that Group Triple P is more costly and less effective than the comparator (dominated) (Figure 5). This confirms there is some uncertainty regarding its effectiveness and cost-effectiveness. Despite the non-cost-effective (according to the Australian WTP threshold value) ICER estimate for the Standard variant, a significant proportion of the uncertainty cloud lies below the cost-effectiveness threshold. The sensitivity analyses did not change the cost-effectiveness results for most assumptions, apart

from variations in the ICERs. However, contrarily to the base-case analysis, Standard Tripe P became cost-effective when assuming no decay in effect through time.

Table 3. Results of the base-case model examining the cost-effectiveness of Group and Standard level 4 Triple P. Costs in AU$ 2013.

	Intervention delivery format	
	Group	**Standard**
Mean ICER (AU$/DALY averted) (95% UI)	9,856 (dominated* - 72 166)	54,535 (19,300-178,096)
DALYs averted (95% UI)	684 (-1,436-2,370)	249 (60-610)
Intervention costs (AU$) (95% UI)		
Government	7.2M (5.2M-9.6M)	10.3M (7.2M-13.6M)
Private	1.2M (772,816-1.7M)	1.4M (875,067-1.9M)
Total	8.4M (6M-11.3M)	11.6M (8.1M-15.4M)
Cost offsets health care (AU$) (95% UI)	690,752 (-910,232-2M)	247,416 (63,803-566,928)
Net costs (AU$) (95% UI)	7.7M (5.3M-10.8M)	11.4M (7.9M-15.1M)

*Proportion of the uncertainty iterations for Group Triple P lie in both the north-west and the north-east quadrants of the cost-effectiveness plane, signifying there is a likelihood that the intervention is more costly and less effective than the comparator (dominated), and that it is more effective and more costly than the comparator.
M - Millions

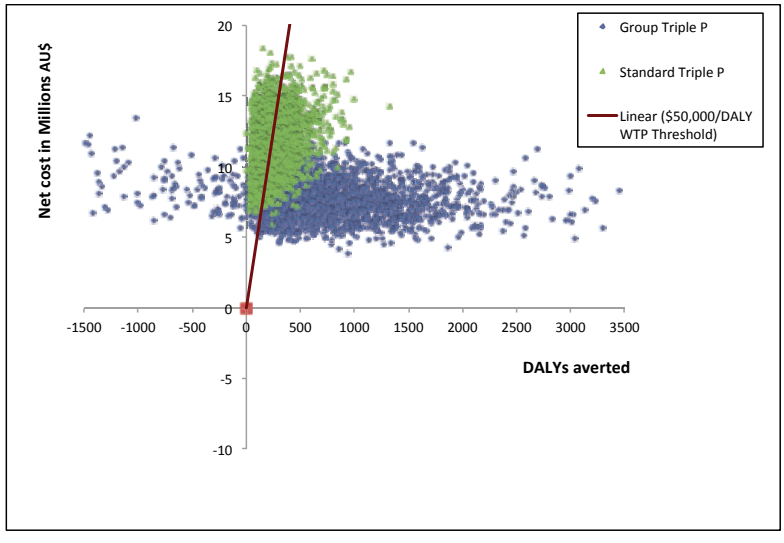


Figure 5. Cost-effectiveness plane of the base-case analysis

5.4.4. Conclusions

Triple P for the treatment of CD among children appears to represent good value for money, when delivered in a Group face-to-face format, at a threshold of $50,000 per DALY averted, but is less likely to be cost-effective when delivered in a Standard individual format. Several limitations need to be acknowledged, such as the uncertainty around the cost-effectiveness estimates, and the insufficient quality of the evidence base for the interventions modelled, thus results should be interpreted with caution. These results do not claim Triple P is not cost-effective, since we only included diagnosed disorder, and excluded children with sub-threshold levels of CD or with some levels of problems, who could also benefit from the intervention.

6. General Discussion

The overall aim of this thesis was to 1) address the methodological challenges of evaluating universal parenting interventions, and 2) evaluate parenting interventions for the prevention and treatment of EBP in children, using different health economic methods, thus contributing to narrowing the knowledge gap in regard to their costs and effects.

6.1. Interpretation of results

Study I assessed the costs and the effects of levels 2 and 3 of Triple P, delivered universally to parents of preschoolers, on child EBP and parental mental health, compared to a waitlist control. The results showed that offering levels 2 and 3 of Triple P universally, with 29% of intervention attendance, did not significantly improve child externalizing behaviour or parental mental health.

Our findings are inconsistent with previous "clinical" trials showing positive effects on child behaviour (102), and parental mental health (103). However, they are in line with other studies, where Triple P was used as a universal intervention, and that found no significant effects on child externalizing behaviour in "non-clinical" settings, where self-selection was allowed (19, 20). The effect sizes in our study are also in accordance with other studies of levels 2 and 3, reporting low effect sizes of 0.21 on child externalizing behaviour, and of 0.19 on parental mental health (103). In our study, baseline scores of EBP were, in average, below the clinical cut-off, and the sample was quite small, which makes it difficult to demonstrate an intervention effect. Greater effects are often shown on larger samples with higher problem scores at baseline (102, 103).

The results also showed that the annual costs of running Triple P were 227 SEK (€24) per child, or 145 SEK (€16) per parent. Including investment costs, Triple P cost 3007 SEK (€323) per child, or 1922 SEK (€207) per parent. A study by Mihalopoulos et al (18) estimated the cost to implement Triple P, based on a hypothetical cohort of 2 year olds, over time to be AU$51 (427 SEK/€46) per child. These values should be compared with caution, as Mihalopoulos based the calculations on population estimates,

whereas we based our estimates on a naturalistic implementation of Triple P. Nevertheless, Mihalopoulos's estimates resemble ours if we add 10% of the investment cost to the running cost, over a 10-year period.

When using traditional analytical methods designed for clinical trials in study I, we could not detect a programme effect. As in public health the purpose is to alter the distribution of a certain risk factor in the population, in study II we tested another way to analyze our trial data with a population health approach in mind, by describing change using the distribution curve of the outcome, child externalizing behaviour, at 12-months follow-up.

The results showed that 12% of the children in the intervention group had a significant improvement in externalizing behaviour, compared to 3% in the control group. The absolute health gain after the intervention was 9%. Carr, 2002 (115) used a similar approach to calculate the impact of single-case design interventions on child mental health. The method he described allowed to estimate the percentage of individuals who benefited from an intervention, however it did not take into account the whole distribution of the target variable.

When dealing with public health interventions, the aim is to assess the impact for the whole target population, taking into account all possible health gains, either improvement in means or in SDs. Thus, we belive that the approach we proposed better serves the purpose of evaluating public health interventions. We used the same approach to estimate the impact of Triple P on child EBP, based on parents' educational level. Approximately 15% of the children with parents with lower educational level improved health outcomes, compared to 6% for those with higher educational level. This difference was not significant, but served for demonstration purposes. Further, these analyses also highlight the potential of the method to help understand how interventions can affect diverse segments of the population, with different socioeconomic or risk profiles, and thus affect social inequities in health.

Study III examined the cost-effectiveness of four group-based face-to-face parenting programmes, and bibliotherapy, compared to a waitlist control, at post-test, targeting CP in children, aged 3-12 years. All interventions, apart from Connect, were effective in reducing child CP, compared to the waitlist. In the original effectiveness study of the same RCT (55), Connect was effective in reducing child CP, on the ECBI intensity scale, although to a lesser extent than the other programmes, but showed no significant effects for children scoring over the 95th percentile.

The literature on the effectiveness of behavioural vs non-behavioural programmes is controversial, with some meta-analyses showing better results for behavioural programmes, and others showing no statistical difference between them (116, 117). A possible explanation for the Connect result may be that non-behavioural programmes need more time to show effectiveness, since they focus on the dynamic change of relationships, which may be a longer process than influencing behaviours. Unfortunately, the short time horizon of our study could not evaluate this possibility.

In our base-case analysis, bibliotherapy was, unsurprisingly, the cheapest option, when comparing the interventions that showed significantly different outcomes from the waitlist. However, when we compared the interventions between themselves, Comet showed better outcomes and higher costs than bibliotherapy, with an ICER of US$8375 per recovered case. As there is no established WTP for a recovered case of CP, the selection of the most appropriate programme, or combination of programmes should be determined by decision-makers' cost-effectiveness thresholds for such outcomes.

The secondary analyses of the joint outcome "recovered+improved", and of intervention completers showed that bibliotherapy was no longer effective, compared to the waitlist. One possible explanation could be the lower dosage of training and no practitioner involvement in bibliotherapy compared to face-to-face programmes (57, 118). Cope, IY, and Comet showed statistically significant differences compared to the waitlist, but not among each other. These analyses appear to have eliminated the differences between programmes, with Cope being the cheapest alternative.

Two other studies have looked at the cost-effectiveness of the IY programme (82, 83), and presented estimates of average costs per child to deliver the programme of similar magnitude to the ones in our study. However, there were some differences in regard to the type of cost items included, and the average number of children per programme (lower in our study). If the average number of children per programme were higher in our study, our average cost estimates would probably be lower. Additionally, a study by Enebrink et al (58) has estimated the operating cost of delivering Comet as an internet-based intervention to be one third of the estimate in our study, thus the internet version of Comet could be a good first step to target child CP.

Study IV evaluated the population cost-effectiveness of Group and Standard level 4 Triple P, compared to no intervention, for the treatment of CD in children, from the health sector perspective, using the Australian population as an example. The results showed that Group Triple was cost-effective, at a threshold of AU$50,000 per DALY averted, however the uncertainty around the ICER was quite large, with the intervention having both a likelihood of

being more effective and more costly than the comparator, and of being more costly and less effective than the comparator. The Standard variant was not cost-effective, but with a large proportion of the uncertainty around the ICER lying *under* the threshold.

These results should be interpreted with caution, as the effectiveness parameters of both interventions were sourced from one study each. This was due to the limited published literature fulfilling our inclusion criteria. There is, thus, uncertainty around the cost-effectiveness of Triple P, which has not been studied previously. Bonin and colleagues, 2011 (17) estimated the costs and longer-term savings of parenting programmes in the UK associated with the reduction in the probability of persistent CD among children. They modelled a "generic" parenting intervention, and based the model inputs on data from a variety of programmes that were likely to be implemented in the English context. Furthermore, this was not a full economic evaluation, but rather a scenario analysis, where inputs were varied according to three different scenarios (base, best and worst cases). In contrast, a strength in our model is that it includes health outcomes, which allows for inference on the cost-effectiveness of the interventions modelled.

6.2. Implications to clinical practice and future directions

Study I is the first evaluation of Triple P, offered universally, in the Swedish context. It contributes to the existing literature with its control group held over a period of 18 months, and an estimation of the costs to deliver the programme universally in "real-world" conditions. The results showed that offering low intensity levels of Triple P universally, with low intervention attendance, does not result in improved outcomes, and may not be a worthwhile use of public health resources. However, as we could not evaluate broader resource use, and hence costs in this study, we could not determine if there were potential cost savings elsewhere. As the estimate of cost per child was very low, further studies, with a greater number of participants to detect small effects, are necessary to specify the intensity and attendance rates needed to produce sustainable effects, and establish possible scenarios for cost-effectiveness of universally offering parenting programmes. In addition, a better registration of actual programme attendance is important. Our study only included parents who had consented to the trial, whereas the intervention was offered to more parents by the municipality. This has resulted in a probable overestimation of cost per child and family.

In Study I, we applied the principles of clinical trials, analysing the data on an individual level, rather than thinking of the issue of EBP in population terms (89, 90). The trial had the characteristics of a true population health approach, with a universal offer, and allowing self-selection. When evaluating the trial in a clinical trial format, low effect sizes and non-significant results were produced. However, we were not sure that the approach to evaluating significance was appropriate for such studies, which have small impacts over large populations. Therefore, in Study II, we proposed an alternative method for evaluating public health interventions, where the focus is on population level and not individual change. Using trial data from study I, we demonstrated that it is possible to calculate the impact of public health interventions by using the distribution of an outcome variable.

This new method produced contradictory results to the first analysis in study I, which is not that surprising, if we consider the different analytical approaches used. Nevertheless, it raises questions about which method is most adequate to assess effects, and how the results ultimately should be interpreted. A conservative standpoint is customary when decisions on policies are advised. Given the low costs per child of delivering Triple P, and that the initial investment had already been made, we suggested the municipality at hand to continue implementing Triple P as a universal offer, but make sure that coverage increased, and that both exposure and costs were registered adequately. A new evaluation is ongoing.

We believe that the new proposed method can be used to evaluate the differential impact of population health measures and their potential to improve health inequities, by assessing intervention effects on different segments of the population, based on risk profiles. However, before this method can become an accepted way of analysing population health trials, it needs to be tested on more empirical datasets. In addition, further methodological development is necessary, such as sensitivity analyses on how different assumptions about the distribution curve affect results. Most importantly, the method should only be used when the trial at hand has a population health approach.

Study III is the first economic evaluation comparing different parenting interventions within the same RCT, conducted in a "real-world" setting. The study shows that bibliotherapy offers a cheap and easily disseminated option to initially target CP in children, when facing a limited budget. Further, Comet could be offered to achieve greater effects, based on decision-makers' willingness to make larger investments. Cope was the cheapest alternative, when targeting broader outcomes, other than clinical caseness. Before definitive conclusions can be made, however, a full collection of resources used should be included in the evaluation.

These results raise the need to further investigate the effectiveness and cost-effectiveness of these interventions as a "stepped-care" approach, based on budget constraints and problem severity. The adoption of stepped-care models with different doses and formats are becoming a common approach to increase treatment availability and cost-effectiveness. Self-directed interventions appear a favourable first step in such models, targeting different areas of child health (58, 119, 120). Further studies are also needed, with control groups held over longer follow-up periods to ascertain the sustainability of the effects, and comprehensive economic evaluations and economic modelling to provide insights on longer-term cost-effectiveness.

Study IV is, to the authors' knowledge, the first study to assess the cost-effectiveness of Triple P for the treatment of CD in children, with the use of a population-based economic modelling approach. Although the context of the study was Australian, the methods and results have international relevance. Triple P was developed in Australia, but is implemented in different countries, thus while referral pathways can differ between countries, the intervention itself would not. In our model, we assumed the interventions, which were the most advanced forms of Triple P, were delivered by psychologists. This was to reflect the common practice within Australian mental health services, as well as the main professional category likely to deliver this level of Triple P.

Our study showed that Triple P, for the treatment of CD in children, appears to represent good value for money, when delivered in a Group face-to-face format, but less likely to be cost-effective when delivered in a Standard individual format. The results should, however, be interpreted with caution due to the uncertainty around the cost-effectiveness estimates. Importantly, our study results do not claims Triple P is not cost-effective, in particular the Standard variant, since we only included diagnosed CD. Children with sub-threshold levels of CD, or with some level of CP, were not included, but could also greatly benefit from the intervention.

6.3. Methodological considerations and limitations of the findings

Limitations regarding costs

Study I and III are not full economic evaluations, and they have very limited costing perspectives, comprising only direct intervention costs. This was due to largely pragmatic reasons, as the economic analyses presented here were conducted after the RCTs were completed, and there was no opportunity to collect any more costing data. In both studies, intervention costs were initial-

ly collected on a group level, from provider and study accounting records. In study III, group level costs were later linked to data on parents' intervention attendance to estimate individual level costs. However, this process does not address fully the issue with individual variation in costs, but should be regarded as a proxy. Study I did not attempt to link costs to health outcomes, but rather provide an insight into the costs of delivering Triple P universally. A fuller costing analysis, in both studies, is needed, with prospective broader resource use collected, as CP in children often result in the excessive use of health care and education services (7). The exclusion of these services limits the comparability with other interventions that may impact differently on the use of the resources aforementioned. Furthermore, study III has a short time horizon (4 months), thus further studies are needed with control groups held over longer follow-up periods.

In study IV, the costing analysis for the cost-offsets was limited and not Australia-specific due to lack of data. The studies used to estimate the costs associated with the treatment of CD are not recent, and were conducted in the UK. Further, some of these costs may have been overestimated, as we used estimates published by Scott and colleagues (121), pertaining to a cohort of 10 year olds followed though to 28 years, to the cohort of 10 to 18 year olds in our model. The distribution of costs throughout time is highly skewed, and substantial costs associated with CD arise early in adulthood, such as costs due to unemployment, and mental health problems.

Limitations regarding outcomes

The sample size in study I was insufficient to detect a small significant effect that is often associated with a light intensity intervention delivered to a non-clinical population (103). As the sample size was limited by lower than expected inclusion in the study, loss to follow-up, and low exposure of the target sample to the intervention, the null effects cannot reliably be assessed.

Moreover, prevalence estimates of child behaviour problems vary according to the measure used (11). In studies I and III, a comprehensive measure of child mental health, the ECBI, was used, as it is a good predictor of CD diagnosis (85). In study I, the DASS, used in the parental sample, is also a good predictor of depression and anxiety diagnoses (94, 122). Both instruments present good sensitivity to detect changes in scores over treatment, and good reliability in both clinical and non-clinical samples (85, 93, 123). Importantly, the inclusion of a multi-attribute utility instrument, sensitive to domains of quality of life impacted by CP in children, would be necessary to measure QALYs, and allow pragmatic estimations of value for money.

The method proposed in study II does not establish an effective cut-off or threshold effect, and does not have implications for clinical significance per

se. Thus, estimating the proportion of the population showing health gain from the intervention will have to be interpreted based on the outcome measure used. By geometric symmetry, gains at one end mean losses at the other end of the distribution curve, although the intervention does not cause such redistribution effects. Moreover, using this method to evaluate outcomes still requires a comparison group to draw inferences on effectiveness. Furthermore, it allows for multiple causality, but one initial concern was the difficulty in controlling for confounding factors. After careful consideration and the input of an external researcher, in the form of an invited commentary to our published study, we were able to address this issue. We suggest standardization of the distribution of the outcome in the control group, using methods proposed by Kumar and Arockiam (124) or Quadrianto (125). By this we mean to adjust the baseline distribution of the outcome in the control group in a way that it will be as close as possible to the distribution of the outcome in the intervention group. This can be done if the size of the control group is relatively large.

Study IV included only studies reporting diagnostic/clinical outcomes (reported as number of prevalent cases) measured using a disease-specific symptom rating scale, with good predictive value of CD (the ECBI). The ECBI discriminates between clinical and non-clinical conditions. However, most studies on the effectiveness of Triple P, for the treatment of CD, often report changes in CD symptomatology with a mean and a SD, which poses difficulties in determining how changes in such estimates translate into changes in number of cases. This limited the number of eligible studies to source the effectiveness parameters used in our model. In addition, the intervention efficacy estimates were based on studies with parents who completed the intervention, thus parents who dropped out prior to programme completion incurred costs but no benefits. Although the proportion of completers was estimated from published literature, the estimate is quite low, which highlights the importance of ensuring intervention engagement and reducing dropout rates for increased cost-effectiveness (126-128).

Finally, in study IV, although DALYs are acceptable to Australian decision-makers, and have the potential to enable comparisons across a range of interventions, their use as outcome measure poses limitations. These pertain, mainly, to the reliability of the DW, and the estimation of the YLDs. One limitation is that the DW estimate accounted for health loss, but did not take into account current or future consequences that occur outside of the disorder's direct health outcomes, nor the burden placed on families or on societal systems (such as welfare or criminal justice). These should be taken into account, as CD is related to a vast range of negative consequences, which place a high disease and economic burden on families and society (7, 8). Additionally, mortality was not included in the calculation of DALYs, as

there was no mortality component attributed to CD (6), thus DALYs in our study were equivalent to YLDs. This is due to the scarce literature showing a direct cause between CD and mortality. However, CD may entail a risk of early mortality due to violence and substance use (6). Finally, CD was modelled along the lines of a chronic rather than episodic disorder, and attributed one single weight (as per the GBD study (28)). A better approach should specify weights, based on disease stages and complications, to reflect heterogeneity in health and functional limitations (129). Moreover, the DW reported in the GBD study was quite large, and is likely to represent the severe end of the symptom continuum of CD (6).

7. Conclusions

Efforts to address the needs of children with mental health problems are increasingly involving collaboration between health and social services, education, and voluntary sector services. To reduce the burden of mental health problems in childhood, the health and social care service system should provide evidence-based interventions on a continuum from prevention, through early intervention, to treatment (21). With the large availability of different interventions targeting different aspects of child and adolescent mental health, the need to investigate their effectiveness and cost-effectiveness is vital, so that public resources can be allocated efficiently.

Parenting interventions have been developed to teach parents strategies to deal with problematic behaviour in their children. Several studies on the effectiveness of parenting interventions have demonstrated they can result in positive changes in child behaviour and parental wellbeing. A majority of the studies on the effectiveness of parenting interventions targeting EBP among children and adolescents are of either selective or indicated preventive interventions, or treatment strategies. Evidence on the effectiveness of universally delivered parenting programmes is controversial, partly due to methodological challenges. Further, parenting interventions for the prevention and treatment of child EBP are often offered and financed with public money in Western countries, and still the evidence on their cost-effectiveness is scarce. The overall aim of this thesis was to 1) address the methodological challenges of evaluating universal parenting interventions, and 2) evaluate parenting interventions for the prevention and treatment of EBP in children, using different health economic methods, thus contributing to narrowing the knowledge gap in regard to their costs and effects.

Our analyses indicate that offering low intensity levels of Triple P universally, with low intervention attendance, does not result in improved outcomes, and may not be a worthwhile use of public health resources. Further, using the distribution of an outcome variable makes it possible to estimate the impact of public health interventions at the population level, and its use was demonstrated on trial data on a universally delivered parenting programme. Additionally, the same method can be used to evaluate the differential impact of population health measures, and their potential to improve health inequities. This thesis also supports offering bibliotherapy to initially target CP in children, when facing a limited budget. The parenting programme

Comet could be offered to achieve greater effects based on decision-makers' willingness to make larger investments, and Cope could be offered when targeting broader outcomes other than clinical caseness. Lastly, our results demonstrated that Triple P for the treatment of CD appears to represent good value for money, when delivered in a Group face-to-face format, but less likely when delivered in an Individual format. However, it needs to be highlighted that our modelling only focused on reducing cases of CD, and did not include benefits in terms of CP. The model built can be used for economic evaluations of other interventions targeting CD, and in other settings.

We believe our results contribute to narrowing the knowledge gap in regard to the effects and costs of parenting interventions, thus assisting decision-makers in resource allocation to this field. Importantly, these results should be regarded as only one puzzle piece in the process of decision-making. This is a complex process, which needs to be complemented by other factors relevant to decision-makers, and other studies tackling the limitations of the studies in the current thesis.

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