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Economic evaluations in paediatric dentistry clinical trials

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Abstract

Economic evaluations play an important role in identifying the cost-effectiveness of alternative healthcare programmes, informing decisions surrounding funding and the allocation of resources. This paper outlines the basic principles of economic evaluation and how it can be conducted alongside a clinical trial. Furthermore, it considers the ways in which evidence from these studies can be used, and the challenges researchers are faced with when conducting economic evaluations in the field of children's oral health.

1 | OVERVIEW

Resources in oral health care are limited. As such, the implementation of a new strategy, regardless of its nature—preventive, diagnostic or treatment—typically involves the reduction or removal of another. Therefore, economic evaluation (EE) studies in dentistry are pertinent in allocating resources to the best strategies available; providing valuable information for policy leaders and clinicians involved in the decision-making process. The pioneering economic studies in the field of oral health date back to the 1960's and assessed the impact of water fluoridation on the cost of children's oral care.¹

Although the late 20th century represented the starting point of economic research in dentistry, only in the 2000's was a considerable increase in the number and quality of EE studies observed.² Currently, in child oral health research there remain relatively few EEs, though there is an upward trend in the number of EEs published each year in this field.³

2 | BASIC PRINCIPLES OF ECONOMIC EVALUATIONS

There are a number of resources involved in health care, including people, time, equipment, facilities and knowledge.⁴ These resources are not limitless, regardless of whether a healthcare system is publicly funded or based on social or private insurance. It is not practicable for every programme to be provided, and hence, a decision must be made to determine which programmes are the best value for money. Importantly, however, through the selection of a programme to fund, there exists an opportunity cost, whereby the benefit of an alternative programme will be forgone. The organisation tasked with making these decisions must be provided with details surrounding the cost and consequences of all relevant alternative programmes to ensure their judgement is well-informed. EEs can provide decision-makers with the information required to enable them to maximise the benefits from healthcare spending; overcome regional variations in access; contain costs and

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manage demand; and provide bargaining power with suppliers of healthcare products.⁵

An EE is typically defined as the comparative analysis of alternative courses of action in terms of both their costs and consequences.⁴ Studies that fail to compare two or more alternatives, such as a cost analysis, or an outcome description, cannot be considered a full EE. Likewise, studies that do not attempt to compare the cost and consequences of a programme with an alternative do not meet the above definition and can only be considered a partial evaluation. Although partial evaluations can still provide an important contribution to knowledge in this field, they cannot be used to answer questions relating to efficiency; that is, the achievement of acceptable efficacy and efficiency with the most appropriate use of resources.^{4,6}

There are three main types of full EE, which vary in terms of outcome. The cost-benefit analysis (CBA) is the broadest form of analysis, characterised by the measurement of all benefits in monetary terms. CBA considers the wider social implications of a programme on the economy as a whole, including the costs and consequences external to the healthcare sector.⁷ Through comparing the incremental benefits with the incremental costs, the net social benefit of the programme can be identified.⁴ Cost-effectiveness analysis (CEA) is the most common form of full EE. It compares the incremental cost of a programme, from a particular viewpoint, with the incremental health improvement attributable to the programme; the latter being measured in natural units specific to the programme under analysis, such as a reduction in dmft/DMFT. Conversely, the cost-utility analysis (CUA) measures benefits in terms of utilities. The most commonly used utility-based measure is the quality-adjusted life year (QALY), which combines the quality of life and length of life gained as a result of a healthcare programme, into a single unit.

There is a fourth type of EE that has created some debate as to whether it fulfils the definition of a full EE. The cost-minimisation analysis (CMA) is historically undertaken in a situation where there is no statistically significant difference between the consequences, or effectiveness, of the alternative programmes. As such, only the costs are compared. CMA has been criticised as the assumption of equivalence overlooks any uncertainty surrounding consequences and fails to capture wider benefits of healthcare programmes.^{8,9}

It is important to establish the perspective of an EE in the early stages of planning, as it may have implications for the trial design.¹⁰ Many EEs in healthcare take the perspective of the healthcare provider, which may be a national health care system (eg, the NHS in the UK), a health insurer or an independent dental surgery. This relatively narrow perspective can be advantageous to groups that are concerned only with the impact and costs of an intervention within a specific organisation.¹⁰ This approach can be widened to include the impacts on patients, which given the widespread nature of co-payments in dentistry is likely to be an important consideration

for oral health evaluations. Nonetheless, broader approaches, termed societal approaches, are increasingly recommended.¹¹ These consider the impact of an intervention on the welfare of the whole of society, for example including costs such as the costs to employers from time off for dental appointments. Understandably, a more inclusive approach such as this can produce differences in cost-effectiveness; hence, it is necessary for researchers to provide clarity on the perspective taken. Furthermore, a pragmatic view is sometimes required, as it may not be feasible to identify all the benefits and costs to society arising from an intervention.

3 | COSTING

The common aspect of all EEs is the incorporation of cost. Although cost may appear to be less conceptually challenging than the different types of outcome measures used in EEs, it is still a potentially complex area. As already described, when cost is considered in economic terms, it is actually opportunity cost that is being measured. So, the cost that is of interest is the benefits forgone by using resources for one intervention or programme rather than the next best alternative. In order to understand the cost, the resources used are measured and are then usually reported in terms of their monetary value. It is important here to clarify that negative outcomes such as pain, distress, whereas often thought of by the public as costs, should be classified as negative outcomes/benefits rather than costs, a common mistake in economic evaluations.¹² If managing these negative benefits incurs a cost, however, these should be added to the costs. Equally, costs averted (or savings) should not be counted as benefits but negative costs.

Costs can be classified in different ways.¹³ The major classification splits direct and indirect costs where direct costs are those incurred by healthcare providers and patients in providing and accessing the healthcare such as consumables, staff time, equipment and estates; indirect costs usually consist of productivity loss due to time away from work. Within direct costs, there are several other categories of costs: total cost will comprise all of the costs measured in an EE but this will depend on decisions about the perspective and scope of an evaluation, which will be explored further; fixed costs are those that remain the same irrespective of how many outputs are produced so for example, the cost of maintaining a dental surgery would not change by the number of patients treated; variable costs are those that vary with the number of outputs, so for example, the number of pre-formed metal crowns will vary depending on how many teeth are treated. Often the question of how much of something should be done is posed, and in these cases, the marginal cost becomes important, where this is the cost of producing one extra unit of output, for example restoring one more tooth.

When a costing is being performed there are several important choices, the most important of which is the perspective that is being taken. Secondly, decisions about the scope of the exercise need to be considered; ideally all possible costs would be included but this is often difficult given that some costs may not be available or may be too time-consuming to collect and so decisions need to be made. Each of these decisions should be justified and reported.¹⁴

Costing can generally be performed in one of two ways. The first way is micro-costing or bottom up, where resources used in providing a programme are identified and then individually costed. This can often be done prospectively in an EE alongside a clinical trial. Alternatively, the top-down approach takes information from existing data sources such as nationally published average data. The bottom up approach is usually more accurate, but more time-consuming and often a mixture of both approaches is used. Two particular types of costs may need special consideration and these are capital costs where there is a large upfront investment, often dealt with by annuitizing the initial outlay over the life time of the equipment but also factoring in depreciation and overhead costs, where some way of splitting the costs over outcomes of unit need to be justified and reported. Another methodological aspect of costing to be considered is discounting.¹⁵ Discounting reflects the fact that people have a time preference for costs such that they would usually prefer costs to be delayed and so costs that are further into the future are usually reduced by an appropriate discount rate. Many countries have their own discount rates, usually in the range of 3-5% per year. The final methodological aspect of costing is where there is uncertainty about the costs because data were poor or not available.¹⁶ This type of uncertainty, termed parameter uncertainty, can be dealt with by sensitivity analysis, which is dealt with later in this paper.

4 | COST-EFFECTIVENESS ANALYSIS

Cost-effectiveness analysis facilitates decision-making by quantifying the trade-off between cost and effectiveness by jointly comparing the two. To allow for such comparisons, effectiveness must be measured for a single shared outcome that is measured in natural units, such as number of decayed teeth.

The cost and effectiveness of a proposed programme relative to some control case—no intervention or a competing intervention—is often graphically illustrated using the cost-effectiveness plane.¹⁷ The cost-effectiveness plane is a set of axes that present the additional, or incremental, cost and effectiveness of the proposed programme relative to the control case on the *y*- and *x*-axes, respectively. There are five possible outcomes when comparing a proposed programme to a control case:

1. Both have the same effectiveness and cost.

2. The proposed programme is more effective and costs no more.
3. The proposed programme is less effective and costs no less.
4. The proposed programme is more effective and costs more.
5. The proposed programme is less effective and costs less.

Cost-effectiveness analysis is indifferent between the programme and the control case for Outcome 1. CEA unambiguously prefers the programme that is simultaneously more effective and less expensive, which is the proposed programme for Outcome 2 and the control programme for Outcome 3. For both, the preferred programme is said to dominate the other programme. For Outcomes 4 and 5, a trade-off between cost and effectiveness is required.

The incremental cost-effectiveness ratio (ICER) is used to measure the size of the trade-off between two programmes. The ICER for two programmes, A and B, is the ratio of the differences in costs and the differences in effect:

$$\text{ICER} = \frac{\Delta\text{Cost}}{\Delta\text{Effect}} = \frac{\text{Cost}_A - \text{Cost}_B}{\text{Effect}_A - \text{Effect}_B}$$

Lower ICERs are preferred as a greater effect is achieved for a lower cost.

Decision-makers can set a threshold ICER which determines the minimum level of cost-effectiveness.¹⁸ Two metrics are used to report cost-effectiveness in relation to the threshold: the incremental net health benefit and the incremental net monetary benefit. The incremental net health benefit measures the additional health effect beyond the health effect of a programme with the same cost and the threshold ICER:

$$\text{Incremental Net Health Benefit} = \Delta\text{Effect} - \frac{\Delta\text{Cost}}{\text{Threshold ICER}}$$

The incremental net monetary benefit measures the cost savings relative to a programme with the same effect size and the threshold ICER:

$$\text{Incremental Net Monetary Benefit} = \text{Threshold ICER} \times \Delta\text{Effect} - \Delta\text{Cost}$$

Although there are a number of methods available for setting thresholds, it is argued that more research is needed into evidence-based approaches for establishing thresholds.

The greatest limitation of CEA is that only programmes aimed at achieving the same outcome can be compared. That vast majority of CEAs undertaken in paediatric dentistry focus on programmes aimed at the reduction of dental caries.³ Even so, CEAs use a wide range of outcome measures including DMFT,¹⁹⁻²¹ number of dental visits for treatment,^{22,23}

survival of molars²⁴ and incidence of dental pain;²⁵ hence, their findings are less comparable. To avoid this problem, the natural effect measure can be replaced by a standardised utility measure as a generic measure of the benefits. By doing so, CEA becomes CUA and broader sets of programmes can be more readily compared.

5 | MEASURING UTILITIES

Utility can be defined as an individual's preferences for health states under uncertainty.²⁶ It is represented by cardinal values, ranging from 1 (best health state possible) to 0 (death), or even negative values for health states considered worse than death.²⁷ The assessment of patients' preferences in an EE provides the decision-maker with not only the results of improvement in oral health, but also the perspective of the individuals' well-being. Utility values are used to obtain the effect measure in CUA and should ideally be determined by the highest sacrifice that a patient is willing to take in order to achieve a health state.²⁸ There are diverse methods for measuring utilities in clinical trials, and the pre-scored multi-attribute health status classification systems are the most common.

5.1 | Scaling methods

5.1.1 | Rating scale (RS)

Patients are instructed to rate the different health states and locate them on a scale, focusing on the interval between states rather than the value to which they correspond.²⁹ The scale is usually a line with marked intervals, labelled with the best and worst outcomes.²⁷ The RS reveals the individuals' ranking of the health states and is simpler than choice-based methods to be used in clinical trials.⁴ One of the main disadvantages of the RS however is that its valuation will vary depending on the context in which it is used (contextual bias).²⁹

5.2 | Choice-based methods

5.2.1 | Standard Gamble (SG)

Subjects will choose between two alternatives: certainty of an intermediate health state; and the probability ' P ' of a better health state *or* a ' $1 - P$ ' probability of a worse state.³⁰ The scenario is explained to the patient, and the probability ' P ' for the best health state varied until the patient is indifferent between the certain health state and the gamble. The P value at which this indifference occurs is recorded and used as the patients utility for the intermediate state.³⁰

5.2.2 | Time trade-off (TTO)

When using a TTO for states preferred to dead patients choose between two certain alternatives: living at full health for time t , or living at less-than-full health for time x (where $t < x$). The utility value is obtained by the variation of the time x until the patient is indifferent between the alternatives.^{4,30} Similarly to the SG method, the TTO involves the idea of sacrifice, but here the main focus is the time for which a patient will maintain a health state.

5.3 | Pre-scored multi-attribute health status classification systems

Using the previously described utility measures in a clinical trial is a complex task, as they are time-consuming and conceptually difficult. An alternative to this are the pre-scored multi-attribute health status classification systems, generic measures of health-related quality of life (HRQoL) comprising different attributes of a health state and used to describe and value health.³¹ Each system will evaluate different attributes that are associated with an individual's quality of life (pain, vitality, mobility, etc.) and utility scores for different responses have been derived already. The main issue with the use of these systems in dentistry is that they comprise attributes that are not usually affected by the main oral conditions, meaning the impact of oral conditions, such as dental caries, may not be detected.³² Moreover, although some of the measures were designed to be responded by children, utility values were obtained from adult population. For this paper, we will briefly introduce the main pre-scored multi-attribute health status classification systems developed for use in paediatric populations to obtain utility values for CUA.

5.3.1 | EQ-5D-Y

The EQ-5D is the most widely used generic preference-based measure and comprises five attributes (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), with a new version containing a five-level scale (EQ-5D-5L).³³ More recently, the EuroQoL group has taken steps to develop an adolescent version of the measure, known as the EQ-5D-Y.³⁴

5.3.2 | HUI2

The Health Utilities Index Mark (HUI)-2 has seven attributes focused on children's capacity (sensation, mobility, emotion, cognition, self-care, pain, fertility), with three, four or five levels.³⁵ The HUI2 was developed for use in children with

cancer, and at present, there are no studies within paediatric dentistry using this measure to obtain utility values.

5.3.3 | AQoL-6D Adolescent

The Assessment of Quality of Life (AQoL)-6D Adolescent is based on the AQoL-6D, which was developed to comprise more dimensions than the existing measures. The adolescent version has six dimensions (independent living, pain, senses, mental health, happiness, coping, relationships, self-worth) with three or four items each and has not been applied to child oral health research.³⁶

5.3.4 | CHU-9D

This is a descriptive child-centred, self-completed system for measuring health-related quality of life in children from 7 to 11 years.³⁷ The CHU-9D has nine attributes (worried; sad; annoyed; tired; pain; sleep; daily routine; work; able to join activities) with a five-level scale. Although it seems like a promising measure to be used in oral health research in paediatric dentistry, a previous study has demonstrated that it cannot detect changes related to dental caries in children.³²

Additional methods of obtaining patients preferences in clinical trials include discrete-choice experiments (DCE) and best-worst scaling (BWS).²⁷ These are both multi-attribute choice-based methods and could be designed in different ways to elucidate adolescent patients' preferences through ordinal data, as they are less cognitively demanding and do not have the same ethical concerns as SG or TTO (no mention of death/risk of death).

The utility values should be measured through a method that suits the health condition, with each method having advantages and disadvantages in trial-based CUA in paediatric dentistry but none being ideal.³⁸ Therefore, there is still a need for a child-centred utility measure for CUA in which children report on their own preferences. This would address the acknowledged need to actively involve children and young people in research and healthcare decisions.^{39,40} Although the use of a child oral health-specific utility measure would negate one of the main advantages of the CUA that is the comparability between different fields.

In a CUA, once utility scores are derived (quality of health gain), they are combined with quantity. The most common outcome measure is the quality-adjusted life year (QALY), which is the product of the utility value of a health state and the time spent on that health state.²⁶ According to a recent systematic review, only one study in child oral health research reported outcomes in QALYs, although it is the main cited outcome measure for CUA in different national agencies.³ The measurement of outcomes in QALYs however has

a number of limitations, primarily in that all QALYs are considered equal, regardless of individual or situational circumstances.⁴¹ Furthermore, although the emphasis of QALYs is on quality of life, they fail to encompass other factors relating to well-being, or process attributes. Two oral health outcome measures for oral health research however have been derived from the QALY, the quality-adjusted tooth year (QATY) and the quality-adjusted prostheses years (QAPY), which incorporate tooth/prosthesis longevity and quality.⁴²

Another outcome measure used in health care research is the disability-adjusted life year (DALY), a generic measure expressed as the number of healthy years lost due to a disability developed by the World Health Organization (WHO) to compare health across different countries. Moreover, the healthy-years equivalents (HYEs) were also proposed for CUA to overcome the concern regarding the QALY's theoretical basis.⁴³

6 | COST-BENEFIT ANALYSIS AND MONETARY VALUATION

Although health state utility measures are widely accepted throughout health, outside of health it is common to value benefits in monetary terms. This method relies on measuring utility in terms of sacrifice with the sacrifice in this instance being measured in the common unit of money. Although using this common unit is appealing as it is conceptually easier than health state utilities, some have raised concerns about the ethical implications of valuing health in monetary terms. It has however been argued that monetary valuation is more in keeping with underlying economic theory and for dentistry it has been argued that it removes some of the problems that health state utility measures carry.⁴⁴ Monetary valuation however brings its own concerns.⁴⁵

In general, the technique of determining monetary valuations through 'revealed preferences', that is studying the amount people are willing to pay through observing what prices they have paid is rarely possible in health due to prices (co-payments) being altered by subsidy or tariffs from a true market rate. Instead, monetary valuation usually relies on 'stated preference' where individuals are asked what they would hypothetically be willing to pay to receive health care or attain a health state if there was a free market for health care.⁴⁶ This can either be done by directly asking for values using the contingent valuation method or by indirectly determining willingness to pay through a Discrete Choice Experiment. Although it is beyond the scope of this paper to outline either of these methods in detail, reviews of both methods in dentistry are available.^{47,48} In either method, the individual is not being asked what they think a fair price should be but what the maximum they would be willing to pay to reflect their value of something. In attaching a

monetary value, all aspects of the benefit derived from an intervention can be derived including non-health benefits. In addition, the respondent can incorporate any dis-benefits of an intervention/state for example pain or inconvenience into their valuation. At its simplest, if someone is willing to pay more for something, they value it more.

One of the common criticisms of willingness to pay is that it will be affected by ability to pay and so those with more money will be willing to pay more even at the same level of value or utility. This can be dealt with by checking for the influence of ability to pay (usually measured through income) on willingness to pay and then if necessary, weighting the results.⁴⁹ In paediatric dentistry, an additional concern, as with health state utilities, is that it will be difficult or impossible for children to answer questions relating to the monetary valuation of health and usually parental valuations are relied on instead.

In order to use monetary valuations in a CBA, it is important to consider the perspective and whether patients are asked for values for their own care, the public are asked for values for the care directly or whether the public are asked for a societal valuation which would include the value of having the option of care available for themselves and others in the future.⁵⁰ In the CBA, the simplest way to use the values is to subtract the costs in monetary from the benefit as measured by willingness to pay, leaving a net social benefit amount.

7 | DECISION MODELLING VERSUS RANDOMISED CONTROLLED TRIALS

Randomised control trials (RCTs) are primarily concerned with the measurement and comparison of relevant outcomes between competing programmes. As the running of RCTs tend to incur large, fixed costs, the additional cost of collecting cost data for an EE tends to be small relative to the benefits. Therefore, including an EE within a trial tends to be cost-effective.⁴ By combining the collection of cost and effect data within the trial's framework, an EE can be delivered from a single RCT. This is termed trial-based EE. Data collected through an RCT design is considered a valuable source of evidence as when a sufficient sample of patients is reliably randomised to the different programmes, the estimation of the average effect is unbiased and the study is said to have high internal validity. The collection of cost data within the RCT design extends the benefits of internal validity to the entire EE.

It is argued that for any EE to be appropriate for decision-making it should be relevant to the decision context with all relevant evidence included in the analysis.⁵¹ This can be achieved in part through a clear definition of the objective of the programmes, the target population and the inclusion of

all relevant programmes, costs and benefits in the evaluation. Not all benefits and costs are realised immediately, so an appropriate time horizon should be set to avoid underestimating any benefits or costs that are realised at later points in time. As evaluations contain a degree of imprecision, further analyses should be conducted to characterise the effect of uncertainty around estimates on the estimated cost-effectiveness of a programme to ensure robust decision-making takes place. Uncertainty can be due to variability in outcomes between identical patients termed stochastic uncertainty, variability between patients based on their observed characteristics termed heterogeneity, structural uncertainty related to the choices made when using decision-analytic modelling which is discussed below, and the uncertainty in the estimation of parameters used in a decision model termed parameter uncertainty.⁵² The analysis of this uncertainty also allows analysts to correctly recommend that further research is required before the final adopt or reject decision is made.

As trial-based EE benefits from the strengths of the RCT design, it also suffers from the potential weaknesses. If the trial sample of patients is not representative of the wider target population of the programme, then the study has low external validity or low generalizability to the decision context. The high costs of RCTs may prohibit the inclusion of all relevant programmes and result in shorter time horizons.⁵¹ Trial-based EE uses the RCT as the single source of evidence and therefore may ignore other relevant evidence.⁵¹ This may lead to incomplete information around uncertainty.⁵¹ Trials may also lead to artificially high compliance, and costs and benefit may be driven by the trial's protocol.⁴

To avoid the limitations of using a single RCT for decision-making covered above, an alternate approach called decision-analytic modelling is used. Decision-analytic modelling presents the options available to the decision-maker in a structured way as a set treatment pathways or movements between health states with outcome measures attached. The movement through pathways or between health states has probabilities attached allowing for the appropriate course of action to be chosen based on the expected benefits and costs of each available intervention. Decision-analytic modelling incorporates evidence from multiple sources making trial-based EE a compliment rather than a substitute to decision-analytic modelling as one form of evidence for populating a model.⁵¹

The modelling process requires well defined and structured models. As models are simplifications of reality, the accuracy of a decision model is limited by the assumptions made regarding the structure. These assumptions should be justified by evidence to limit structural uncertainty.⁴

Rich comparisons of the available interventions can be made when a model is populated with parameters estimated with strong evidence including the examination of heterogeneity between subgroups based upon clinical and

socio-demographic characteristics,⁵³ the extrapolation beyond observed data to consider appropriate time horizons⁵⁴ and further sensitivity analyses. Sensitivity analysis involves varying one (one-way sensitivity) or more (multiway sensitivity) parameter inputs, or the probability distribution of a parameter estimates (probabilistic sensitivity analysis) to measure the effect of parameter uncertainty on the cost-effectiveness of a programme. Sensitivity analyses can become more informative by drawing from sources of evidence beyond trials as the most important parameters can be more easily identified and the possible distribution of parameter inputs can be informed by evidence such as the policymakers or healthcare providers influence over the parameters when implementing a programme. Decision-analytic modelling allows for the full evaluation of uncertainty in the model, which may result in the conclusion that more research is required before a decision is made.⁵⁵

There are two main frameworks used in decision-analytic modelling: decision tree models and Markov models. Decision tree models map patient pathways onto probability trees. Probability trees usually start with an initial choice node at which the intervention is chosen. The tree then splits to map possible patient pathways at chance nodes to different outcomes each with a probability attached. For example, comparing school-based programmes for fluoride varnish and rinsing to a control case as the choice node and the differences in the prevalence of enamel and dentin caries and the associated cost savings of avoided fillings as the chance nodes.⁵⁶ Although most patient pathways can be represented by a decision tree, if events in the pathway are recurrent then a decision tree can become infinitely large. In this case, a Markov model is preferred.⁵⁷ A Markov model allows for recurrent pathways by modelling the probability a patient moves between a finite set of health states. For example, the movement between a healthy state to an unhealthy state defined by carious teeth and back to a healthy state after treatment.⁵⁸ If models require interactions between individuals or have large number of possible health states, then other methods may be required.⁵⁷

8 | HOW WE USE ECONOMIC EVALUATIONS

Economic evaluations answer questions of efficiency (ie, what is the best use of resources to maximize health). There are two types of efficiency questions with technical efficiency questions relating to comparisons of interventions for the same outcome to determine which intervention will produce the most output for a given resource and allocative efficiency questions revolving around whether a particular output should be produced or how much of it should be produced. So for example, whether we use one

type of material or another for a restoration would be a technical efficiency question whereas whether we should invest in restorative care or periodontal care is an allocative efficiency question.

Cost-minimisation analysis, CEAs and CUAs can all help answer technical efficiency questions, and decisions are easy when one alternative is found to be less costly and more effective than an alternative. A more common situation however is that one alternative is more effective and more costly (ie, it has a higher ICER). In this case an allocative question must be asked as to whether there is something else that should be given up to invest in the better alternative. For allocative decisions, in order to compare programmes with different outcomes, a common unit of benefit is needed and so CUAs and CBAs are required. Even these however are still difficult to use in allocative decisions as a proper decision would require an understanding of the cost per QALY or net social benefit for all potential programmes.⁵⁹ Even in a small field such as paediatric dentistry, it is very unlikely that this data will exist for all potential programmes and so decisions are often made with partial information which is unlikely to maximize efficiency. Sometimes this decision-making will be aided by the use of a threshold such that all programme that have cost per QALY lower than the agreed threshold will be invested in but this may still result in more programmes being recommended than the total budget can fund.⁶⁰ Alternative approaches to allocative decisions have been suggested including integer programming,^{12,61} or more pragmatic multi-criteria decision analysis tools such as programme budgeting and marginal analysis,⁶² although there have been very few uses in dentistry.^{63,64}

9 | SPECIFIC ISSUES IN DENTISTRY AND CHILD ORAL HEALTH RESEARCH

EEs in child oral health research are insufficiently reported.³ The use of guidelines offers a means of addressing this issue by indicating the crucial aspects needed for a high-quality EE and standardising reports. Checklists are available for the conduct and reporting of EEs, such as the Drummond checklist⁶⁵ and the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement, respectively.¹⁴ The CHEERS format is based on the CONSORT (Consolidated Standards of Reporting Trials) and is endorsed by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) in its latest report of good research practices for trial-based CEAs.⁶⁶

As mentioned earlier, the key problem with CEA in dentistry relates to the lack of comparability of the findings through the use of a broad range of clinical outcome measures; a particular concern in caries research. This can

prevent data from being maximised through systematic reviews and ultimately disrupts the dissemination of study findings across the world.^{67,68} This led to the commencement of the Outcomes in Trials for Management of Caries Lesions (OuTMac) study, which aims to develop a core outcome set for trials investigating clinical management of caries lesions in primary or permanent teeth.⁶⁹ This may improve the measurement of benefits in CEA within child oral health research.

Despite the advantages in terms of comparability, in dentistry, there may be a number of difficulties in generating QALYs. For example, if a programme has an effect on only one tooth, such as a type of restoration, it would not be possible to determine whether the reported impacts related to that particular tooth, or another tooth in the mouth, or perhaps another oral health problems that they may be experiencing, such as oral ulcers.⁷⁰ Moreover, it is acknowledged that many children do not experience symptoms from carious primary teeth, there is unlikely to be a notable gain in QALYs noted following provision of an programme to address the caries.^{71,72} For these reasons, a preference-based measure suitable for the condition and population in question may be more applicable to oral health promotion strategies, rather than individual tooth-level programmes, to increase the sensitivity of preference-based instruments, allowing for changes in QALYs to be identified.

Although the conception of QATYs initially offered potential for CUA, there has been little development over the years. Since utilities for four different tooth states were originally published,⁷³ our knowledge of caries has increased substantially. Importantly, it is now understood that the disease is a dynamic process, moving between demineralisation and remineralisation;⁷⁴ hence, these utilities are unlikely to reflect the full range of dental states represented on the caries continuum. Furthermore, its applicability to the primary dentition has not yet been explored, nor has its comparability across different programmes.⁷⁵ Moreover, the QATY may fail to acknowledge the wider impacts of caries beyond the tooth itself. These limitations currently preclude the wider use of the QATY as the primary means of measuring the benefits of dental programmes.

It should be acknowledged that a substantial amount of funding is required to conduct clinical trials. This cost is even greater when investigating a condition such as dental caries, which may take years to develop. This is one of the key factors precluding the undertaking of EEs alongside clinical trials and demonstrates the need for decision modelling studies in oral health research.

Importantly, the decision-making processes in dentistry are often not as centralised as in other areas of healthcare. In many health systems, for example, decisions surrounding the funding and implementation of oral health promotion strategies are undertaken at a local level. Although this approach

can help to ensure that services are tailored to meet the requirements of the local population, an absence of centralised decision-making can lead to regional variation, which may serve to increase inequalities further.

10 | CONCLUSION

Economic evaluation is an important aspect of understanding clinical interventions and programmes in paediatric dentistry. Any economic evaluation must carefully measure both costs and consequences, both of which require several considerations. The measurement of outcomes is particularly difficult in paediatric dentistry, and further work is required in the field of utility measurement. Although economic evaluations can be done alongside a clinical trial, this is often difficult in oral health and modelling-based approaches may be more appropriate in some instances.

AUTHOR CONTRIBUTIONS

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REFERENCES

1. Ast DB, Cons NC, Pollard ST, Garfinkel J. Time and cost factors to provide regular, periodic dental care for children in a fluoridated and nonfluoridated area: final report. *J Am Dent Assoc.* 1970;80(4):770–776.
2. Tonmukayakul U, Calache H, Clark R, Wasiak J, Faggion CM. Systematic review and quality appraisal of economic evaluation publications in dentistry. *J Dent Res.* 2015;94(10):1348–1354.
3. Rogers HJ, Rodd HD, Vermaire JH, et al. A systematic review of the quality and scope of economic evaluations in child oral health research. *BMC Oral Health.* 2019;19(1):132.
4. Drummond M, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. Critical assessment of economic evaluation. In: Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW, eds. *Methods for the economic evaluation of health care programmes.* 4th edn. Oxford, UK: Oxford University Press; 2015.
5. Morris S, Devlin N, Parkin D, Spencer A. *Economic Analysis in Healthcare.* Wiley; 2014.
6. Mackenzie R, Dixon AK. Measuring the effects of imaging: an evaluative framework. *Clin Radiol.* 1995;50(8):513–518.
7. Parkin D, Morris S, Devlin N. *Economic Appraisal in Public Healthcare: Assessing Efficiency and Equity,* 6th edn. Oxford University Press; 2015.

8. Briggs AH, O'Brien BJ. The death of cost-minimization analysis? *Health Econ.* 2001;10(2):179–184.
9. Dakin H, Wordsworth S. Cost-minimisation analysis versus cost-effectiveness analysis, revisited. *Health Econ.* 2013;22(1):22–34.
10. Byford S, Raftery J. Perspectives in economic evaluation. *BMJ.* 1998;316(7143):1529–1530.
11. Johannesson M. A note on the depreciation of the societal perspective in economic evaluation of health care. *Health Policy.* 1995;33(1):59–66.
12. Birch S, Donaldson C. Applications of cost-benefit analysis to health care: Departures from welfare economic theory. *J. Health Econ.* 1987;6(3):211–225.
13. Špaćirová Z, Epstein D, García-Mochón L, et al. A general framework for classifying costing methods for economic evaluation of health care. *Eur J Health Econ.* 2020;21(4):529–542.
14. Husereau D, Drummond M, Petrou S, et al. Consolidated Health economic evaluation reporting standards (CHEERS)-explanation and elaboration: A report of the ISPOR health economic evaluation publication guidelines good reporting practices task force. *Value Health.* 2013;16(2):231–250.
15. Attema AE, Brouwer WBF, Claxton K. Discounting in economic evaluations. *Pharmacoeconomics.* 2018;36(7):745–758.
16. Briggs AH, Gray AM. Handling uncertainty in economic evaluations of healthcare interventions. *BMJ.* 1999;319(7210):635.
17. Black WC. The CE plane: a graphic representation of cost-effectiveness. *Med Decis Making.* 1990;10(3):212–214.
18. Gafni A, Birch S. Incremental cost-effectiveness ratios (ICERs): The silence of the lambda. *Soc Sci Med.* 2006;62(9):2091–2100.
19. Davies G, Worthington H, Ellwood R, et al. An assessment of the cost effectiveness of a postal toothpaste programme to prevent caries among five-year-old children in the North West of England. *Community Dent Health.* 2003;20(4):207–210.
20. Marino R, Fajardo J, Morgan M. Cost-effectiveness models for dental caries prevention programmes among Chilean schoolchildren. *Community Dent Health.* 2012;29(4):302–308.
21. Goldman AS, Chen X, Fan M, Frencken JE. Cost-effectiveness, in a randomized trial, of glass-ionomer-based and resin sealant materials after 4 yr. *Eur J Oral Sci.* 2016;124(5):472–479.
22. Stearns SC, Rozier RG, Kranz AM, Pahel BT, Quinonez RB. Cost-effectiveness of preventive oral health care in medical offices for young Medicaid enrollees. *Arch Pediatr Adolesc Med.* 2012;166(10):945–951.
23. Samnaliev M, Wijeratne R, Kwon EG, Ohiomoba H, Ng MW. Cost-effectiveness of a disease management program for early childhood caries. *J Public Health Dent.* 2015;75(1):24–33.
24. Schwendicke F, Krois J, Robertson M, Splieth C, Santamaria R, Innes N. Cost-effectiveness of the hall technique in a randomized trial. *J Dent Res.* 2019;98(1):61–67.
25. Homer T, Maguire A, Douglas GVA, et al. Cost-effectiveness of child caries management: a randomised controlled trial (FICTION trial). *BMC Oral Health.* 2020;20(1):45.
26. Torrance GW, Feeny D. Utilities and quality-adjusted life years. *Int J Technol Assess Health Care.* 1989;5(4):559–575.
27. Brazier J. *Measuring and Valuing Health Benefits for Economic Evaluation.* 2nd edn. Oxford, UK: Oxford University Press; 2017.
28. Birch S, Ismail AI. Patient preferences and the measurement of utilities in the evaluation of dental technologies. *J Dent Res.* 2002;81(7):446–450.
29. Bleichrodt H, Johannesson M. An experimental test of a theoretical foundation for rating-scale valuations. *Med Decis Making.* 1997;17(2):208–216.
30. Torrance GW, Thomas WH, Sackett DL. A utility maximization model for evaluation of health care programs. *Health Serv Res.* 1972;7(2):118–133.
31. Feeny D, Furlong W, Boyle M, Torrance GW. Multi-attribute health status classification systems. Health Utilities Index. *Pharmacoeconomics.* 1995;7(6):490–502.
32. Foster Page LA, Beckett DM, Cameron CM, Thomson WM. Can the Child Health Utility 9D measure be useful in oral health research? *Int J Pediatr Dent.* 2015;25(5):349–357.
33. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res.* 2011;20(10):1727–1736.
34. Dalziel K, Catchpool M, García-Lorenzo B, Gorostiza I, Norman R, Feasibility R-A. Validity and differences in adolescent and adult EQ-5D-Y health state valuation in Australia and Spain: an application of best-worst scaling. *Pharmacoeconomics.* 2020;38(5):499–513.
35. Torrance WG, Feeny HD, Furlong JW, Barr DR, Zhang DY, Wang DQ. Multiattribute utility function for a comprehensive health status classification system: health utilities index mark 2. *Med Care.* 1996;34(7):702–722.
36. Moodie M, Richardson J, Rankin B, Iezzi A, Sinha K. Predicting time trade-off health state valuations of adolescents in four pacific countries using the assessment of quality-of-life (AQoL-6D) instrument. *Value Health.* 2010;13(8):1014–1027.
37. Stevens K. Valuation of the child health utility 9D index. *Pharmacoeconomics.* 2012;30(8):729–747.
38. Wolowacz SE, Briggs A, Belozeroff V, et al. Estimating health-state utility for economic models in clinical studies: an ISPOR good research practices task force report. *Value Health.* 2016;19(6):704–719.
39. United Nations. *General Comment No. 12: The Right of the Child to be Heard (No.UN=CRC=C=GC=12).* Geneva, Switzerland: United Nations; 2009.
40. Marshman Z, Gupta E, Baker SR, et al. Seen and heard: towards child participation in dental research. *Int J Paediatr Dent.* 2015;25(5):375–382.
41. Pettitt D, Raza S, Naughton B, et al. The limitations of QALY: a literature review. *J Stem Cell Res Ther.* 2016;6(4):334
42. Birch S. Measuring dental health: improvements on the DMF index. *Community Dent Health.* 1986;3(4):303–311.
43. Birch S, Gafni A, Markham B, Marriott M, Lewis D, Main P. Health years equivalents as a measurement of preferences for dental interventions. *Community Dent Health.* 1998;15(4):233–242.
44. Matthews DC, Gafni A, Birch S. Preference based measurements in dentistry: a review of the literature and recommendations for research. *Community Dent Health.* 1999;16(1):5–11.
45. Ryan M, Watson V, Amaya-Amaya M. Methodological issues in the monetary valuation of benefits in healthcare. *Expert Rev Pharmacoecon Outcomes Res.* 2003;3(6):717–727.
46. Donaldson C, Shackley P. Economic studies. In: Detels R et al., eds. *Oxford Textbook of Public Health.* 3rd ed. Oxford, UK: Oxford University Press. 1997.
47. Tan SHX, Vernazza CR, Nair R. Critical review of willingness to pay for clinical oral health interventions. *J Dent.* 2017;64:1–12.
48. Barber S, Pavitt S, Khambay B, Bekker H, Meads D. Eliciting preferences in dentistry with multiattribute stated

- preference methods: a systematic review. *JDR Clin Trans Res.* 2018;3(4):326–335.
49. Donaldson C. Valuing the benefits of publicly-provided health care: does 'ability to pay' preclude the use of 'willingness to pay'? *Soc Sci Med.* 1999;49(4):551–563.
 50. O'Brien B, Gafni A. When do the "dollars" make sense? Toward a conceptual framework for contingent valuation studies in health care. *Med Decis Making.* 1996;16(3):288–299.
 51. Sculpher MJ, Claxton K, Drummond M, McCabe C. Whither trial-based economic evaluation for health care decision making? *Health Econ.* 2006;15(7):677–687.
 52. Briggs AH, Weinstein MC, Fenwick EAL, Karnon J, Sculpher MJ, Paltiel AD. Model parameter estimation and uncertainty: a report of the ISPOR-SMDM modeling good research practices task force-6. *Value Health.* 2012;15(6):835–842.
 53. Sculpher M. Subgroups and heterogeneity in cost-effectiveness analysis. *Pharmacoeconomics.* 2008;26(9):799–806.
 54. Gray AM, Clarke PM, Wolstenholme JL, Wordsworth S. *Applied Methods of Cost-Effectiveness Analysis in Healthcare*, Vol. 3, Oxford University Press, 2011.
 55. Claxton K, Ginnelly L, Sculpher M, Philips Z, Palmer S. A pilot study on the use of decision theory and value of information analysis as part of the NHS Health Technology Assessment programme. *Health Technol Assess.* 2004;8(31):1–103.
 56. Skold UM, Petersson LG, Birkhed D, Norlund A. Cost-analysis of school-based fluoride varnish and fluoride rinsing programs. *Acta Odontol Scand.* 2008;66(5):286–292.
 57. Barton P, Bryan S, Robinson S. Modelling in the economic evaluation of health care: selecting the appropriate approach. *J Health Serv Res Policy.* 2004;9(2):110–118.
 58. Pukallus M, Plonka K, Kularatna S, et al. Cost-effectiveness of a telephone-delivered education programme to prevent early childhood caries in a disadvantaged area: a cohort study. *BMJ Open.* 2013;3(5):e002579.
 59. Gerard K, Mooney G. QALY league tables: handle with care. *Health Econ.* 1993;2(1):59–64.
 60. Bertram MY, Lauer JA, De Joncheere K, et al. Cost-effectiveness thresholds: pros and cons. *Bull World Health Organ.* 2016;94(12):925–930.
 61. Birch S, Gafni A. Cost effectiveness/utility analyses: Do current decision rules lead us to where we want to be? *J Health Econ.* 1992;11(3):279–296.
 62. Peacock S, Ruta D, Mitton C, Donaldson C, Bate A, Murtagh M. Using economics to set pragmatic and ethical priorities. *BMJ.* 2006;332(7539):482–485.
 63. Tianviwat S, Chongsuvivatwong V, Birch S. Optimizing the mix of basic dental services for Southern Thai schoolchildren based on resource consumption, service needs and parental preference. *Commun Dent Oral Epidemiol.* 2009;37(4):372–380.
 64. Vernazza CR, Carr K, Wildman J, et al. Resource allocation in NHS dentistry: recognition of societal preferences (RAINDROP): study protocol. *BMC Health Serv Res.* 2018;18(1):487.
 65. Drummond M, Jefferson T. Guidelines for authors and peer reviewers of economic submissions to the BMJ. *BMJ.* 1996;313(7052):275.
 66. Ramsey SD, Willke RJ, Glick H, et al. Cost-effectiveness analysis alongside clinical trials II-An ISPOR Good Research Practices Task Force report. *Value Health.* 2015;18(2):161–172.
 67. Ricketts D, Lamont T, Innes N, Kidd E, Clarkson JE. Operative caries management in adults and children. *Cochrane Database Syst Rev.* 2013; Art. No.: CD003808(3).
 68. Schwendicke F, Stolpe M, Meyer-Lueckel H, Paris S, Dorfer CE. Cost-effectiveness of one- and two-step incomplete and complete excavations. *J Dent Res.* 2013;92(10):880–887.
 69. Schwendicke F, Lamont T, Innes N. Outcomes in trials for management of caries lesions (OuTMaC): protocol. *Trials.* 2015;16(1):397.
 70. Krisdapong S, Prasertsom P, Rattananangsim K, Sheiham A. Relationships between oral diseases and impacts on Thai schoolchildren's quality of life: Evidence from a Thai national oral health survey of 12- and 15-year-olds. *Commun Dent Oral Epidemiol.* 2012;40(6):550–559.
 71. Milsom K, Tickle M, Blinkhorn A. Dental pain and dental treatment of young children attending the general dental service. *Br Dent J.* 2002;192(5):280–284.
 72. Tickle M, Milsom K, King D, Kearney-Mitchell P, Blinkhorn A. The fate of the carious primary teeth of children who regularly attend the general dental service. *Br Dent J.* 2002;192(4):219.
 73. Fyffe HE, Kay EJ. Assessment of dental health state utilities. *Commun Dent Oral Epidemiol.* 1992;20(5):269–273.
 74. Featherstone J. Dental caries: a dynamic disease process. *Aust Dent J.* 2008;53(3):286–291.
 75. Chestnutt IG, Hutchings S, Playle R, et al. Seal or varnish? A randomised controlled trial to determine the relative cost and effectiveness of pit and fissure sealant and fluoride varnish in preventing dental decay. *Health Technol Assess.* 2017;21(21):1–256.

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