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REVIEW ARTICLE

Is Screening and Integrated Care for Gestational Diabetes Cost Effective?

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An introduction to Cost effectiveness Analysis

Cost effectiveness analysis is a health economic tool that measures the benefits associated with an intervention relative to its cost. The cost-effectiveness ratio (CE ratio) is calculated using the following equation:

Benefit of an intervention can be measured in different ways such as an adverse outcome averted or as quality adjusted life years (QALY) gained or disability adjusted life years (DALY) prevented. According to the WHO CHOISE analysis any intervention in a given country is considered Highly cost-effective if its cost is less than

$$\frac{(\textit{Cost}\ \text{of intervention - Costs averted by intervention})}{\textit{Benefits}\ \text{of intervention}}$$

its annual GDP per capita; Cost-effective when it is between one and three times GDP per capita; and Not cost-effective when it is more than three times GDP per capita (1).

Health interventions do not occur in isolation and different interventions for the same objective may have differing costs and outcomes depending on the interplay with other elements of the health system. To assess which of the interventions is more beneficial a comparative cost and benefit analysis for different interventions compared to the base case which maybe the current

$$\frac{\text{Total Cost Intervention 1 - Total Cost Intervention 2}}{\text{QALYs/DALYs Intervention 1 - QALYs/DALYs Intervention 2}}$$

practice - in case there is an existing policy; or, to no intervention is done. This analysis is called incremental cost effectiveness analysis and is expressed as a ratio which is called Incremental Cost Effectiveness Ratio (ICER) and is defined as the difference in costs between two interventions divided by the difference in benefits of the two interventions.

When the benefits are also valued in monetary terms using valuations of people's observed or stated preferences, such as the willingness-to-pay (WTP) approach the cost effectiveness analysis is termed as Cost Utility Analysis.

Perspective

Perception of what is cost beneficial varies depending upon the viewpoint of who makes the judgement. Therefore any cost benefit evaluation must describe the perception. The viewpoint may be that of the patient, hospital/clinic, healthcare system or society. So while a specific intervention maybe cost beneficial from an individual perspective it may not be so from a societal perspective for example general cost effectiveness analysis shows that treating tuberculosis with the DOTS strategy is highly cost-effective and providing liver transplants in cases of alcoholic cirrhosis is highly cost-ineffective from a societal perspective (2). Thus cost-effectiveness analysis (CEA) is useful in making resource allocations.

Sectorial versus Societal: The growing use of cost-effectiveness analysis (CEA) to evaluate the costs and health effects of specific interventions is dominated by studies of prospective new interventions compared to current practice. This type of analysis does not explicitly take a sectorialor societal perspective where the costs and effectiveness of all possible interventions are compared in order to select the mix that maximizes health for a given set of resource constraints. The estimated cost-effectiveness of a single proposed new intervention is compared either with the cost effectiveness of a set of existing interventions reported in the literature or with a fixed price cut-off point representing the assumed social willingness to pay for an additional unit of health. The implicit assumption that the required additional resources would need to be transferred from another health intervention or from another sector is rarely discussed (2). On the flip side of this, are interventions that may cascade a set of further interventions that spill into other health sectors and create health benefits in the life course of individuals and sometimes into the life course of the next generations such as interventions for GDM screening and diagnosis. If the delayed health benefits accruing from these are not taken into account because of compartmentalization of budget and resources then the initial intervention may seem cost ineffective for the particular health sector resulting in missed opportunities to create overall health benefits and save costs from a societal perspective.

Opportunity Costs

Traditionally opportunity cost of investing in a healthcare intervention is the other healthcare programs that are displaced by its introduction. This is best measured by the health benefits that could have been achieved had the money been spent on the next best alternative healthcare intervention. In the example above failure to make the investment in the intervention because of a short term immediate outlook approach may result in opportunity cost to gain future health benefits.

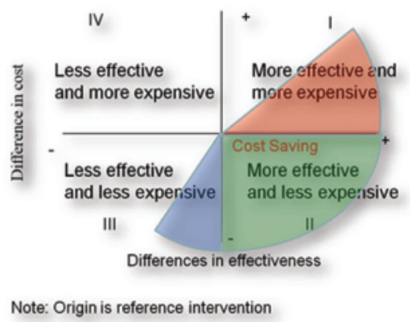
Discounting

In the context of cost benefit analysis it is important to understand that costs and benefits incurred today are usually valued more highly than costs and benefits occurring in the future. In cost effectiveness analysis this is accounted for through discounting. Discounting health benefits reflects society's preference for benefits to be experienced in the present rather than the future. Discounting costs reflects society's preference for costs to be experienced in the future rather than the present. To ensure that cost benefit analyses are comparable one needs to use standard rate of discounting. The standard approach is to use WHO-CHOICE recommendations, with both costs and health effects discounted at 3%. In the sensitivity analysis testing, the sensitivity of the results can be tested at 0% discount rate for health effects and a rate of 6% for costs (2).

Modelling and its Limitation

Cost benefit analysis are done using mathematical modelling where input costs are based on actual consumption of direct resources and allocated costs ofcommon manpower and material resources based on actual utilization. Benefits are estimated based on published studies and their applicability in the

Figure 1: Cost effectiveness Plane



given context. The quality of existing evidence, its applicability in the given context and weightage given to the evidence as well as apportioning of costs of common resources; results in unavoidable bias and some degree of arbitrariness to cost effectiveness analysis. Standardization of methods of data collection and applying sensitivity analysis can correct some of these biases; none the less cost effectiveness analysis should primarily be used in conjunction with other sources of information to make policy decision.

Cost Effectiveness Plane

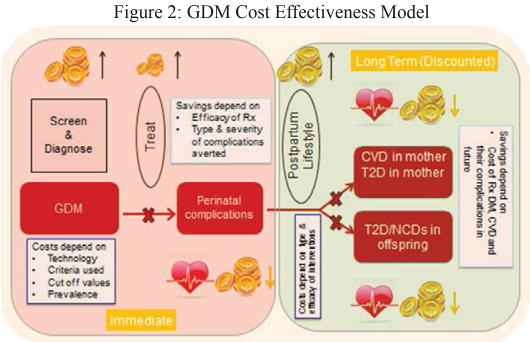
The cost-effectiveness plane (CE plane) is an important tool to present cost-effectiveness analysis visually. It clearly illustrates the differences in costs and effects between different strategies. By visually representing the relative value of strategies, the CE plane helps its viewer evaluate multiple strategies and make informed decisions. The cost-effectiveness plane consists of a four-quadrant diagram where the X axis represents the incremental level of effectiveness of an outcome and the Y axis represents the additional total cost of implementing this outcome. For example, the further right you move on the X axis, the more effective the outcome. Importantly, the X axis also allows less effective interventions to be represented on the left-hand side of the graph. Similarly, the further up you move on the Y axis, the more costly the outcome. Cost-saving interventions are in the lower half of the graph.

When considering both parameters together, the CE plane allows one to determine the relative cost and relative effectiveness. The fact that the four quadrants can represent all combinations of possible outcomes is important, since sensitivity analyses will produce a cloud of results which may span multiple quadrants. In fact, the spread of results can be an important aspect of the ICER to understand, since it is a measure the ICER's degree of uncertainty. This is one reason why the CE plane is such a valuable visual tool, since it provides a quick visual snapshot of the distribution of the ICER and a summary of how cost and outcomes are likely to behave. Interventions that are more effective and cost less than the base case are cost saving and must be implemented. Interventions that cost slightly more than the base case but are relatively more effective, as well as interventions that are slightly less effective but cost considerably less are also cost effective (Fig. 1). An intervention that has higher costs and worse outcomes than an alternative intervention is referred to as dominant. When the incremental cost-effectiveness ratio (ICER) for a given treatment alternative is higher than that of the next, more effective, alternative (that is, it is dominated by the combination of two alternatives) it is called extended dominance and this alternative should not be used.

Gestational Diabetes Mellitus Cost Effectiveness Model

Available evidence shows that hyperglycemia in pregnancy is associated with high risk of maternal and perinatal morbidity and mortality and poor pregnancy outcome (3-5). It is also shown that women with history of GDM are at a high future risk of diabetes and CVD (6-8) and offering these women post-partum lifestyle intervention prevents or delays the onset of diabetes and CVD (9-11) and thusprovides the opportunity for primary prevention. In addition offsprings of GDM pregnanciesare at high risk of metabolic problems (12, 13) including early onset type 2 diabetes (14). While

Figure 2: GDM Cost Effectiveness Model



treatment of maternal diabetes is expected to reduce these risks there is still limited evidence from high quality studies (15, 16).

GDM screening and integrated care cost effectiveness model must take into account all the three elements described above. Figure 2 shows the various elements of input costs and health benefits that must be included in such a model. Here, both the immediate and long term costs have been considered. In terms of costs and benefits the longer term intervention will require discounting.

Screening and Diagnosis of GDM: This is a key input cost and the efficacy of public health programs to screen and correctly identify women with GDM who will most benefit from treatment is a key element. The criteria, technology and cut off value used for testing and diagnosis are important determinants of this cost. Traditionally, the risk factor based approach has been popular in Europe. Given the high rates of diabetes and IGT in the background population and documented high rates of hyperglycemia in pregnancy in India and South Asia,where additionally, ascertainment of risk factors is poor due to low levels of education and awareness and poor record keeping, universal testing seems an appropriate strategy (17).

Treatment of Women with GDM: Proportion of women with different degrees of hyperglycemia requiring different types of treatment and level of monitoring to ensure euglycemia and prevent fetal and maternal complications will determine the next input cost.

Prevention of perinatal complications listed in table 1provides the immediate health benefit from the

Table 1: Risks Associated with Hyperglycemia in Pregnancy

FOETAL RISKS	MATERNAL RISKS
Spontaneous abortion, intrauterine death & still birth	Polyhydramnios
Lethal or handicapping congenital malformation	Pregnancy Induced Hypertension & Preeclampsia,
Shoulder dystocia & birth injuries	Prolonged labor, Obstructed labor, Assisted delivery & C-section
Neonatal hypoglycemia	Uterine atonia and Post-partum Hemorrhage
Infant Respiratory Distress Syndrome (IRDS)	Infections
	Progression of retinopathy

intervention with resultant savings.

In a model that limits itself to the short term, the CE analysis is limited to this time point.

Life Course Approach: In an integrated model, the life course approach,including the post-partum periodis used.Here,in addition to the costs and benefits described above, additional input costs include post-partum screening and life style / pharmacological intervention to prevent diabetes and CVD in the mother and appropriate counselling and follow up of the offspring to prevent/ delay type 2 diabetes/ metabolic syndrome. The costs depend on the type, intensity and efficacy of the interventions and benefits are calculated based on quality adjusted life years (QALYs) gained or disability adjusted life years (DALYs) averted free from diabetes/ CVD and their debilitating and costly complications in both the mother and offspring. These costs and benefits are discounted at appropriate rates for the duration of intervention.

Studies on Cost effectiveness of Interventions

There are only a few studies thathave evaluated the cost effectiveness of an integrated approach to GDM screening and care that also include the post-partum prevention of diabetes and CVD. Most studies have evaluated the cost effectives of one screening strategy over another e.g., selective screening versus universal screening or the IADPDSG criteria over the WHO 2009 criteria or the ADA/ACOG criteria. Some of these studies are summarized in table 2 and described below.

Using a decision analysis tool GeDiForCE® that assesses the full range of costs and benefits of GDM screening and intervention in specified populations developed by the authors, Marseille et al (18) report data from India and Israel and show that the intervention is highly cost effective both in India and Israel. The program costs in international dollars per 1000 pregnant women was $259,139 in India and $259,929 in Israel. Net costs, adjusted for averted disease, were $194,358 and $76,102, respectively. The cost per DALY averted were $1626 in India and $1830 in Israel. Sensitivity analysis findings ranged from $628 to $3681 per DALY averted in India and net savings of $72 420–8432 per DALY avertedin Israel.

Another decision analysis modelling study reported by Werner et al from USA (19) compared the cost-utility of three strategies to identify GDM: 1) no screening, 2) current screening practice (1-h 50-g glucose challenge test between 24 and 28 weeks followed by 3-h 100-g

Table 2: Summary of some GDM Cost effectiveness studies

Study	Comment	ICER
Marseille et al.	Cost of screening and related gestational diabetes costs, prevalence, adverse event risk and intervention efficacy considered	1,626 International dollars (India) 1,830 International dollars (Israel) per DALY averted
Moss et al.	ICE based on data from the ACHOIS trial. Serious perinatal complication defined as ≥ 1 of the following: death, shoulder dystocia, bone fracture, nerve palsy.	AU$27,503 per perinatal complication; AU$60,506 per perinatal death and AU$2,988 per life-year saved
Mission et al.	Decision model treating vs not treating patients in category 5 of HAPO. Pre-eclampsia, mode of delivery, maternal death, macrosomia, shoulder dystocia, brachial plexus injury (permanent and transient), hypoglycemia, hyperbilirubinemia and neonatal death included as maternal and neonatal outcomes.	US$44,203 per QALY.
Ohno et al.	Treating versus not treating mild gestational diabetes. Maternal outcomes included pre-eclampsia, shoulder dystocia, caesarean vs vaginal delivery & maternal death; neonatal outcomes included macrosomia (> 4000 g), brachial plexus injury (permanent or transient), hypoglycemia, admission to NICU, hyperbilirubinemia and neonatal death.	US$20,412 per QALY
Werner et al.	Compared 3 strategies of no screening, current practice (1 hour 50 g GCT between 24 weeks and 28 weeks followed by 3 hour 100 g OGTT) or screening according to IADPSG criteria.	IADPSG recommendations cost effective with an ICER of US$20,336 per QALY when potential long-term maternal benefits included)

glucose tolerance test when indicated), or 3) screening practice proposed by the IADPSG. Assumptions in the study included that 1) women diagnosed with GDM received additional prenatal monitoring; mitigating the risks of preeclampsia, shoulder dystocia, and birth injury; and 2) GDM women had opportunity for intensive post-delivery counseling and behavior modification to reduce future diabetes risks. The primary outcome measure was the incremental cost-effectiveness ratio (ICER). For every 100,000 women screened, 6,178 quality-adjusted life-years (QALYs) are gained, at a cost of $125,633,826. The ICER for the IADPSG strategy compared with the current standard was $20,336 per QALY gained. When post-delivery care was not accomplished, the IADPSG strategy was no longer cost-effective. These results were robust in sensitivity analyses.

Mission et al. (20) developed a decision analysis model to compare the cost effectiveness of treating patients with GDM versus not treating in the USA. They considered patients in HAPO (Hyperglycemia and Adverse Pregnancy Outcome) Category 5 (top 3–12% of fasting glucose levels) which is consistent with diagnosis of marginal patients according to the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) recommendations. Pre-eclampsia, mode of delivery, maternal death, macrosomia, shoulder dystocia, brachial plexus injury (permanent and transient), hypoglycaemia, hyperbilirubinemia and neonatal death were included as maternal and neonatal outcomes. Treating patients was found to be cost effective at a cost of US$44,203 per QALY. A one-way sensitivity analysis suggested that treatment remained cost effective when it met 64% of its reported efficacy.

Ohno et al. (21) compared treating versus not treating mild gestational diabetes from a societal perspective. Maternal outcomes included pre-eclampsia, shoulder dystocia, caesarean versus vaginal delivery and maternal death; neonatal outcomes included macrosomia (more than 4000 g), brachial plexus injury (permanent or transient), hypoglycemia, admission to a neonatal intensive care unit, hyperbilirubinemia and neonatal death. In the base case analysis, treatment was found to be cost effective (below a WTP threshold of US$100,000) at US$20,412 per QALY. Sensitivity analyses showed that treatment remained cost effective when the incremental cost to treat was less than US$3,555 or when the reported efficacy was at least 49% (at baseline cost).

An Australian study (22) compared treatment of women with mild gestational diabetes by dietary advice, blood glucose monitoring and when required insulin therapy with routine pregnancy care from a health system perspective. Based on data from the Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) trial, the incremental cost per additional serious perinatal complication (defined as 1 or more of the following: death, shoulder dystocia, bone fracture, nerve palsy) prevented was estimated as AU$27,503. The incremental cost per perinatal death prevented was calculated as AU$60,506 and AU$2,988 per life-year saved.

Given the high risk of future diabetes in women with GDM and evidence from prospective studies that lifestyle and pharmacological intervention for prevention of diabetes is as effective in women with GDM as in non GDM women with IGT and men with IGT (9-11), and that these interventions are regarded as highly cost effective (23-26), and that treatment of GDM is cost effective in preventing perinatal complications (20-22). It seems intuitive that screening and comprehensive care for GDM should be overall highly cost effective even in the absence of more comprehensive cost effectiveness data.

The key challenge from a program's perspective is the ability of the health system to be able to track and follow up the GDM mother child pair and continuously engage and empower them to adapt a healthy lifestyle (27). Without adequate focus on post-partum care, the strategy for screening and treatment of GDM will be only half as effective. Focusing only on the short-term survival in terms of lowered maternal and perinatal morbidity and mortality does not capture outcomes that have longer-term implications for adult health, life expectancy, quality of life and accumulation of human capital (28). Pregnancy offers a window of opportunity to provide maternal care services, not only to reduce the traditionally known maternal and perinatal morbidity and mortality indicators, but also for intergenerational prevention of several chronic diseases (29). There are several barriers in achieving these objectives. These barriers related to GDM, for example, have been recently described in a systematic review [30].

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