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ORIGINAL ARTICLE

The cost-effectiveness of gestational diabetes screening including prevention of type 2 diabetes: application of a new model in India and Israel

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Abstract

Objective: Gestational diabetes mellitus (GDM) is associated with elevated risks of perinatal complications and type 2 diabetes mellitus, and screening and intervention can reduce these risks. We quantified the cost, health impact and cost-effectiveness of GDM screening and intervention in India and Israel, settings with contrasting epidemiologic and cost environments.
Methods: We developed a decision-analysis tool (the GeDiForCE™) to assess cost-effectiveness. Using both local data and published estimates, we applied the model for a general medical facility in Chennai, India and for the largest HMO in Israel. We computed costs (discounted international dollars), averted disability-adjusted life years (DALYs) and net cost per DALY averted, compared with no GDM screening.
Results: The programme costs per 1000 pregnant women are $259 139 in India and $259 929 in Israel. Net costs, adjusted for averted disease, are $194 358 and $76 102, respectively. The cost per DALY averted is $1626 in India and $1830 in Israel. Sensitivity analysis findings range from $628 to $3681 per DALY averted in India and net savings of $72 420–8432 per DALY averted in Israel.
Conclusion: GDM interventions are highly cost-effective in both Indian and Israeli settings, by World Health Organization standards. Noting large differences between these countries in GDM prevalence and costs, GDM intervention may be cost-effective in diverse settings.

Keywords

Cost-effectiveness analysis, costs, diagnosis, gestational diabetes mellitus, management, type 2 diabetes mellitus

History

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Introduction

Gestational diabetes mellitus (GDM) causes severe perinatal complications [1–4] and elevates the long-term risk of type 2 diabetes mellitus (T2DM), for both mother and offspring [5–7]. Prevalence is 2–10% across global regions [8] higher than 25% in some settings [9], and will likely increase due to rising obesity.

There is no worldwide standard of practice for the diagnosis and management of GDM [8]. Most high-income countries have national guidelines, while many low- and middle-income countries are considering the addition of GDM management to antenatal care. To facilitate decision-making, countries need reliable information on the cost and cost-effectiveness of GDM screening and treatment. Almost all cost-effectiveness analyses have assessed only short-term complications [10], omitting consideration of reductions in long-term T2DM. A recent study evaluated the potential cost-effectiveness of new GDM screening criteria for both time periods [11] (for a modelled US cohort, finding GDM screening to cost $20 326 per QALY gained). We know of no comprehensive analyses for varied global health setting.

The GeDiForCE™ decision-analysis model assesses the full range of costs and benefits of GDM screening and intervention in specified populations. It compares the cost and cost-effectiveness of no GDM screening with one or more GDM screening and intervention strategies. We use this model to assess the costs, health benefits and cost-effectiveness of GDM screening and treatment in two disparate settings: Chennai, India at a general medical facility; and in a large Health Maintenance Organization in Israel.

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We quantified the health and cost effects of screening for GDM and applying pharmaceutical and behavioural interventions to reduce perinatal adverse events (PAEs) and long-term T2DM. Inputs included cost, GDM prevalence, adverse event (AE) risk and intervention efficacy, derived from local data and published literature. We calculated the occurrence of AEs with and without screening and intervention, and translated these outcomes into overall costs and disability-adjusted life years (DALYs), a measure of disease burden. We conducted sensitivity analyses to assess the importance of uncertainties in input values. Methods are summarized below; further detail appears in a Supplemental Digital Content file (S1).

Methods

Model description

The GeDiForCE™ assesses the costs and consequences of GDM screening in any setting, by specifying appropriate epidemiologic and cost input values. It was developed at the University of California, San Francisco and Health Strategies International. It is implemented in Microsoft Excel© and is available *gratis*.

Each intervention strategy is defined by a set of screening tests, antenatal management interventions and post-partum diabetes prevention interventions. The model computes the cost of each strategy; the expected incidence and cost of perinatal complications and T2DM; and the cost per averted DALY compared with no intervention. We applied the model in Israel and in India. Results are in ''International dollars'', using purchasing power parity to adjust unit costs of specified services, and per-capita medical care spending to adjust general medical care costs (e.g. for T2DM). All results are discounted at 3% per year to 2011.

Study sites

India

The Chennai Corporation Maternity Hospital (CCMH) is a general medical facility. The outpatient unit has an active diabetes screening programme and refers a large portion of GDM cases to the Diabetes Care and Research Institute (DCRI) for antenatal monitoring and treatment. DCRI is a multi-disciplinary hospital that provides comprehensive inpatient and outpatient diabetes services, including patient education, lab investigations and diagnosis and treatment. (We also conducted analyses for facilities in Maharashtra and Punjab, see Supplemental Digital Content, S1.)

Israel

Clalit, a health maintenance organization, serves 60% of Israel's population (all ethnic groups) with a network of 14 hospitals and 1300 primary and specialized care clinics, including 40 women's health centres. Pregnancy-related services include a dedicated certified nurse throughout pregnancy, and health promotion workshops from pre- through post-pregnancy.

Input values

The model inputs used in the analysis are summarized in Table 1.

GDM services

CCMH and DCRI. Data on GDM costs were obtained using an ingredients-based micro-costing [12] of resources used for screening tests at CCMH, antenatal care for GDM-positive mothers at DCRI, and post-partum follow-up and care. We included direct service costs and a portion of administrative and facility overhead.

Clalit. We obtained GDM service costs through queries of the central Clalit cost database. These queries compiled the units of service and associated costs (personnel, supplies and administration) for 501 GDM-positive women.

Prevalence of GDM

At CCMH, record abstraction for September 2009 through August 2010 yielded a prevalence of 9.1% via 75 g oral glucose tolerance test (OGTT), for 1864 women tested. In Clalit, GDM prevalence was 2.6% in the cohort of women tested.

Test performance (sensitivity and specificity)

CCMH uses the 75 g, 2 h OGTT to diagnose GDM, and Clalit uses either the 75 g, 2 h OGTT or the 50 g glucose challenge test followed by the 100 g OGTT for diagnosis. For comparability, we assumed use of 75 g, 2 h OGTT for both sites. Since this test was used to diagnose T2DM for most studies of T2DM incidence following GDM, we considered it the ''gold standard'' test and thus assign specificity and sensitivity of 100%. In a sensitivity analysis, we examine the test performance of 75 g, 2 h OGTT if using 100 g, 3 h OGTT as the gold standard (sensitivity 57.6%, specificity 85.1%) [13].

Intervention costs: initial screening; antenatal care for GDM+ women

CCMH. The cost of initial screening was $6.59 (58.2% personnel, 39.1% test kit and other supplies, 2.7% overhead and capital). Subsequent antenatal care costs were $327 per woman with GDM (diet and exercise counselling, glucose control medications and monitoring, including HbA1c tests, foetal ultrasound, echocardiogram and alpha-fetoprotein tests).

Clalit. Antenatal screening averaged $26 per woman including the GDM test kit, personnel and overhead. Subsequent antenatal services (laboratory monitoring, diet and lifestyle counselling, foetal monitoring via ultrasound and echocardiograms, and glycaemic control medications) cost $649 per woman.

Intervention costs: post-partum care to reduce the risk of T2DM in GDM+ women

In two randomized clinical trials, the US-based Diabetes Prevention Program (DPP) and the Indian Diabetes Prevention Program (IDPP), metformin and/or lifestyle management interventions were provided to people with impaired glucose tolerance to reduce T2DM risk. We extrapolated the costs of the DPP to $7533 (Israel) and the IDPP to $2424 (India).

Table 1. Model inputs: base-case values, ranges for sensitivity analyses and data sources.

Input type	Input	Input values*: India	Input values*: Israel	Sensitivity analyses range	Sources
Miscellaneous	Cohort size	1000		N/A	User input
	Discount rate – annual	3.0%		±50%	[14]
	Per capita health spending	$122	$2093	N/A	[44]
Epidemic	Prevalence of GDM in screened women	9.1%	2.6%	India: ±10%; Israel: ±50%	Israel: Clalit; India: CCMH
	Normal life expectancy from GDM intervention: Mother	39	49	N/A	[22]
	Normal life expectancy from GDM intervention: Child	46	57	N/A	[22]
Intervention characteristics	Screening regimen	75 g 2 h, OGTT		N/A	Israel: Clalit; India: CCMH
	Test performance: sensitivity	1.0		57.6%	''Gold standard'' test
	Test performance: specificity	1.0		85.1%	''Gold standard'' test
	Initial GDM screening cost	$7	$26	±50%	Israel: Clalit; India: CCMH; DCRI
	Antenatal care cost	$327	$649	±50%	
	Post-partum care cost (net present value)	$2846	$7533	±50%	India: IDPP [24] Israel: DPP [21,23]
	Proportion of women diagnosed with GDM who initiate post-partum intervention	80.0%		N/A	Assumption
	Proportion of women receiving ongoing post-partum intervention who have IGT	22.0%		N/A	[45]
DALYs	PAEs: Mother + Child (weighted mean) – No GDM intervention	0.23	0.23	±50%	[16]
	PAEs: Mother + Child (weighted mean) – With GDM intervention	0.16	0.17	±50%	[16]
	Type 2 diabetes: Mother	11.2	14.3	±50%	CORE model
	Type 2 diabetes: Child	13.7	16.1	±50%	CORE model
Incidence (incremental, lifetime)	Perinatal death: Mother	0.00		5.0%	No documented reductions
	Perinatal death: Child	0.00		5.0%	No documented reductions
	Type 2 diabetes (lifetime): Mother	0.49		±50%	[20,21,46,47]
	Type 2 diabetes (lifetime): Child	0.25		±50%	[20,21,46,47]
Effectiveness: Relative risk reduction	Perinatal death: Mother	0.00		25%	No documented reductions
	Perinatal death: Child	0.00		25%	No documented reductions
	Type 2 Diabetes: Mother	0.40		±50%	[47,48], See Technical Appendix
	Type 2 Diabetes: Child	0.40		±50%	[47,48], See Technical Appendix
Ave. age of T2DM onset	GDM+ mothers	40		N/A	Authors' estimate
	Children of GDM+ mothers	25		N/A	Authors' estimate
Cost of illness	PAEs: Mother + Child (weighted mean): No GDM intervention	$1566	$4926	±50%	Israel: Clalit; India: CCMH, Chennai
	PAEs: Mother + Child (weighted mean): With GDM intervention	$1163	$3817	±50%	Israel: Clalit; India: CCMH, Chennai
	Perinatal death: Mother	$0		N/A	No documented reductions
	Perinatal death: Child	$0		N/A	No documented reductions
	Type 2 Diabetes: Mother	$2628	$45 090	±50%	[28,29,31–34]
	Type 2 Diabetes: Child	$2628	$45 090	±50%	[28,29,31–34]

*All costs are denominated in International dollars, which adjusts for differences in purchasing power between countries.

Proportion of women diagnosed with GDM who initiate post-partum intervention

We assume that 80% of women diagnosed with GDM receive post-partum care, either lifestyle counselling or metformin or both.

DALYs, incidence and effectiveness: PAEs

DALYs reflect the number of years lost due to ill health, disability or early death, where one DALY equals one year of healthy life lost [14]. GDM is associated with a higher risk of PAEs and T2DM, in the mother and child. DALYs for PAEs were estimated from data on health state utilities and discounted to the present if long-term (brachial plexus injury following shoulder dystocia) [15,16]. The baseline incidence of PAEs was estimated from local data (Clalit) or the literature (CCMH). The effectiveness of antenatal interventions in reducing PAEs was derived from published literature [3,4,17,18] (Kahn J, Marseille E, Malekinejad M. Global health intervention review: gestational diabetes mellitus. Working paper, 2011). See Supplemental Digital Content (S1: Technical Appendix) for details on PAE incidence and efficacy of interventions.

DALYS, incidence and efficacy: T2DM

Estimates of the lifetime cumulative incidence of T2DM in mothers with a history of GDM and their offspring were derived from published literature. We found divergent values due to different follow-up periods, populations and diagnostic criteria. We used a cumulative incidence of 0.49 in the model [19,20]. See Supplemental Digital Content (S1: Technical Appendix) for details on T2DM incidence estimation.

The lifetime discounted DALYs associated with developing T2DM in the mother and in the child was obtained by comparing disability-adjusted life expectancy with and without T2DM at the estimated age of onset of T2DM. Normal life expectancy was derived from country-specific WHO life tables for 2009 [21]. We relied on the Center for Outcomes Research (CORE) Diabetes Model, a web-based interactive simulation, to estimate the health and cost outcomes of each T2DM case, using an all-female version of the UK Prospective Diabetes Study cohort.

Interventions to reduce T2DM incidence have been found effective in populations with impaired glucose tolerance (IGT), including women with a history of gestational diabetes. Based on results from the US DPP [20,22] and Indian IDPP [23], we estimated 40% as the lifetime reduction in T2DM incidence due to post-partum lifestyle management interventions (and metformin in IDPP).

Incidence and effectiveness: perinatal death

The base case assumes no GDM-attributable perinatal mortality, for mother or child. We are aware of no data that firmly supports non-zero values. However, this issue is debated [24]. Particularly in settings with limited health infrastructure, undiagnosed GDM could lead to perinatal death due to, for example, post-natal hypoglycaemia in the child or post-partum maternal haemorrhage. The effect of GDM-related perinatal mortality is explored in sensitivity analyses.

Costs: PAEs

CCMH. Cost estimates were derived from personal communications regarding the inpatient days required per AE and the cost per inpatient day. There were no significant outpatient costs (Personal communication: Githa K. Resource requirements for treating perinatal adverse events associated with gestational diabetes in Chennai, India. 2011).

Clalit. The costs of treating AEs were derived from the Clalit cost database, for the GDM cohort.

Costs: T2DM

The cost of treating T2DM was estimated from published literature [25–32] and from the CORE model [33] assuming 100% females and costs from Canada [34] and the US [35,36]. We adjusted the median cost over nine studies to our study sites using national health care spending per capita, estimating $45 090 for Israel and $2628 for India.

Sensitivity analyses

In order to assess the influence of variations in the value of key model inputs on cost-effectiveness, we performed one-way sensitivity analyses on 16 variables and displayed the results in a tornado diagram. All values were varied from 50% to 150% of the base case. A Monte Carlo simulation (@RISK Version 5.7.1, Palisade Corporation, Ithaca, NY) was also conducted. The cost variables were assigned log-normal distributions with a standard deviation of 0.25 with the base-case value standardized to 1.0. The health inputs assumed beta distributions with alpha and beta parameters of 2. We also explored the effect of lower screening test performance, and of delayed rather than prevented cases of T2DM.

Results

Base case

Table 2 presents results based on most likely input values. The GDM screening and treatment intervention costs per 1000 pregnant women are estimated at $259 139 for CCMH in India and $259 920 for Clalit in Israel. In CCMH, initial screening, antenatal interventions, and post-partum interventions constituted 9.4%, 21.5% and 69.1% of these costs, respectively. In Clalit, the cost breakdown is 9.9%, 29.7% and 60.3%, respectively.

Net incremental costs compared to no screening and treatment, i.e. adjusted for offsetting savings due to averted GDM-associated adverse outcomes including future T2DM, are $194 358 for CCMH and $76 102 for Clalit.

Table 2. Results of analysis of costs, health effects and cost-effectiveness of GDM screening in Indian and Israeli settings for a cohort of 1000 pregnant women.

	Cost-effectiveness comparison	DALYs incurred	Incremental DALYs averted	Intervention costs	Costs of illness	Total cost	Incremental cost	Incremental cost – effectiveness ratio
India – CCMH, Chennai	No GDM screening	375	n/a	$0	$241 278	$241 278		n/a
	75 g 2 h, OGTT	256	120	$259 139	$176 496	$435 636	$194 358	$1626
Israel – Clalit HMO	No GDM screening	132	n/a	$0	$620 746	$620 746		n/a
	75 g 2 h, OGTT	90	42	$259 920	$436 928	$696 848	$76 102	$1830

All costs in 2011 International dollars; costs discounted at 3% per annum.

The interventions avert an estimated 120 discounted DALYs for CCMH and 42 DALYs for Clalit. Since most PAEs resolve quickly, the number of estimated DALYs resulting from perinatal AE events is low. Most DALYs from perinatal complications are due to shoulder dystocia causing brachial plexus injury. PAEs account for 5.7% and 4.6% of the DALYs in the CCMH and Clalit settings, respectively. Thus, 95.4% of DALYs averted are due to T2DM prevention.

The cost per DALY averted is $1626 for India and $1830 for Israel.

Sensitivity analyses

We present one-way and multivariate sensitivity analyses by setting.

India

In Figure 1, each horizontal bar represents the range in cost per DALY averted across the uncertainty interval for one of 16 key inputs. The input with the greatest influence on cost-effectiveness is the cost of post-partum care; at 50–150% of the $2846 base case value, the ICER ranges from $887 to $2385 per DALY averted. The next most important influences on cost-effectiveness are the incidence of T2DM in mothers with GDM, the effectiveness of GDM-related interventions in reducing this incidence and the discount rate. If we use sensitivity and specificity values for the 75g 2 h OGTT test of 0.58 and 0.85, respectively, the CE ratio rises more than three-fold to $5365.

For every 1000 women screened for GDM, 57.5 cases of T2DM are averted in women and 29.4 in children. If we assume that only 60% of cases are prevented and the others are merely delayed by 5 years, the ICER rises to $2557 per DALY averted.

The base case assumes that GDM interventions have no effect on perinatal maternal or child mortality. If instead we assume that perinatal mortality for GDM-affected mothers and children is 50% higher than in the general population, and that screening and antenatal interventions reduced this excess mortality by 50%, the CE ratio drops to $1367 per DALY averted.

If the reduction in T2DM were only 20% (versus 40% in the base case), the cost per DALY averted rises to $3353. With no effect on T2DM incidence, the cost per DALY averted rises sharply to $37 647.

In the base case, 80% of women diagnosed with GDM receive post-partum care. If follow-up rates were 50%, the CE ratio would rise to $1810 per DALY averted.

A Monte Carlo simulation with 20 000 trials yielded a 90% confidence interval (CI) for the incremental cost-effectiveness ratio of $543–$3957 per DALY averted (Figure 2).

Israel

Similar to India, the inputs with the greatest influence on the cost-effectiveness of GDM screening and intervention are the effectiveness in reducing T2DM in mothers, the estimated incidence of T2DM in these women, and the cost of post-partum care designed to achieve the reductions. As incidence and effectiveness range from 50% to 150% of base-case values, the ICER varied from $338 per DALY averted to $4681 per DALY averted. When the cost of post-partum care is similarly varied, the ICER ranges from a small net saving to a cost of $3677 per DALY averted.

With prevalence of GDM in the screened caseload at 5% rather than the base-case value of 2.6%, the ICER becomes more favourable, at $794 per DALY averted. If the 75g 2 h OGTT test has a performance of 0.58 and 0.85, for sensitivity and specificity, respectively, the ICER rises substantially to $34 486 per DALY averted at 2.6% GDM prevalence, or $17 373 at 5% prevalence. Test performance has a greater effect at Clalit than at CCMH due to the lower GDM prevalence, leading to an unfavourable positive predictive value.

For every 1000 women screened for GDM, 4.1 cases of T2DM would be averted in mothers and 2.1 cases in children. Assuming that only 60% of cases are prevented and the rest delayed by five years, the ICER rises to $4722 per DALY averted. If the relative reduction in the risk of T2DM were

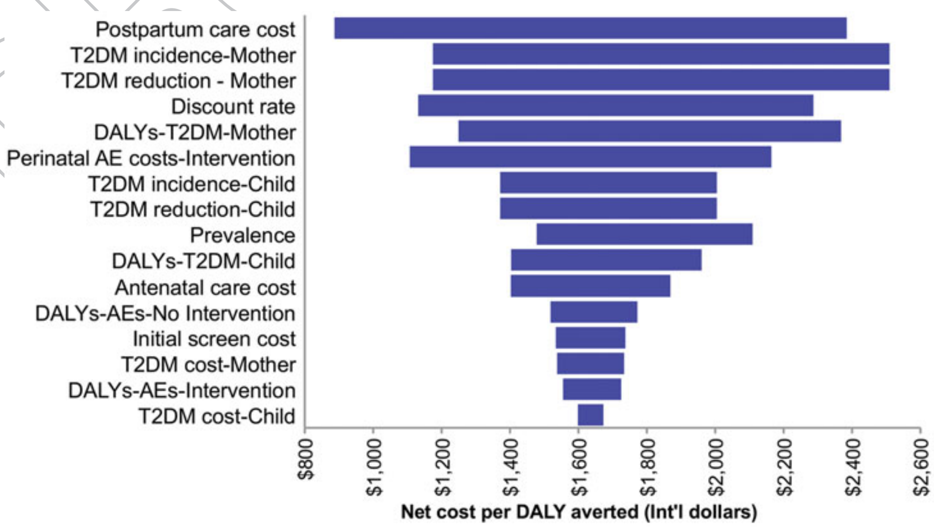

Figure 1. CCMH: tornado diagram showing one-way sensitivity of the mean ICER of 16 key inputs varied.
Source: CCMH, Chennai, India.
Inputs were varied from 50% to 150% of their respective base case value as shown in Table 1.

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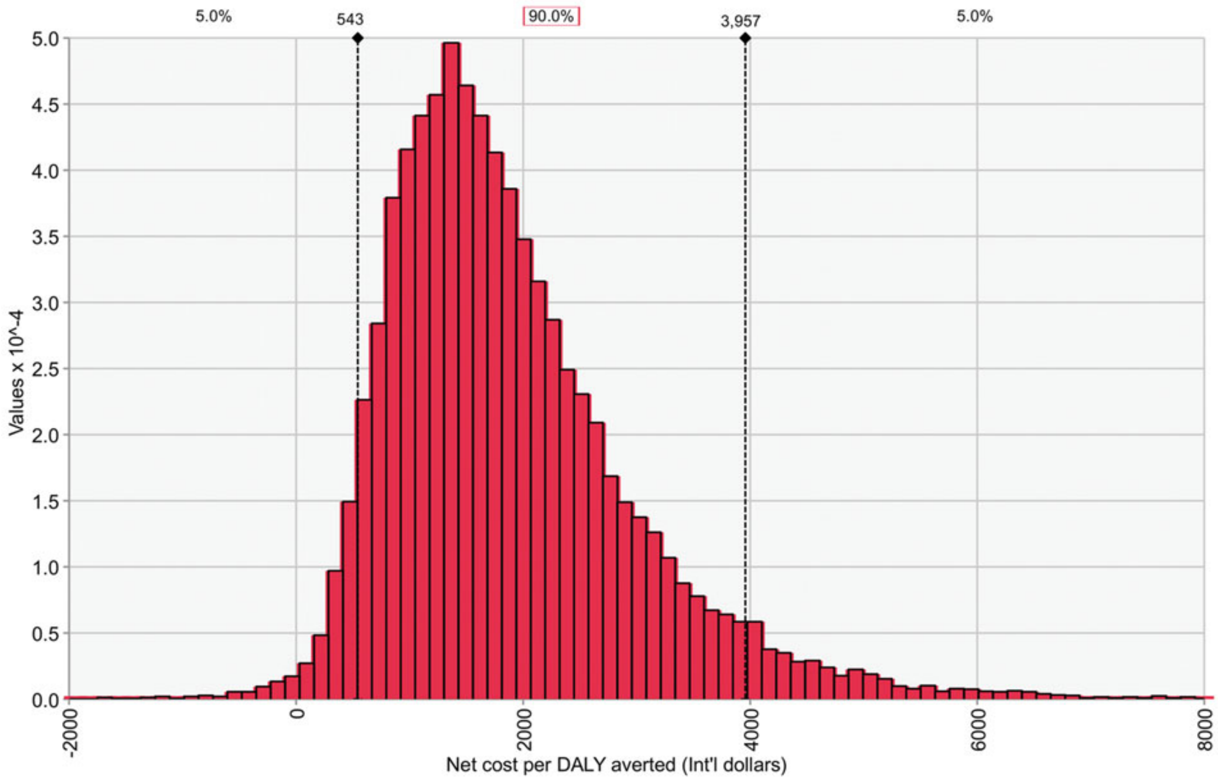

Figure 2. Results of a 20 000-trial Monte Carlo simulation.
Source: CCMH, Chennai, India.
The figure shows the distribution of ICER values and the 90% CI. The 16 input values had beta distributions with minima and maxima set at 50% and 150% of the case values shown in Table 1.

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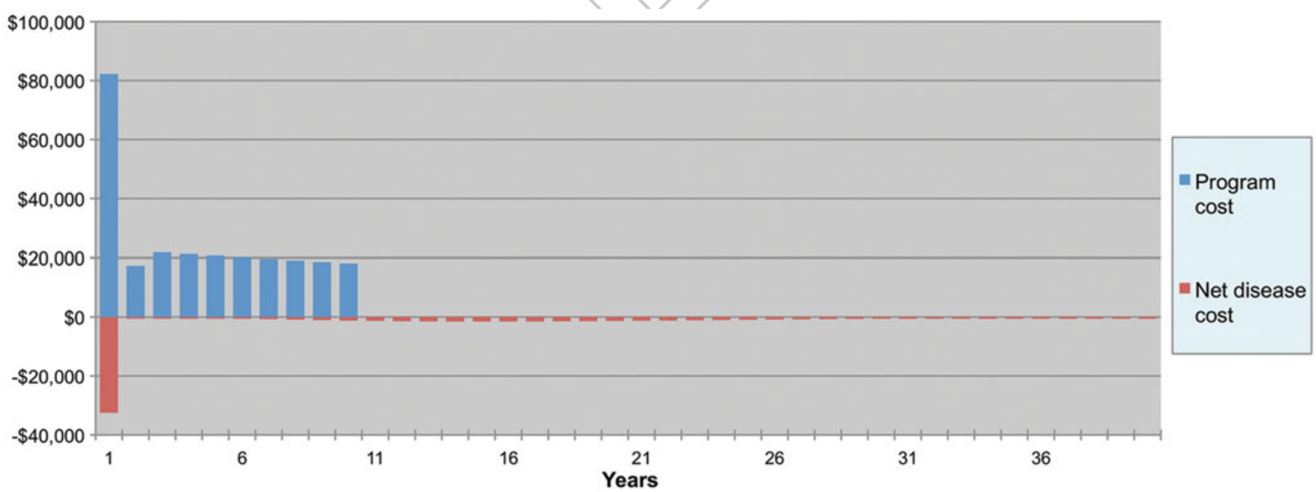

Figure 3. Annual discounted programme costs and net disease costs for one cohort of 1000 women screened.
Source: CCMH, Chennai, India.
Net disease costs calculated as intervention minus no intervention. Costs in International dollars and discounted at 3% per annum.

20%, rather than the base case 40%, the cost per DALY averted rises to $7242. With no benefit in reducing T2DM, the cost per DALY averted rises to $182 750.

In the base case, 80% of women diagnosed with GDM receive post-partum care. If follow-up rates were 50%, the ICERs would rise to $2895 per DALY averted.

A Monte Carlo simulation of 20 000 trials yielded a 90% CI for the incremental cost-effectiveness ratio of GDM screening and treatment of net savings of $1269 to a cost of $8039 per DALY averted. See Supplemental Digital Content (S1: Technical Appendix) for cost-effectiveness results assuming uniform distributions for the input values.

Time course of costs and savings

Figure 3 displays the distribution of costs over time for one cohort of women screened for GDM at CCMH (India). Programme costs are heavily concentrated in the initial years, when screening and antenatal care occur.

Figure 4 shows a simulation of cumulative costs over time for 40 annual cohorts of 1000 women. Discounted annual

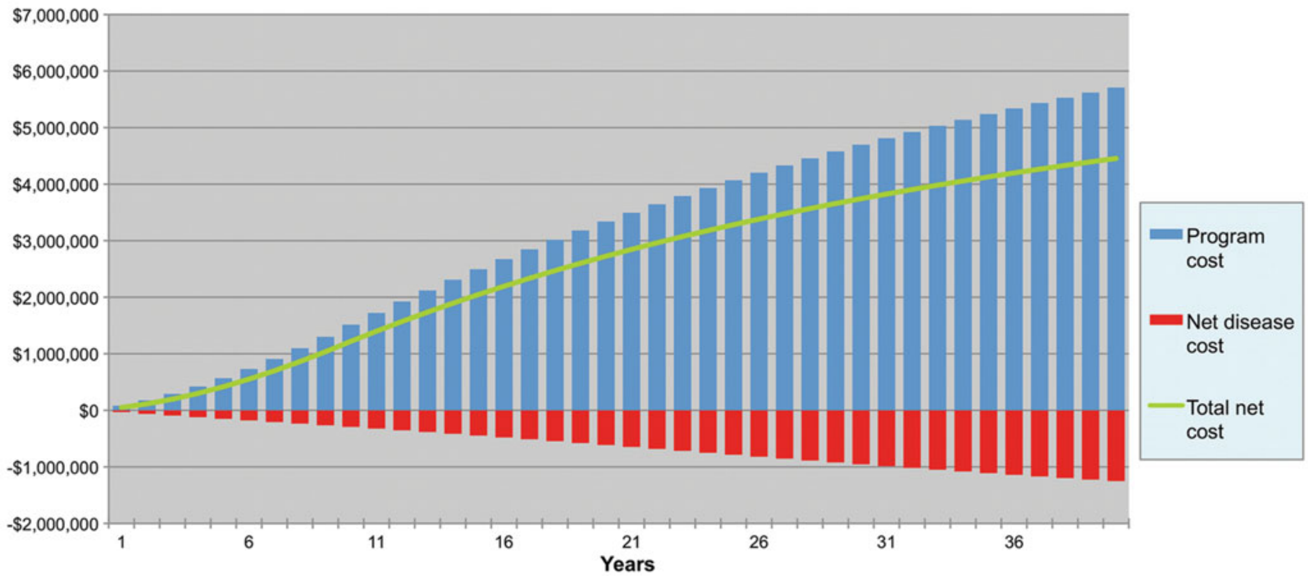

Figure 4. Annual discounted programme costs, net disease costs and total net cost for 40 GDM cohorts.
Source: CCMH, Chennai, India.
Each cohort consisted of 1000 women screened. Net disease costs calculated as intervention minus no intervention. Costs in International dollars and discounted at 3% per annum.

programme costs plateau in year 40 at $5.7 million and total net costs reach $4.5 million at year 40.

Discussion

This study estimated that screening and treating gestational diabetes, considering adverse perinatal events and future diabetes, has an incremental cost-effectiveness of $1626 per DALY averted for a general hospital in India, and $1830 per DALY averted for an HMO in Israel. The World Health Organization has proposed that interventions costing less than the per capita GDP of a country be deemed ''highly cost-effective'', and those costing up to three times per-capita GDP ''cost-effective'' [37]. Since the 2010 per-capita GDP of India and Israel are $3500 and $29 800 [38], respectively, the interventions are ''highly cost-effective''.

In both settings, cost-effectiveness was sensitive to the incidence of T2DM and to the costs and effectiveness of post-partum intervention. This poses a practical problem. In contrast to quick and inexpensive screening, effective post-partum care may require 5–10 years of follow-up. For this reason, it is the most costly portion of the three aspects of GDM intervention – screening, antenatal care and post-partum management. Programme managers are challenged to control costs without compromising benefits. The IDPP and DPP studies have documented the components and associated costs of effective post-partum management. These studies provide an evidence-based template on which other such programmes can be designed or adapted [39,40].

This study has a number of limitations. First, we had imperfect or imprecise data on important inputs such as the lifetime discounted cost of treating T2DM and the DALYs associated with PAEs and T2DM. Second, the need to extrapolate health care costs between countries via national per-capita health spending levels is a serviceable but second-best expedience in the absence of a full set of cost data for GDM and T2DM. Third, the WHO standards for cost-effectiveness are based only on the relevant nation's per-capita GDP. These thresholds do not account for the fact that even in the case of ''very cost-effective'' options, there may be better uses of available resources. Finally, we do not account for the association between untreated GDM and the elevated risk of GDM in future pregnancies [41].

Our findings are consistent with the WHO standard for ''very cost-effective'' across all of the inputs for Israel (Clalit) and across most of the plausible sets of input values for India (DCRI). Since these countries differ in GDM prevalence, per-capita health spending and per-capita GDP, GDM interventions may be cost-effective in many other settings. Screening and subsequent management of GDM presents an important opportunity to reduce T2DM and its attendant societal costs.

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Declaration of interest

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