

BMJ Open Cost-effectiveness of the New Zealand diabetes in pregnancy guideline screening recommendations

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ABSTRACT

Objective: To compare the cost-effectiveness of 2 possible screening strategies for gestational diabetes mellitus (GDM) from the perspective of the New Zealand health system, developed as part of a gestational diabetes guideline.

Design: A decision analytic model was built comparing 2-step screening (glycated haemoglobin (HbA1c) test at first booking and a 2 h 75 g oral glucose tolerance test (OGTT) as a single test at 24–28 weeks) with 3-step screening (HbA1c test at first booking and a 1 h glucose challenge test (GCT) followed by a 2 h 75 g OGTT when indicated from 24–28 weeks) using a 9-month time horizon.

Setting: A hypothetical cohort of 62 000 pregnant women in New Zealand.

Methods: Probabilities, costs and benefits were derived from the literature, and supplementary data was obtained from National Women's Annual Clinical Reports. Main outcome measures, screening and treatment costs (NZ\$2013) and effect on health outcomes (incidence of complications).

Results: The total cost for both strategies under baseline assumptions shows that the 2-step screening strategy would cost NZ\$1.38 m more than the 3-step screening strategy overall. The additional cost per case detected was NZ\$12 460 per case. The model found that the 2-step screening strategy identifies 12 more women with diabetes and 111 more women with GDM when compared against the 3-step screening strategy. We assessed the effect of changing the sensitivity and specificity of the OGTT. The baseline model assumed that the 2 h 75 g OGTT has a sensitivity and specificity of 95%. The 2-step strategy becomes more cost-effective when the diagnostic accuracy measures are improved.

Conclusions: Adopting a 2-step strategy would moderately increase the number of GDM cases detected at the same time as moderately increasing the number of women with false negatives at a significant cost to the health system. Further evidence on the benefits of the 2 different approaches would be welcome.

BACKGROUND

Gestational diabetes mellitus (GDM) is a form of diabetes that occurs in pregnancy. Although the condition usually resolves

Strengths and limitations of this study

- This study used a whole-system approach as all women are offered the screen, and all women may have benefits or harms, and will incur costs.
- We have included all relevant outcomes, and we have considered a wide range of costs.
- We used nationally representative data sources to increase generalisability, and performed sensitivity analysis to quantify the uncertainty in our cost-effectiveness estimates.
- The New Zealand health system perspective may limit the applicability of the findings to other country settings.

following birth, it is associated with a risk of complications during the pregnancy such as preeclampsia and caesarean section.^{1 2} Babies born to mothers with GDM are at increased risk of being large for gestational age (potentially leading to delivery complications), having low blood sugar, and respiratory distress syndrome.³ Both the mother and baby are also at increased risk of developing type 2 diabetes (T2D) later in life.^{3 4} There is strong evidence suggesting a clear benefit in maternal and infant outcomes when women with GDM are treated with dietary and lifestyle advice.^{5 6} There is also evidence that oral hypoglycaemics and/or insulin are effective for women with poor glucose control.⁵

GDM is a growing problem in New Zealand with increasing rates over the past 5 years.⁶ Data presented at the New Zealand Society for the Study of Diabetes Conference reported that the number of pregnancies associated with GDM has increased from 1.3% in 2001 to 2% in 2006, and to 4.9% in 2012. The highest prevalence is in the Auckland region (8%).⁶

There are considerable variations across New Zealand in the management of women with diabetes in pregnancy. There are also variations in the screening for diabetes in spite of national guidance for GDM in pregnancy published in 2008 that recommended

a 2-step strategy at 24–28 weeks of glucose challenge test (GCT), followed by an oral glucose tolerance test (OGTT) if the GCT is abnormal (≥ 7.8 to < 11.0 mmol/L).⁷ There are also a range of different international diagnostic criteria being used that means the observed prevalence of hyperglycaemia in pregnancy can range from 7.9% to 24.9% in the same group of women using the same 2 h, 75 g OGTT.⁸

In 2010, the International Association of Diabetes in Pregnancy Groups (IADPSG) proposed new diagnostic criteria.⁹ These suggested different clinical thresholds for the detection of diabetes in pregnancy and, importantly, recommended relying on the result of a single test (plasma glucose concentration equal to or exceeding the thresholds of 5.1, 10.0 and 8.5 mmol/L for fasting, 1 and 2 h postglucose load glucose values, respectively) rather than the standard 2-step approach widely used in New Zealand. Women are usually offered a 50 g, 1 h oral GCT at 24–28 weeks followed by a 75 g, 2 h OGTT for those who have had a positive result (plasma glucose ≥ 7.8 to < 11.0 mmol/L) from the initial test. The proposed diagnostic criteria created controversy as it would lead to a major rise in the prevalence of GDM, potentially adding to the cost of care for diagnosed pregnant women.

NEW ZEALAND GESTATIONAL DIABETES GUIDELINE

Increasing prevalence of GDM, the benefits of treatment, and variations in practice nationally and internationally led the New Zealand Ministry of Health to commission the development of a clinical practice guideline ('Screening, Diagnosis and Management of GDM in New Zealand: A Clinical Practice Guideline'⁶). For further details of the guideline methodology there is a link to the full guideline contained in the reference list. A quick reference guide is also available for download (see 'Diabetes in pregnancy: Quick reference guide for health professionals').

The Guideline Development Team considered five screening strategies, including the current screening approach used in New Zealand. The Guideline Development Team noted that although there was some observational data that suggested that the IADPSG criteria may identify women and infants with worse outcomes who may benefit from treatment, there was no randomised controlled trial evidence to support this.

After a review of all the available evidence, a series of recommendations and good practice points were

developed.⁶ The Guideline Development Team recommended at the first antenatal booking (providing it was < 20 weeks):

- ▶ Offer a glycated haemoglobin (HbA1c) test to all pregnant women not known to have diabetes in order to detect undiagnosed T2D (HbA1c > 50 mmol/L) and prediabetes (HbA1c 41–49 mmol/L).

The Guideline Development Team recommended at 24–28 weeks:

- ▶ Offer all women not previously diagnosed with diabetes who are at high risk of GDM (HbA1c 41–49,) a 2 h, 75 g OGTT.
 - If fasting glucose ≥ 5.5 mmol/L or 2 h value ≥ 9 mmol/L, refer to diabetes in pregnancy clinic.
- ▶ Offer all other women a 1 h, 50 g, oral GCT.
 - If glucose ≥ 11.1 mmol/L, refer directly to diabetes in pregnancy clinic without further testing.
 - If glucose ≥ 7.8 to < 11.0 mmol/L, then arrange a 75 g, 2 h OGTT without delay.⁶

Current screening practice differs widely between regional centres, and it was not feasible to identify or consider all strategies in the model. We developed a decision analytical model to evaluate the cost-effectiveness of two screening strategies, namely the 2-step strategy (eventually not recommended) and the 3-step strategy that was recommended by the Guideline Development Team.

METHODS

We developed a decision tree model with a 9-month time horizon that compared the expected costs and health outcomes of two different screening strategies from the health system perspective using Microsoft Excel. The two strategies are outlined in [table 1](#).

We have undertaken a whole-system approach, and therefore the model evaluated the benefits, harms and costs of an annual cohort of 62 000 pregnant women (annual number of births in 2011),¹⁰ but not including women with known diabetes, assigning women to one of six categories:

- ▶ True positive (GDM): women correctly tested positive for GDM.
- ▶ True positive (T2D): women correctly tested positive for T2D.
- ▶ True negative (non-GDM/non-T2D): women correctly tested negative for GDM and previously undiagnosed T2D.

Table 1 Screening and diagnostic strategies

Strategy	Screening test First booking	Screening test 24–28 weeks	Diagnostic test 24–28 weeks	Type 2 postnatal screening test
2-step	HbA1c	–	OGTT All women HbA1c < 50 mmol/L	HbA1c
3-step	HbA1c	GCT All women HbA1c < 40 mmol/L	OGTT All women HbA1c 41–49 mmol/L	HbA1c

GCT, 1 h 50 g glucose challenge test; HbA1c, glycated haemoglobin; OGTT, 2 h 75 g oral glucose tolerance test.

- ▶ False positive (non-GDM/non-T2D): women without GDM and T2D who incorrectly test positive.
- ▶ False negative (GDM): women with GDM who incorrectly test negative or who are not tested.
- ▶ False negative (T2D): women with T2D who incorrectly test negative or who are not tested.

Attached to these categories are various treatment costs and health outcome cost probabilities (table 2). Regardless of which category a woman is in, she was considered to be at risk for particular maternal outcomes, and to incur both screening and treatment costs. A false negative woman, untreated for GDM, has a higher risk of complications than a true positive woman being treated for GDM. For example a true positive (GDM) woman has a lower risk of preeclampsia (0.12) compared to a false negative (GDM) woman (0.18).⁶ This also applies to neonatal outcomes used in the model.

Maternal outcomes included: preeclampsia, induction of labour, caesarean section and vaginal birth. Neonatal outcomes included: perinatal death/stillbirth, shoulder dystocia, hyperbilirubinaemia, and neonatal intensive care admission. Data from systematic reviews conducted as part of a New Zealand guideline 'Screening, Diagnosis and Management of gestational diabetes in New Zealand: A Clinical Practice Guideline' were used to provide estimates of the effect of diagnosing and treating diabetes on health outcomes, dependant on the group (GDM, non-GDM, or T2D).⁶ If systematic review data was not available, National Women's Annual Clinical Reports,¹¹ other published literature, and the expert opinion of the Guideline Development Team were utilised.

Screening strategies

Both strategies begin by offering all women not known to have diabetes an HbA1c screening test at the first antenatal appointment, providing the visit was before 20 weeks gestation. This test is used to identify women with undiagnosed T2D (≥ 50 mmol/L) and prediabetes (41–49 mmol/L).

2-step screening strategy

At 24–28 weeks, the 2-step strategy offers all women a 2 h OGTT as a single test (cut-off values—fasting 5.5 mmol/L or 2 h value ≥ 9.0 mmol/L).

3-step screening strategy

Women with an HbA1c between 41 and 49 mmol/L from the screening test at booking before 20 weeks are offered a 2 h OGTT as they are at increased risk of GDM. All other women are offered a 1 h 50 g oral GCT at 24–28 weeks gestation to screen for GDM. If this test is positive (if glucose value ≥ 7.8 to 11.0 mmol/L), a further 2 h 75 g OGTT is offered to diagnose GDM. If the result is ≥ 11.1 mmol/L, the women are referred directly to a clinic for diabetes in pregnancy.

Both strategies offer all women with GDM an HbA1c test 12 weeks postnatally to identify women with undiagnosed T2D.

Decision tree

The basic structure of the 2-step decision tree used in developing the model is shown in online supplementary figure S1. Women with previously undiagnosed T2D (≥ 50 mmol/L) testing positive with the HbA1c test are included in the model but do not continue on to the subsequent screening branches of the tree. The decision tree separates pregnant women who undertake screening from those who are not screened. The 'not-screened' arm includes women who have either presented late for antenatal care or refused screening. The screening part of the model includes diagnostic accuracy measures to identify the likely numbers of false positive and false negative test results. This makes it necessary to divide the women into 'GDM' and 'No GDM' categories, using prevalence estimates, before the result of the test is known. The model endpoint estimates the number of women that will be identified as having GDM, prediabetes and T2D. The labels 'true positive', 'false positive', 'true negative' and 'false negative' are attached at this point, although some women will not have been tested for diabetes.

Prevalence data

The prevalence of GDM and prediabetes varies within different regions of New Zealand, and the prevalence rate is also affected by local screening practices. Prevalence of GDM has been reported to range from 1.4 to 8.2 across the country, with the highest rates reported in the most populated areas.⁶ Therefore, an overall estimated national average of 6.5% prevalence of GDM was assumed. Data published in 2013 used information from the 2008/2009 New Zealand Adult Nutrition Survey to identify the prevalence of diagnosed and undiagnosed diabetes and prediabetes in (non-pregnant) adults. The New Zealand prevalence of prediabetes in women, using self-reported diabetes, and the 2010 American Diabetes Association cut-off values for HbA1c, was recently reported to be 8.5%.¹² We reduced this rate to 7% to allow for the lower cut-off values that were applied in this survey.

We estimated that 80% of women with prediabetes would be diagnosed with GDM.¹³ As a result of this high rate of GDM diagnosis among women with prediabetes, the remaining cohort of women with normal glucose tolerance was left with an estimated GDM diagnosis rate of 1%. The prevalence of previously undiagnosed T2D in women is reported to be 1.1%.¹² This rate was multiplied by a sensitivity of the HbA1c test of 40%,¹⁴ reducing the rate to 0.4%. This means that less than 1% (n=409) of the women going through the model will have undetected T2D. This was considered to be an acceptably small number that was unlikely to substantially affect the validity of the model (see online supplementary table S1 for full details of diagnostic accuracy and prevalence estimates).

Table 2 Probabilities, costs and outcomes used in the model

Parameter	Costs												
	FN PD/GDM		TP PD/GDM		FN T2D		TP T2D		TN ALL		FP PD/GDM		
		Prob	Cost	Prob	Cost	Prob	Cost	Prob	Cost	Prob	Cost	Prob	Cost
GDM treatment													
Diabetes clinic	\$300 per clinic												
Insulin	\$3 per day												
Blood glucose monitor	\$20												
Test strips	\$11 per 50												
Metformin	\$0.06 per day												
Ultrasound	\$140 per US												
Total cost of treatment													
Health outcomes													
Preeclampsia	\$8144	0.12	\$1013	0.07	\$569	0.20	\$1629	0.02	\$181	0.03	\$236	0.03	\$236
Induction of labour	\$58	0.29	\$17	0.34	\$20	0.56	\$33	0.60	\$35	0.21	\$12	0.21	\$12
Caesarean section (excluding preeclampsia)	\$6398	0.27	\$1727	0.25	\$1600	0.40	\$2559	0.11	\$711	0.21	\$1344	0.21	\$1344
Vaginal delivery (excluding preeclampsia)	\$2260	0.63	\$1424	0.71	\$1593	0.60	\$1356	0.89	\$2011	0.76	\$1718	0.76	\$1718
Shoulder dystocia	\$1351	0.04	\$49	0.01	\$18	0.15	\$209	0.15	\$203	0.06	\$81	0.06	\$81
Perinatal death/stillbirth	\$7383	0.005	\$34	0.00	\$	0.13	\$984	0.00	\$	0.00	\$	0.00	\$
Hyperbilirubinaemia/phototherapy	\$1125	0.10	\$116	0.08	\$86	0.09	\$105	0.05	\$61	0.12	\$135	0.12	\$135
Admitted to NICU	\$5010	0.14	\$701	0.16	\$782	0.21	\$1068	0.24	\$1190	0.09	\$465	0.09	\$465

All costs are expressed as \$0.00k.

FN, false negative; FP, false positive; GDM, gestational diabetes mellitus; NICU, neonatal intensive care; PD, prediabetes; Prob, probabilities; T2D, type 2 diabetes; TN, true negative; TP, true positive; US, ultrasound.

Screening and treatment assumptions

A New Zealand report found that 61% of women would accept the 1 h GCT.¹⁵ This study focussed on a comparatively socially deprived area where 38.4% of women either engage with antenatal services late (after 18 weeks) or do not engage with maternity services at all.¹⁶ We estimated that the national uptake of GCT screening would be higher (80% test acceptance). Women receiving a positive result from the 1 h GCT were also expected to be more willing to undertake the 2 h OGTT test (90% test acceptance). The rate of postnatal glucose tolerance testing among women with GDM averages 70% over the previous 5 years.¹¹ It was assumed that the postnatal type 2 screening HbA1c test acceptance rate would be higher due to the more convenient nature of the test. We assumed that women would not be offered a postnatal type 2 screening test if they were diagnosed as having prediabetes without a GDM diagnosis. Women diagnosed with T2D as a result of the HbA1c screening test or the 1 h GCT, were also assumed not to need any further testing. The proportion of women that was estimated not to undertake any GDM screening was the same in both strategies (19%). The predictive value of a screening or diagnostic test is determined by the test's sensitivity and specificity, and by the prevalence of GDM. We assume the 2 h 75 g OGTT has a sensitivity and specificity of 95%. Although the OGTT is considered the 'gold standard diagnostic test', it is generally accepted that it does not have perfect sensitivity and specificity,¹⁷ and reproducibility of the test is poor.¹⁸

We estimated that women with GDM would need four multidisciplinary clinic visits after diagnosis, and women with T2D would require 10 (personal communication. Email from ADHB Charge Midwife confirmed the costs of obstetric clinics and ultrasounds, September 2013). These visits include nutritional counselling, instruction and supplies for home glucose monitoring. Women classified as false positive were assumed to have fewer clinic visits and no diabetes medication costs, because it was considered that treatment would most likely discontinue once normal blood glucose measures were detected. Estimates of metformin and insulin use for women with GDM were derived from metformin in a GDM cohort study.¹⁹ Fifty per cent of the women diagnosed with GDM were estimated to require insulin, and 38% metformin. It was assumed that all the women with T2D would be treated with insulin at an average of 100 international units per day. The cost of one pregnancy ultrasound (NZ\$140) was included for all women. Women with T2D and GDM were assumed to have two ultrasounds (see online supplementary table S2).

Baseline probabilities: maternal outcomes

Preeclampsia, induction of labour, caesarean section and vaginal delivery

The baseline probabilities for preeclampsia, induction of labour, caesarean section and vaginal delivery for women with GDM were derived directly from a recently

updated systematic review of combined diet and lifestyle interventions for GDM.⁵ The interventions include any treatment package for GDM such as a programme of diet and/or exercise, other education media and supplementary pharmacological intervention (if required) compared with usual or standard care.⁶

The baseline probabilities for preeclampsia, caesarean section, and vaginal delivery for women with T2D were derived from a 2012 systematic review of different intensities of glycaemic control for pregnant women with diabetes.²⁰ Data from a recently published New Zealand Maternity Report were used to obtain rates for caesarean section and vaginal delivery for women without diabetes.¹⁰ All probability rates for caesarean section and vaginal delivery were adjusted to avoid double counting the costs of these outcomes for women with preeclampsia.

National Women's data was used to provide induction of labour probabilities for women treated with T2D (true positive T2D).¹¹ Induction of labour probabilities for women with untreated T2D (false negative T2D) was difficult to source resulting in the use of National Women's data reporting on women postnatally diagnosed with T2D.¹¹ These women were most likely treated for GDM. National Women's data was also used to provide preeclampsia and induction of labour probabilities for women without diabetes¹¹ (see online supplementary table S2).

Baseline probabilities: neonatal outcomes

Shoulder dystocia, perinatal death/stillbirth, hyperbilirubinaemia and admission to neonatal intensive care

The baseline probabilities for shoulder dystocia and hyperbilirubinaemia in infants of women with GDM were taken directly from a recently updated systematic review described above.⁵ The probabilities for shoulder dystocia in infants of women with T2D and women without diabetes were taken from a population-based study of 11 000 deliveries in Israel.²¹ National Women's Health reports were used to derive probabilities of shoulder dystocia for the undiagnosed T2D group using the proportional difference in large for gestational age infants between these groups.

Perinatal death/stillbirth probabilities for infants of women with T2D were obtained from a systematic review comparing tight-moderate versus loose-glycaemic control for pregnant women with T2D.²⁰ The remaining perinatal death probabilities were obtained from a New Zealand perinatal mortality report.²²

The baseline probabilities for hyperbilirubinaemia in infants of women with T2D were taken from RCT data from New Zealand and Australian women.²³ The hyperbilirubinaemia rates for infants of women without diabetes were derived from National Women's reports.¹¹

Baseline probabilities for neonatal intensive care admission in infants of women with GDM were taken directly from metformin in a GDM prospective study.¹⁹ National Women's data was used to provide probabilities

of neonatal intensive care admission in infants of women with T2D and women without diabetes¹¹ (see online supplementary table S2).

Costs

All costs are in 2013 New Zealand dollars. The costs of most health outcomes were based on the average cost determined using weighted inlier equivalent separation data.²⁴ Prices were inflated to 2013 values according to consumer price index tables from Statistics New Zealand. We did not apply discounting because the time horizon of the analysis was less than 1 year. The costs of birth were categorised into three groups irrespective of the mode of delivery. Preeclampsia was the most expensive followed by caesarean section and then vaginal delivery. The cost of preeclampsia was based on the average costs for admissions with a diagnosis of preeclampsia (personal communication. Email from ADHB data analyst, September 2013). The cost of induction of labour was derived from a cost-effectiveness analysis undertaken in the UK.⁴ This price was converted from UK pounds using purchasing power parities and inflated as appropriate to the price year 2012/2013. The costs of insulin, blood glucose monitoring and test strips were taken from the New Zealand Pharmaceutical Schedule.²⁵ The estimated cost of shoulder dystocia amounted to NZ\$1350. This amount did not include the cost associated with potential damage to the perineum and any subsequent surgery. The risk of brain injury to an infant during delivery was not included in the model. The costs of the HbA1c screening test, the 1 h GCT and the 2 h OGTT were obtained from the Ministry of Health and an Auckland-based laboratory (personal communication. Email from senior project manager at the Ministry of Health, and a phone call to the ADHB laboratory confirmed the cost of diagnostic tests, November 2013). Full details of the methods for deriving costs are given in online supplementary table S2.

RESULTS

The results from the baseline model are given based on a population of 62 000 pregnant women, and assume an overall prevalence of GDM of 6.5% (table 3). The total cost for both strategies under baseline assumptions shows that the 2-step screening strategy would cost NZ \$1.38 m more than the 3-step screening strategy overall. The additional cost per case detected is NZ\$12 460. The model found that the 2-step screening strategy identifies 12 more women with T2D and 111 more women with GDM when compared against the 3-step screening strategy. The 2-step strategy results in 111 fewer women not being diagnosed with GDM (false negatives) and 1220 more women being incorrectly diagnosed with GDM (false positives). Adopting a 2-step strategy would moderately increase the number of GDM cases detected at the same time as moderately increasing the number of women with false negatives at a significant cost to the health system.

Table 3 Baseline results

Costs	2-Step				3-Step				Total
	TP	FP	FN	TN	TP	FP	FN	TN	
Screening	0.213	0.096	0.012	2.025	0.212	0.043	0.014	1.561	1.832
Treatment	7.358	1.733	0.084	7.736	7.115	0.830	84.112	7.906	15.954
Health outcomes	17.640	9.346	3.146	220.496	17.069	4.477	3.805	225.364	250.629
Total	25.212	11.176	3.242	230.258	24.398	5.351	3.921	234.832	268.504
Outcomes (number of women)									
New T2D diagnoses	322	0	33	0	310	0	45	0	355
Missed T2D diagnoses	0	0	409	0	0	0	409	0	409
Hyperglycaemia (prediabetes and gestational diabetes)	3477	2342	568	55 258	3366	1122	679	56 478	61 645

All 62 000 annual births are represented. All costs expressed as \$0.000m. TP, true positive; FP, false positive; FN, false negative; TN, true negative; T2D, type 2 diabetes.

The total screening cost was NZ\$2.35 m for the 2-step strategy versus NZ\$1.83 m for the 3-step strategy, a marginal cost difference of NZ\$515 845. The total cost of treatment was NZ\$16.9 m for the 2-step strategy versus NZ\$15.9 m for the 3-step strategy, a marginal cost difference of NZ\$957 251. The total cost of health outcomes was NZ\$250.50 m versus NZ\$250.58 m for the 3-step strategy, a marginal cost difference of NZ\$88 423.

Sensitivity analysis

The model was examined at different GDM prevalence rates. A higher overall prevalence of GDM was found to favour the 2-step screening strategy. If the prevalence of GDM is increased to 10%, the additional cost per case detected is reduced to NZ\$5161. If the overall prevalence of GDM is reduced to 5%, the additional cost per case detected is increased to NZ\$233 616. We also assessed the effect of changing the sensitivity and specificity of the OGTT (table 4). The baseline model assumed that the 2 h 75 g OGTT has a sensitivity and specificity of 95%. The 2-step strategy becomes more cost-effective when the diagnostic accuracy measures are improved. An OGTT sensitivity and specificity of 98% reduces the overall total cost difference to NZ\$695 281, making the cost per additional case detected NZ\$5919. We also assessed the impact of reducing the test acceptance in women who present after 20 weeks of pregnancy, and increasing the likelihood that these women have GDM. This did not impact the overall results significantly. Similarly, changing the costs of health outcomes by 20% and increasing the test acceptance to 90% did not significantly alter the results. Reducing the estimated rate of GDM diagnosis in women with prediabetes, and increasing the rate of GDM diagnosis in women with normal glucose tolerance did not significantly alter the overall results, making the 2-step strategy only slightly less expensive.

DISCUSSION

We have reported a cost-effectiveness analysis of two different strategies for screening pregnant women in order to identify women with GDM in pregnancy. A 2-step strategy of an HbA1c followed by an OGTT was compared with a 3-step strategy of an HbA1c and a GCT followed by an OGTT, and was associated with a small increase in the overall numbers of women with GDM in pregnancy being identified, but would also incur significant costs to the New Zealand healthcare system. If the prevalence of GDM were higher than predicted, then the costs would decrease.

We consider that our cost-effectiveness model has merit. We have taken a whole-system approach, as all women are offered the screen, and all women may have benefits or harms, and will incur costs. We have included all relevant outcomes and we have considered a wide range of costs. We have used sensitivity analysis to explore different prevalences, sensitivities and specificities, test acceptance and changing costs of health outcomes.

As with any cost-effectiveness analysis, there are several limitations to this study. We could not find any data reporting on the sensitivity and specificity of the HbA1c test in determining a prediabetes diagnosis. This means that some of the women treated as having prediabetes may have had normal glucose tolerance or T2D. These women (90%) will most likely undertake further screening tests during the course of their pregnancy. Similarly, we could not find data reporting the sensitivity and specificity of the GCT for women with prediabetes. The same rates were applied (88% and 84%) regardless of whether the woman had prediabetes or normal glucose tolerance. The model attaches the same outcome probabilities and costs to women with prediabetes (HbA1c 41–49 mmol/L) that have not been diagnosed with GDM as women with an HbA1c below 40 mmol/L (normal glucose tolerance). This may have underestimated the cost of treatment and affected the reliability

Table 4 Sensitivity analysis

GDM diagnoses (numbers of women)		Total cost	Total cost	Cost difference	Cost difference
2-Step	3-Step	2-Step	3-Step	(per case detected)	(total cost)
6.5% GDM prevalence (baseline)					
3477	3366	\$269.889	\$268.504	\$0.012	−\$1.384
5% GDM prevalence					
2841	2777	\$266.732	\$266.563	\$0.002	−\$0.169
10% GDM prevalence					
5395	5064	\$273.148	\$272.672	\$0.001	−\$0.476
OGTT S and S 90%					
3301	3201	\$271.063	\$268.529	\$0.025	−\$2.533
OGTT S and S 98%					
3582	3465	\$269.185	\$268.490	\$0.005	−\$0.695
OGTT S and S 100%					
3653	3531	\$268.715	\$268.480	\$0.001	−\$0.235

GDM prevalence and diagnostic accuracy of the oral glucose tolerance test. All costs are expressed as \$0.000m. GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test; S and S, sensitivity and specificity.

of the baseline estimates of health outcomes for this group (approximately 1.5% of women being modelled).

Our study did not analyse the cost-effectiveness of screening over a lifetime, the analysis was also limited to the time frame from the beginning of the pregnancy to the 12-week postnatal visit. The model did not include the costs to women and families such as time off work and travel to appointments because it was modelled from the health system perspective. Some women may find the tests inconvenient and unpleasant. Women identified as being at higher risk, either by risk factors or a previous screening test, may be more likely to accept a screening test. However, risk-based screening has the potential to miss up to one-third of women with GDM.²⁶ Universal screening will identify more women with GDM than risk factor-based screening, but the effect of subsequent management on health outcomes is unclear.

A clinical trial is currently underway to compare whether the IADPSG criteria, compared with the current Ministry of Health recommended criteria used in New Zealand, reduces the risk of the infant being large for gestational age, and significant perinatal morbidity without increased maternal physical and psychological risk, and to determine cost consequences.²⁷

The Guideline Development Team took into consideration the high prevalence of previously undiagnosed diabetes and GDM in certain areas of New Zealand, and the high chance that many women would have one or more risk factors. It decided that using universal screening at booking would be more appropriate in the New Zealand context than risk-based screening in early pregnancy.

The Guideline Development Team accepted that HbA1c is used to diagnose diabetes in the non-pregnant population and, although the evidence is mostly indirect, it felt that there was sufficient emerging evidence to support the use of HbA1c in early pregnancy for the detection of probable undiagnosed diabetes and prediabetes. Further research is required to determine whether the HbA1c test, universally performed during the first part of the pregnancy, is cost-effective.

Our analysis has been preceded by several other recent reports comparing different screening strategies. In the USA, the lifetime cost-effectiveness of three strategies to identify GDM was analysed—no screening, current screening practice (1 h 50 g GCT followed by 3 h 100 g OGTT when indicated), or screening practice proposed by the IADPSG.²⁸ This study found that for any screening strategy to be cost-effective, long-term postpartum risk reduction measures needed to be successful. Another cost analysis study from the USA investigated the cost-effectiveness of GDM screening using the IADPSG guidelines from a societal perspective.²⁹ This model compared routine screening with a 2 h OGTT versus the 1 h GCT. Screening at 24–28 weeks gestational age under the new IADPSG guidelines with the 2 h OGTT was found to be expensive but cost-effective in improving maternal and neonatal outcomes.

The National Institute of Health and Clinical Excellence developed a single cost-effectiveness model addressing screening, diagnosis and treatment for GDM.⁴ All screening methods, including risk factor-based screening, screening blood tests and universal diagnostic tests, were considered (in isolation and combinations of tests). They proposed that a strategy of offering women at increased risk a 1-step diagnostic test would be cost-effective when compared with no screening and/or treatment.

The results of international cost-effectiveness studies are not always immediately generalisable to the New Zealand context. For example, the Guideline Development Team considered offering all high-risk women a 1-step screening, but as we had recommended that all women are screened who book before 20 weeks with HbA1c, then the focus was shifted from high risk because of ethnicity or body mass index to those at high risk because they had prediabetes according to their HbA1c at booking. Furthermore, in some regions of the country, we recognised that high risk would apply to more than 50% of the population of pregnant women (on the basis of ethnicity and BMI), and that adding a simple blood test to the booking schedule would make more sense and improve the likelihood of the test being complete and would avoid stigmatisation.

CONCLUSIONS

We developed a decision tree model that compared the expected costs and health outcomes of two possible screening strategies. The results have shown that adopting a 2-step screening strategy (without lowering the diagnostic thresholds) will result in a small number of additional women being diagnosed with GDM at considerable cost to the health system. The additional cost of the 2-step approach as compared with the 3-step approach (as adopted by the New Zealand Guidelines for Gestational Diabetes published in 2014) was an additional NZ\$12 460 per case. The prevalence of GDM and the diagnostic accuracy of the screening tests were shown to be important variables in determining the most cost-effective approach.

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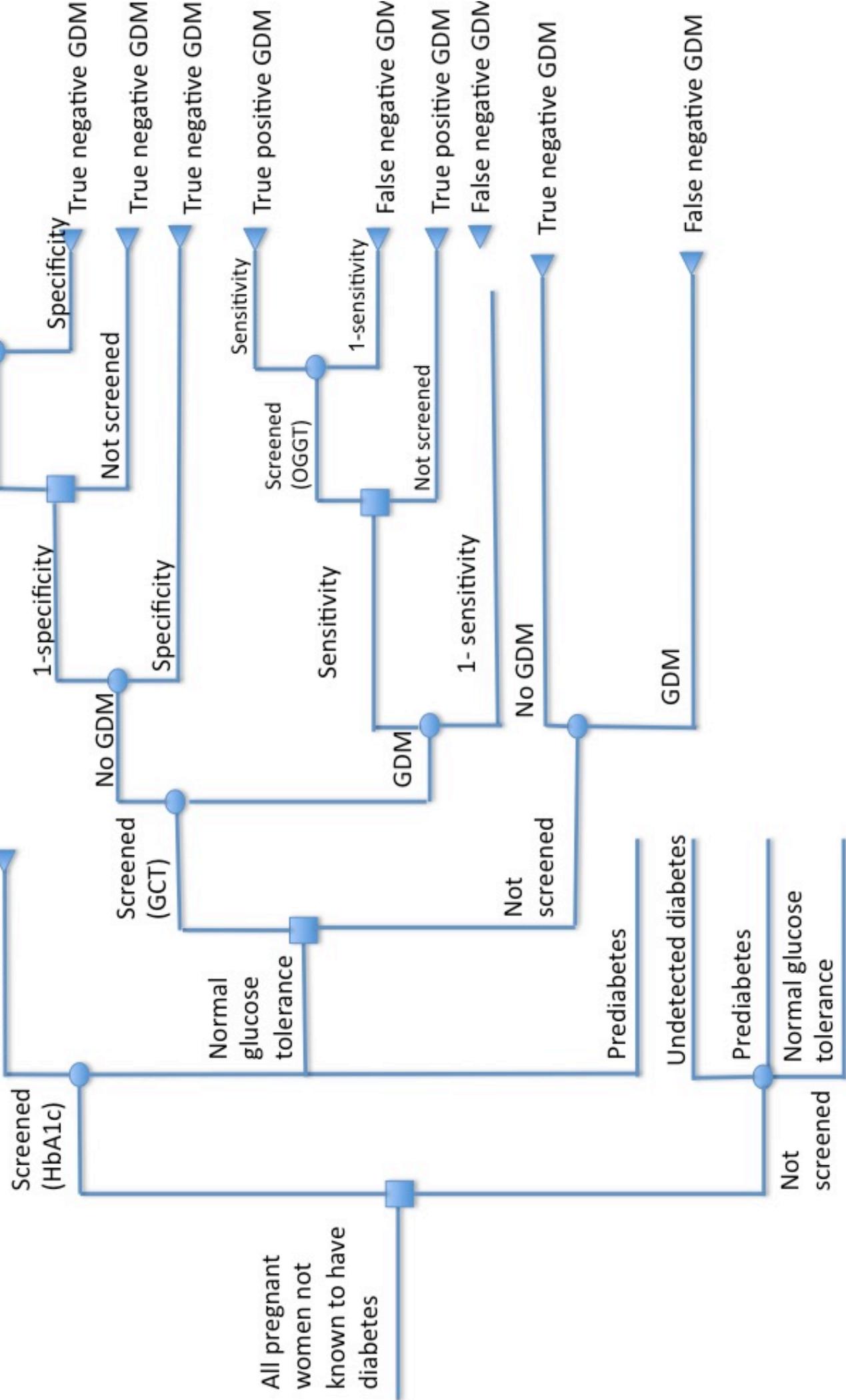
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Supplementary Figure 1: The 3-step decision tree structure. Not all branches are shown to facilitate display. Lines that do not end in a triangle indicate that the tree is truncated.



HbA1c – glycated haemoglobin, T2D – type 2 diabetes, GCT – 1 hour, 50g glucose challenge test, GDM – gestational diabetes, OGGT – 2 hour, 75g oral glucose tolerance test

Supplementary table 1: Screening model parameters

Description	Estimate	Source
Prevalence or disease distribution (%)		
Undiagnosed type 2 diabetes (≥ 50mmol/L)	1.1	Extrapolated from Coppell, 2013
Prediabetes (41-49mmol/L)	7.0 (8.5)	Extrapolated from Coppell, 2013
Normal glucose tolerance (≤ 40mmol/L)	92.0	Extrapolated from Coppell, 2013
Diagnostic accuracy (%)		
1-hour, 50g GCT		
Sensitivity	88	Hartling, 2012
Specificity	84	Hartling, 2012
2-hour, 75g OGGT		
Sensitivity	95	Expert opinion
Specificity	95	Expert opinion
Sensitivity of the HbA1c in detecting type 2 diabetes (%)	40	Burlingame, 2012
Test acceptance (%)		
Initial HbA1c screening	80	Auckland District Health Board (ADHB) 2007-2011
GCT screening 24-28 weeks	80 (61)	Extrapolated from Wijayaratna, 2011
2-hour OGGT screening following positive GCT	90	Expert opinion
Postnatal screening HbA1c	80 (50)	Extrapolated from ADHB, 2007-2011

GCT – glucose challenge test

OGGT –oral glucose tolerance test

HbA1c – Glycated haemoglobin

Supplementary table 2: Costs and outcome probabilities.

Screening, self-monitoring of blood glucose and treatment

Variable	Cost NZD\$	Source	Notes
Screening	\$22 HbA1c \$10 GCT \$24 OGTT	Personal communication (2013a)	Glycated haemoglobin 1 hour, 50g oral glucose challenge test 2 hour, 75g oral glucose tolerance test
Diabetes Clinic	\$300	Personal communication (2013a)	Assumed 4 visits for women with gestational diabetes and 10 visits for women with type 2 diabetes. MOH purchase units ranged from \$142 for midwife consultation to \$413 for a first time attendance with a dietitian
Insulin	\$3/day	Pharmaceutical management agency (2013)	Based on a dose of 86 international units (iu) per day for women with gestational diabetes and 100iu per day for women diagnosed with type 2 diabetes. Based on a cost of \$52.15 for 1500iu
Blood glucose monitor	\$20	Pharmaceutical management agency (2013)	1 meter with 50 lancets, a lancing device, and 10 diagnostic strips
Test strips	\$11 per 50	Pharmaceutical management agency (2013)	Based on testing 4x per day
Ultrasound	\$140 per U/S	Personal communication (2013a)	Based on a relative value unit of \$137.66 per exam

Health outcomes

Variable	Cost NZD\$	Source	Notes
Preeclampsia	\$8,144	Personal communication (2013)	May underestimate the outpatient costs
Induction of labour	\$58	National Institute for Health and Care Excellence (2008)	£20 cost updated to 2013 prices converted using OECD price and purchasing power parities and inflated according to consumer price index tables from Statistics New Zealand
Caesarean section	\$6,398	WIESNZ 12	O01A - Caesarean delivery without catastrophic or severe complication or comorbidity \$6152 inflated to 2013 prices
Vaginal delivery	\$2,260	WIESNZ 12	O60Z - Vaginal delivery \$2173 inflated to 2013 prices
Shoulder dystocia	\$1,351	WIESNZ 12	P67D - Neonate, Admission weight >2499g without significant operating room procedure without problem \$1082 inflated to 2013 prices. Assumed 4% with brachial plexus injury \$4817 inflated to 2013 prices.
Perinatal death/stillbirth	\$7,383	WIESNZ 12	P60A - Neonate, Died or Transferred <5 Days of Admission, without significant operating room procedure, born Here \$2282 inflated to 2013

			prices AND P67C - Neonate, Admission weight >2499 g without significant operating room procedure with other problem \$4817 inflated to 2013 prices
Phototherapy	\$1,125	WIESNZ 12	P67D - Neonate, admission weight >2499 g without significant operating room procedure without problem \$1082 inflated to 2013 prices.
Admission to NICU	\$5,010	WIESNZ 12	P67C - Neonate, Admission weight >2499 g without significant operating room procedure with other problem \$4817 inflated to 2013 prices

OECD PPPs - Organisation for Economic Co-operation and Development, WIESNZ - Weighted Inlier Equivalent Separations New Zealand

Outcome probabilities. GDM estimates were also applied to prediabetes.

Variable	Treatment	Mean	Source	No treatment	Mean	Source
Preeclampsia	TP GDM	0.07	MOH, Unpublished	FN GDM	0.12	MOH, Unpublished
	TP T2D	0.02	Middleton, 2012	FN T2D	0.20	Middleton, 2012
	FP GDM	0.03	ADHB, 2007-2011	TN ALL	0.03	ADHB, 2007-2011
Induction	TP GDM	0.34	MOH, Unpublished	FN GDM	0.29	MOH, Unpublished
	TP T2D	0.60	ADHB, 2007-2011	FN T2D	0.56	*ADHB, 2007-2011
	FP GDM	0.21	ADHB, 2007-2011	TN ALL	0.21	ADHB, 2007-2011
Caesarean section	TP GDM	0.25	MOH, Unpublished	FN GDM	0.27	MOH, Unpublished
	TP T2D	0.11	Middleton, 2012	FN T2D	0.40	Middleton, 2012
	FP GDM	0.21	MOH, 2011	TN ALL	0.21	MOH, 2011
Vaginal delivery	TP GDM	0.71	MOH, Unpublished	FN GDM	0.63	MOH, Unpublished
	TP T2D	0.89	Middleton, 2012	FN T2D	0.60	Middleton, 2012
	FP GDM	0.76	MOH, 2011	TN ALL	0.76	MOH, 2011
Shoulder dystocia	TP GDM	0.01	MOH, Unpublished	FN GDM	0.04	MOH, Unpublished
	TP T2D	0.15	Tsur, 2012	FN T2D	0.15	ADHB, 2007-2011
	FP GDM	0.06	Tsur, 2012	TN ALL	0.06	Tsur, 2012
Perinatal death/stillbirth	TP GDM	0.00	Cundy, 2000	FN GDM	0.005	Cundy, 2000
	TP T2D	0.00	Middleton, 2012	FN T2D	0.13	Middleton, 2012
	FP GDM	0.00	Cundy, 2000	TN ALL	0.00	Cundy, 2000
Phototherapy	TP GDM	0.08	MOH, Unpublished	FN GDM	0.10	MOH, Unpublished
	TP T2D	0.05	†Rowan, 2010	FN T2D	0.09	†Rowan, 2010
	FP GDM	0.12	ADHB, 2007-2011	TN ALL	0.12	ADHB, 2007-2011
Admission to neonatal intensive care	TP GDM	0.16	Goh et al, 2011	FN GDM	0.14	Goh et al, 2011
	TP T2D	0.24	ADHB, 2007-2011	FN T2D	0.21	§Goh et al, 2011
	FP GDM	0.09	ADHB, 2007-2011	TN ALL	0.09	ADHB, 2007-2011

TP – true positive, FN – false negative, FP – false positive, TN – true negative, MOH – Ministry of Health, HbA1c – glycated haemoglobin, GCT – oral glucose challenge test, OGTT – oral glucose tolerance test

* National Women's Health report data reporting on outcomes among babies of women postnatally diagnosed with type 2 diabetes. These women were most likely treated for gestational diabetes.

† Due to a lack of data the gestational diabetes rates were re-applied to this group

§ Due to a lack of data the proportional difference in rates for the gestational diabetes groups (TP & FN) were re-applied using the TP type 2 diabetes rate of admission to neonatal intensive care (0.24)