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Cost effectiveness of 1-step and 2-step screening for gestational diabetes: Evaluation of a hypothetical cohort using a decision analytic model

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Abstract

Objective To compare the cost effectiveness of two possible screening strategies for gestational diabetes in women, from the perspective of the New Zealand health system.

Design A decision analytic model was built comparing 1-step screening strategy (2 hour 75g OGTT as a single test at 24-28 weeks) with 2-step screening (1 hour GCT followed by a 2 hour 75g OGTT when indicated) 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 (NZD$ 2013) and affect on health outcomes (incidence of complications and associated affect on costs).

Results The total cost for both strategies under baseline assumptions shows that the 1-step screening strategy would cost NZD$1,38m more than the 2-step screening strategy overall. The additional cost per case detected is NZD$12,460. The model found that the 1-step screening strategy identifies 12 more women with diabetes and 111 more women with GDM when compared against the 2-step screening strategy. We assessed the effect of changing the sensitivity and specificity of the OGTT. The baseline model assumed that the 2 hour 75g OGTT has a sensitivity and specificity of 95%. The 1-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 $695,281, making the cost per additional case detected $5,919.

Conclusion Adopting a 1-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 two different approaches would be welcome.

Article summary

Strengths and limitations of this study

- This study used a whole of 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.

Background

Gestational diabetes mellitus (GDM) is a form of diabetes that occurs in pregnancy. Although the condition usually resolves 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 gestational diabetes 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 later in life [3 4]. There is strong evidence suggesting a clear benefit in maternal and infant outcomes when women with gestational diabetes 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].

Gestational diabetes is a growing problem in New Zealand with increasing rates over the past five years [6]. Data presented at the New Zealand Society for the Study of Diabetes Conference reported that the number of pregnancies associated with gestational diabetes has increased from 1.3% in 2001 to 2% in 2006 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 gestational diabetes in pregnancy published in 2008 which 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]. There are also a range of different international diagnostic criteria being used which means that the prevalence of hyperglycaemia in pregnancy can range from 7.9% to 24.9% in the same group of women using the same 2 hour, 75g 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 just one test (plasma glucose concentration equal to or exceeds the thresholds of 5.1mmol/L, 10.0mmol/L and 8.5mmol/L for fasting, one-hour and 2 hour post-glucose load glucose values respectively) rather than the standard 2-step

approach widely used in New Zealand. Women are usually offered a 50g, 1 hour oral glucose challenge test (GCT) at 24-28 weeks followed by a 75 g, 2 hour oral glucose tolerance test (OGTT) for those that have had a positive result (plasma glucose ≥ 7.8 mmol/L 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 gestational diabetes, potentially adding to the cost of care for many pregnant women.

New Zealand Gestational Diabetes Guideline

Increasing gestational diabetes prevalence, 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 gestational diabetes in New Zealand: A Clinical Practice Guideline.' [6]). 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 type 2 diabetes (HbA1c > 50mmol/L) and prediabetes (HbA1c 41 to 49mmol/L)

The guideline development team recommended at 24-28 weeks:

- Offer all women not previously diagnosed with diabetes who are at high risk of gestational diabetes (HbA1c 41 to 49,) a 2 hour, 75 g oral glucose tolerance test
    - If fasting glucose ≥ 5.5 mmol/L or 2 hour value ≥ 9 mmol/L refer to diabetes in pregnancy clinic
- Offer all other women a 1 hour, 50 g, oral glucose challenge test
    - If glucose ≥ 11.1 mmol/L refer directly to diabetes in pregnancy clinic without further testing
    - If glucose ≥ 7.8mmol/L to < 11.0mmol/L then arrange a 75g, 2 hour oral glucose tolerance test 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 analytic model to evaluate the cost-effectiveness of two screening strategies, namely the 1-step strategy (eventually not recommended) and the 2-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 of 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 gestational diabetes.
- True Positive (T2D): Women correctly tested positive for type 2 diabetes.
- True Negative (non GDM/non-T2D): Women correctly tested negative for gestational diabetes and previously undiagnosed type 2 diabetes.
- False Positive (non-GDM/non-T2D): Women without gestational diabetes and type 2 diabetes who incorrectly test positive.
- False Negative (GDM): Women with gestational diabetes who incorrectly test negative or who are not tested.
- False Negative (T2D): Women with type 2 diabetes who incorrectly test negative or who are not tested

Attached to these categories are various treatment costs and health outcome cost probabilities (see 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 gestational diabetes, has a higher risk of complications than a true positive woman being treated for gestational diabetes. 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, hyperbilirubinanaemia, and neonatal intensive care admission. Data from systematic reviews were used to provide estimates of the effect of diagnosing and treating diabetes on health outcomes, dependant on the group (GDM, non-GDM, or type 2 diabetes) [6]. If systematic review data was not available National Women's Annual Clinical Reports [11], other published literature, and the expert opinion 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 type 2 diabetes (≥50mmol/L) and prediabetes (41 to 49mmol/L).

1-step screening strategy

At 24-28 weeks, the 1-step strategy offers all women a 2 hour oral glucose tolerance test (OGTT) as a single test (cut-off values - Fasting 5.5 mmol/L or 2 hour value ≥9.0 mmol/L).

2-step screening strategy

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

Both strategies offer all women with gestational diabetes an HbA1c test 12 weeks postnatally to identify women with undiagnosed type 2 diabetes.

Decision Tree

The basic structure of the 2-step decision tree used in developing the model is shown in Figure 1. Women with previously undiagnosed type 2 diabetes (≥50mmol/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 gestational diabetes, prediabetes, and type 2 diabetes. 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 gestational diabetes and prediabetes varies within different regions of New Zealand and the prevalence rate is also affected by local screening practices. Prevalence of gestational diabetes 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 gestational diabetes was assumed. Data published in 2013 used information from the 2008/9 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 8.5b% [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 gestational diabetes [13]. As a result of this high rate of gestational diabetes diagnosis amongst women with prediabetes, the remaining cohort of women with normal glucose tolerance were left with an estimated gestational diabetes diagnosis rate of 1%. The prevalence of previously undiagnosed type 2 diabetes 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 type 2 diabetes. This was considered to be an acceptably small number that was unlikely to substantially affect the validity of the model. (See Supplementary Table 1 for full details of diagnostic accuracy and prevalence estimates)

Screening and treatment assumptions

A recent New Zealand report found that 61% of women would accept the 1 hour glucose challenge test [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 glucose challenge test screening would be higher (80% test acceptance). Women receiving a positive result from the 1 hour GCT were also expected to be more willing to undertake the 2 hour OGTT test (90% test acceptance). The rate of postnatal glucose tolerance testing among women with gestational diabetes 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 gestational diabetes diagnosis. Women diagnosed with type 2 diabetes as a result of the HbA1c screening test or the 1 hour GCT, were also assumed not to need any further testing. The proportion of women that were estimated not to undertake any gestational diabetes 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 gestational diabetes. We assume the 2 hour 75g oral glucose tolerance test 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].

We estimated that women with gestational diabetes would need four multidisciplinary clinic visits after diagnosis and women with type 2 diabetes would require ten [18]. These visits include nutritional counselling, instruction and supplies for home glucose monitoring. Women classified as false positive were assumed to have less 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 a metformin in gestational diabetes cohort study [19]. Fifty percent of the women diagnosed with gestational diabetes were estimated to require insulin and 38% percent metformin. It was assumed that all of the women with type 2 diabetes would be treated with insulin at an average of 100 international units per day. The cost of one pregnancy ultrasound (NZD$140) was included for all women. Women with type 2 diabetes and gestational diabetes were assumed to have two ultrasounds. (See Supplementary Table 2)

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 gestational diabetes were derived directly from a recently updated systematic review of combined diet and lifestyle interventions for gestational diabetes [5]. The interventions include any treatment package for gestational diabetes 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 type 2 diabetes 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 caesarean section and vaginal delivery rates for non-diabetic women [10]. All probability rates for caesarean section and vaginal delivery were adjusted to avoid double counting the cost of these outcomes for women with preeclampsia.

National Women's data was used to provide induction of labour probabilities for women treated with type 2 diabetes (True Positive T2D) [11]. Induction of labour probabilities for women with untreated type 2 diabetes (False negative T2D) was difficult to source resulting in the use of National Women's data reporting on women postnatally diagnosed with type 2 diabetes [11]. These women were most likely treated for gestational diabetes. National Women's data was also used to provide

preeclampsia and induction of labour probabilities for non-diabetic women [11]. (See Supplementary table 2)

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 gestational diabetes and were taken directly from a recently updated systematic review described above [5]. The probabilities for shoulder dystocia in infants of women with type 2 diabetes and non-diabetic women were taken from a population-based study of 11,000 deliveries in Israel [21]. National Women's Health reports were used to derive shoulder dystocia probabilities for the undiagnosed type 2 diabetes group using the proportional difference in large for gestational age infants between these groups.

Perinatal death/still birth probabilities for infants of women with type 2 diabetes were obtained from a systematic review comparing tight-moderate versus loose glycaemic control for pregnant women with type 2 diabetes [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 type 2 diabetes were taken from RCT data from New Zealand and Australian women [23]. The hyperbilirubinaemia rates for infants of non-diabetic women were derived from National Women's reports [11].

Baseline probabilities for neonatal intensive care admission in infants of women with gestational diabetes were taken directly from a metformin in gestational diabetes prospective study [19]. National Women's data was used to provide neonatal intensive care admission probabilities in infants of women with type 2 diabetes and non-diabetic women [11]. (See supplementary table 2)

Costs

All costs are in 2013 New Zealand dollars. The cost of most health outcomes were based on the average cost determined using weighted inlier equivalent separation data [24]. Prices were inflated to 2013 according to CPI tables from Statistics New Zealand. We did not apply discounting because the time horizon of the analysis was less than one 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 [25]. 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 2013/2013. The estimated cost of shoulder dystocia amounted to NZD$1,350. 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 hour GCT and the 2 hour OGTT were prices obtained from the Ministry of Health and an Auckland based laboratory [26] Full details of the methods for deriving costs are given in Supplementary Table 2.

Results

The results from the baseline model are given based on a population of 62,000 pregnant women and assume an overall gestational diabetes prevalence of 6.5%. (See Table 3) The total cost for both strategies under baseline assumptions shows that the 1-step screening strategy would cost NZD$1,38m more than the 2-step screening strategy overall. The additional cost per case detected is NZD$12,460. The model found that the 1-step screening strategy identifies 12 more women with type 2 diabetes and 111 more women with gestational diabetes when compared against the 2-step screening strategy. The 1-step strategy results in 111 fewer women not being diagnosed with gestational diabetes (false negatives) and 1220 more women being incorrectly diagnosed with gestational diabetes (false positives). Adopting a 1-step strategy would moderately increase the number of gestational diabetes cases detected at the same time as moderately increasing the number of women with false negatives at a significant cost to the health system.

Sensitivity analysis

The model was examined at different gestational diabetes prevalence rates. A higher overall prevalence of gestational diabetes was found to favour the 1-step screening strategy. If the prevalence of gestational diabetes is increased to 10% the additional cost per case detected is reduced to NZD$5,161. If the overall prevalence of gestational diabetes is reduced to 5% the additional cost per case detected is increased to NZD$42,022. We also assessed the effect of changing the sensitivity and specificity of the oral glucose tolerance test (See Table 4). The baseline model assumed that the 2 hour 75g OGTT has a sensitivity and specificity of 95%. The 1-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 NZD$695,281, making the cost per additional case detected NZD$5,919. 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 gestational diabetes. 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 1-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 gestational diabetes in pregnancy. A one step strategy of OGTT was compared with a two step strategy of a GCT followed by an OGTT and was associated with a small increase in the overall numbers of women with gestational diabetes in pregnancy being identified but would also incur significant costs to the New Zealand health care system. If the prevalence of gestational diabetes were higher than predicted then the costs would decrease.

We consider that our cost effectiveness model has merit. We have taken a whole of 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 prevalence's, sensitivities and specificities etc.

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 type 2 diabetes. These women will most likely (90%) undertake further screening tests during the course of their pregnancy. Similarly, we could not find data reporting the sensitivity and specificity of the GCT test 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 to 49mmol/L) as women with an HbA1c below 40mmol/L (normal glucose tolerance). This may have underestimated the cost of treatment and affected the reliability of the baseline estimates of health outcomes for this group.

Our analysis has been preceded by several other recent reports with similar conclusions. In the United States the lifetime cost effectiveness of three strategies to identify gestational diabetes was analysed - no screening, current screening practice (1 hour 50g GCT followed by 3 hour 100g OGTT when indicated), or screening practice proposed by the IADPSG [27]. 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 United States investigated the cost effectiveness of gestational diabetes screening using the IADPSG guidelines from a societal perspective [28]. The United States model compared routine

screening with a 2 hour OGTT versus the 1 hour GCT. Screening at 24 to 28 weeks gestational age under the new IADPSG guidelines with the 2 hour 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 gestational diabetes [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 one 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 one 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 percent 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 avoid labeling.

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 1-step screening strategy (without lowering the diagnostic thresholds) will result in a small number of additional women being diagnosed with gestational diabetes at considerable cost to the health system. The prevalence of gestational diabetes 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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Footnotes

Contributors CC is the guarantor. All the authors were involved in preparing this manuscript. CC was responsible for the overall study design, data analysis and interpretation of data, and wrote the initial draft of the manuscript. All other authors

contributed to the study design, analysis and interpretation of data, and critical revision of the manuscript. RE, JB, and CF also provided supervision.

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Competing interests None.

Ethics There were no human subjects involved in this study.

Data sharing statement The results from further sensitivity analyses are available by emailing Catherine Coop, catherinecoop6@gmail.com.

What is already known on this topic

There is strong evidence that treating women with gestational diabetes will improve maternal and infant outcomes

There are variations in the screening and management of gestational diabetes

Screening for gestational diabetes has been shown to be cost-effective when compared with not screening

What this study adds

Adopting a one step screening strategy without lowering the diagnostic thresholds will result in a small number of additional women being diagnosed with gestational diabetes at considerable cost to the health system

The one step strategy becomes more cost effective when the diagnostic test accuracy is improved or the prevalence of GDM increases

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Competing interest declaration

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that (1) [initials of relevant authors] have support from [name of company] for the submitted work; (2) [initials of relevant authors] have [no or specified] relationships with [name of companies] that might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners, or children have [specified] financial relationships that may be relevant to the submitted work; and (4) [initials of relevant authors] have no [or specified] non-financial interests that may be relevant to the submitted work.

Transparency declaration

The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.
*The manuscript's guarantor.

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Table 1: Screening and diagnostic strategies

Strategy	Screening test – first booking	Screening test	Diagnostic test	Type 2 postnatal screening test
1-step	HbA1c	-	OGTT	HbA1c
2-step	HbA1c	GCT	OGTT	HbA1c

HbA1c – glycated haemoglobin, GCT- 1 hour 50g glucose challenge test, OGTT – 2 hour 75g oral glucose tolerance test

Table 2: Probabilities, costs and outcomes used in the model. All costs are expressed as $0.00k

Parameter	Costs	FN PD/GDM		TP PD/GDM		FN T2D		TP T2D		TN ALL		FP PD/GDM	
GDM Treatment	No treatment	Treatment		No treatment		Treatment		No treatment		No treatment		Treatment	
Diabetes clinic	$300 per clinic	$-		$1200		$-		$3000		$-		$ 600	
Insulin	$3 per day	$-		$ 135		$-		$ 798		$-		$-	
Blood gluocse monitor	$20	$-		$ 20		$-		$ 20		$-		$-	
Test strips	$11 per 50	$-		$ 77		$-		$ 231		$-		$-	
Metformin	$0.06 per day	$-		$ 2		$-		$ 16		$-		$-	
Ultrasound	$140 per U/S	$ 140		$ 280		$ 140		$ 280		$ 140		$ 140	
Total cost of treatment		$ 140		$1714		$ 140		$4345		$ 140		$ 740	
		Prob	**Cost**	**Prob**	**Cost**	**Prob**	**Cost**	**Prob**	**Cost**	**Prob**	**Cost**	**Prob**	**Cost**
Health Outcomes													
Preeclampsia	$8,144	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 (excl preeclampsia)	$6,398	0.27	$1727	0.25	$1600	0.40	$2559	0.11	$ 711	0.21	$1344	0.21	$1344
Vaginal delivery (excl preeclampsia)	$2,260	0.63	$1424	0.71	$1593	0.60	$1356	0.89	$2011	0.76	$1718	0.76	$1718
Shoulder dystocia	$1,351	0.04	$ 49	0.01	$ 18	0.15	$ 209	0.15	$ 203	0.06	$ 81	0.06	$81
Perinatal death/stillbirth	$7,383	0.005	$ 34	0.00	$ -	0.13	$ 984	0.00	$ -	0.00	$ -	0.00	$ -
Hyperbilirubinaemia/phototherapy	$1,125	0.10	$ 116	0.08	$ 86	0.09	$ 105	0.05	$ 61	0.12	$ 135	0.12	$135
Admitted to NICU	$5,010	0.14	$ 701	0.16	$ 782	0.21	$1068	0.24	$1190	0.09	$ 465	0.09	$465

FN – false negative, PD – prediabetes, GDM – gestational diabetes, TP – true positive, TN – true negative, T2D – type 2 diabetes, FP – false positive, U/S – ultrasound, Prob – probabilities, NICU – neonatal intensive care,

Table 3: Baseline results. All 62,000 annual births are represented. All costs expressed as $0.000m

	1-step					2-step				
Costs:	**TP**	**FP**	**FN**	**TN**	**Total**	**TP**	**FP**	**FN**	**TN**	**Total**
Screening	0.218	0.097	0.009	2.025	**2.351**	0.218	0.044	0.011	1.560	**1.835**
Treatment/Outcomes	25.885	11.243	2.505	228.089	**267.722**	25.071	5.472	3.181	233.128	**266.854**
Total	26.103	11.341	2.514	230.114	**270.074**	25.289	5.517	3.194	234.689	**268.689**
Outcomes (number of women):										
New T2D diagnoses	322	0	33	0	355	310	0	45	0	355
Missed T2D diagnoses	0	0	409	0	409	0	0	409	0	409
Hyperglycaemia (prediabetes & gestational diabetes)	3616	2377	429	55223	61645	3505	1157	540	56443	61645

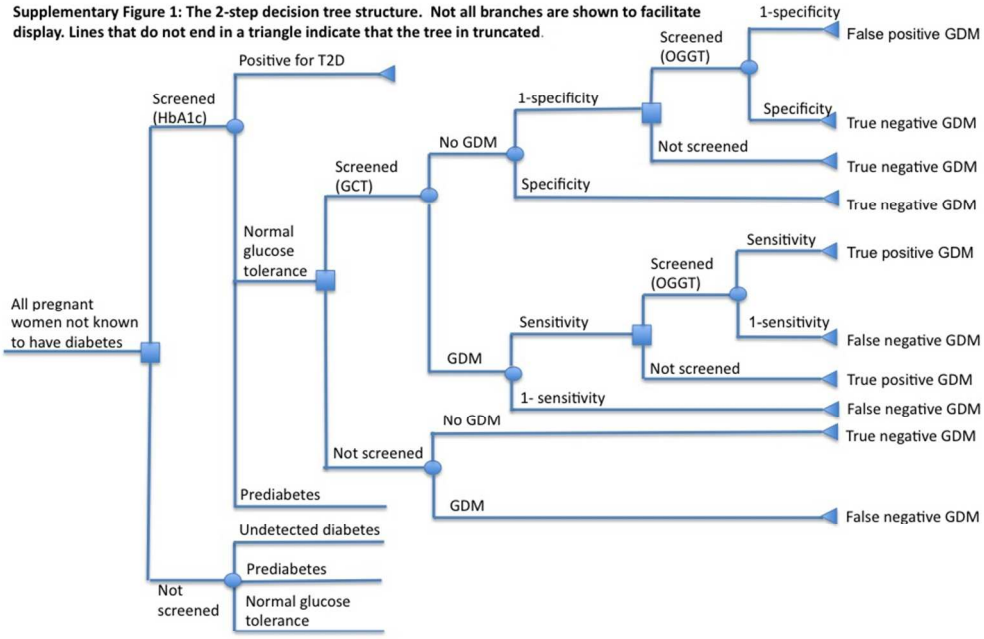
TP – true positive, FP – false positive, FN – false negative, TN – true negative, T2D - type 2 diabetes.

Table 4: Sensitivity analysis. Gestational diabetes prevalence and diagnostic accuracy of the oral glucose tolerance test. All costs are expressed as $0.000m

GDM diagnoses (numbers of women)		Total cost	Total cost	Cost difference (per case detected)	Cost difference (total cost)
1-step	2-step	1-step	2-step		
6.5% GDM prevalence (Baseline)					
3616	3505	$270.074	$268.689	$0.012	-$1.384
5% GDM prevalence					
2818	2788	$268.097	$266.851	$0.042	-$1.245
10% GDM prevalence					
5271	4969	$274.351	$272.792	$0.005	-$1.558
OGTT S & S 90%					
3440	3340	$271.247	$268.714	$0.025	-$2.533
OGTT S & S 98%					
3721	3604	$269.369	$268.674	$0.005	-$0.695
OGTT S & S 100%					
3792	3670	$268.900	$268.664	$0.001	-$0.235

GDM – gestational diabetes, OGTT – oral glucose tolerance test, S & S = sensitivity and specificity-$0.688

Supplementary Figure 1: The 2-step decision tree structure. Not all branches are shown to facilitate display. Lines that do not end in a triangle indicate that the tree in 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

352x264mm (72 x 72 DPI)

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 comordibity $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)

CHEERS Checklist
Items to include when reporting economic evaluations of health interventions

The CHEERS checklist is part of the CHEERS statement, as well as the ISPOR CHEERS explanation and elaboration task force report.

Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement please see:
http://download.journals.elsevierhealth.com/pdfs/journals/1098-3015/PIIS109830151300065X.pdf

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 evaluations publication guidelines good reporting practices task force. Value Health 2013;16:231-50.
http://www.ispor.org/ValueInHealth/ShowValueInHealth.aspx?issue=3D35FDBC-D569-431D-8C27-378B8F99EC67

CHEERS checklist—Items to include when reporting economic evaluations of health interventions

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	P1 Title
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Abstract
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	P1 & 2
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	3/13-15
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	2/12 & 3/ 7
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	3/11
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	1/49 & 4/11-26
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	3/5
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	7/50

Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	3/46
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	n/a
	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	3/48-55
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	n/a
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	n/a
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	7/4 &43
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	7/46
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	4/34
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	4/55 & 5/31
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	8/35
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly	Supp Table 1

BMJ Open

Cost effectiveness of 2-step and 3-step screening for gestational diabetes: Evaluation of a hypothetical cohort using a decision analytic model

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Cost effectiveness of 2-step and 3-step screening for gestational diabetes: Evaluation of a hypothetical cohort using a decision analytic model

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Cost effectiveness of 2-step and 3-step screening for gestational diabetes: Evaluation of a hypothetical cohort using a decision analytic model

Abstract

Objective To compare the cost effectiveness of two possible screening strategies for gestational diabetes in women, from the perspective of the New Zealand health system as part of the gestational diabetes guideline development.

Design A decision analytic model was built comparing 2-step screening strategy (HbA1c test at first booking and a 2 hour 75g OGTT as a single test at 24-28 weeks) with 3-step screening (HbA1c test at first booking and a 1 hour GCT followed by a 2 hour 75g OGTT when indicated from 24 to 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 (NZD$ 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 NZD$1.38m more than the 3-step screening strategy overall. The additional cost per case detected (as adopted by the New Zealand Guidelines for Gestational Diabetes published in 2014) was NZD$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 hour 75g OGTT has a sensitivity and specificity of 95%. The 2-step strategy becomes more cost effective when the diagnostic accuracy measures are improved.

Conclusion 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 two different approaches would be welcome.

Article summary

Strengths and limitations of this study

- This study used a whole of 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.

Background

Gestational diabetes mellitus (GDM) is a form of diabetes that occurs in pregnancy. Although the condition usually resolves 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 gestational diabetes 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 later in life [3 4]. There is strong evidence suggesting a clear benefit in maternal and infant outcomes when women with gestational diabetes 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].

Gestational diabetes is a growing problem in New Zealand with increasing rates over the past five years [6]. Data presented at the New Zealand Society for the Study of Diabetes Conference reported that the number of pregnancies associated with gestational diabetes has increased from 1.3% in 2001 to 2% in 2006 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 gestational diabetes 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 mmol/L 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 hour, 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 mmol/L, 10.0 mmol/L and 8.5 mmol/L for fasting, one-hour and 2

hour post-glucose load glucose values respectively) rather than the standard 2-step approach widely used in New Zealand. Women are usually offered a 50 g, 1 hour oral glucose challenge test (GCT) at 24-28 weeks followed by a 75 g, 2 hour oral glucose tolerance test (OGTT) for those who have had a positive result (plasma glucose ≥ 7.8 mmol/L 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 gestational diabetes, potentially adding to the cost of care for diagnosed pregnant women.

New Zealand Gestational Diabetes Guideline

Increasing gestational diabetes prevalence, 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 gestational diabetes in New Zealand: A Clinical Practice Guideline.' [6]). 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 type 2 diabetes (HbA1c > 50 mmol/L) and prediabetes (HbA1c 41 to 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 gestational diabetes (HbA1c 41 to 49,) a 2 hour, 75 g oral glucose tolerance test
    - If fasting glucose ≥ 5.5 mmol/L or 2 hour value ≥ 9 mmol/L refer to diabetes in pregnancy clinic
- Offer all other women a 1 hour, 50 g, oral glucose challenge test
    - If glucose ≥ 11.1 mmol/L refer directly to diabetes in pregnancy clinic without further testing
    - If glucose ≥ 7.8mmol/L to < 11.0 mmol/L then arrange a 75 g, 2 hour oral glucose tolerance test 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 analytic 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 of 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 gestational diabetes.
- True Positive (T2D): Women correctly tested positive for type 2 diabetes.
- True Negative (non-GDM/non-T2D): Women correctly tested negative for gestational diabetes and previously undiagnosed type 2 diabetes.
- False Positive (non-GDM/non-T2D): Women without gestational diabetes and type 2 diabetes who incorrectly test positive.
- False Negative (GDM): Women with gestational diabetes who incorrectly test negative or who are not tested.
- False Negative (T2D): Women with type 2 diabetes 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 gestational diabetes, has a higher risk of complications than a true positive woman being treated for gestational diabetes. 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, hyperbilirubinanaemia, and neonatal intensive care admission. Data from systematic reviews 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 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 type 2 diabetes (≥50 mmol/L) and prediabetes (41 to 49 mmol/L).

2-step screening strategy

At 24-28 weeks, the 2-step strategy offers all women a 2 hour oral glucose tolerance test (OGTT) as a single test (cut-off values - Fasting 5.5 mmol/L or 2 hour value ≥9.0 mmol/L).

3-step screening strategy

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

Both strategies offer all women with gestational diabetes an HbA1c test 12 weeks postnatally to identify women with undiagnosed type 2 diabetes.

Decision Tree

The basic structure of the 2-step decision tree used in developing the model is shown in Supplementary Figure 1. Women with previously undiagnosed type 2 diabetes (≥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 gestational diabetes, prediabetes, and type 2 diabetes. 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 gestational diabetes and prediabetes varies within different regions of New Zealand and the prevalence rate is also affected by local screening practices. Prevalence of gestational diabetes 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 gestational diabetes was assumed. Data published in 2013 used information from the 2008/9 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 gestational diabetes [13]. As a result of this high rate of gestational diabetes diagnosis amongst women with prediabetes, the remaining cohort of women with normal glucose tolerance were left with an estimated gestational diabetes diagnosis rate of 1%. The prevalence of previously undiagnosed type 2 diabetes 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 type 2 diabetes. This was considered to be an acceptably small number that was unlikely to substantially affect the validity of the model. (See Supplementary Table 1 for full details of diagnostic accuracy and prevalence estimates)

Screening and treatment assumptions

A recent New Zealand report found that 61% of women would accept the 1 hour glucose challenge test [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 glucose challenge test screening would be higher (80% test acceptance). Women receiving a positive result from the 1 hour GCT were also expected to be more willing to undertake the 2 hour OGTT test (90% test acceptance). The rate of postnatal glucose tolerance testing among women with gestational diabetes 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 gestational diabetes diagnosis. Women diagnosed with type 2 diabetes as a result of the HbA1c screening test or the 1 hour GCT, were also assumed not to need any further testing. The proportion of women that were

estimated not to undertake any gestational diabetes 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 gestational diabetes. We assume the 2 hour 75 g oral glucose tolerance test 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].

We estimated that women with gestational diabetes would need four multidisciplinary clinic visits after diagnosis and women with type 2 diabetes would require ten [18]. 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 a metformin in gestational diabetes cohort study [19]. Fifty per cent of the women diagnosed with gestational diabetes were estimated to require insulin and 38% metformin. It was assumed that all of the women with type 2 diabetes would be treated with insulin at an average of 100 international units per day. The cost of one pregnancy ultrasound (NZD$140) was included for all women. Women with type 2 diabetes and gestational diabetes were assumed to have two ultrasounds (Supplementary Table 2).

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 gestational diabetes were derived directly from a recently updated systematic review of combined diet and lifestyle interventions for gestational diabetes [5]. The interventions include any treatment package for gestational diabetes 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 caesarean section and vaginal delivery rates for non-diabetic women [10]. All probability rates for caesarean section and vaginal delivery were adjusted to avoid double counting the cost of these outcomes for women with preeclampsia.

National Women's data was used to provide induction of labour probabilities for women treated with type 2 diabetes (True Positive T2D) [11]. Induction of labour probabilities for women with untreated type 2 diabetes (False negative T2D) was difficult to source resulting in the use of National Women's data reporting on women postnatally diagnosed with type 2 diabetes [11]. These women were most likely treated for gestational diabetes. National Women's data was also used to provide preeclampsia and induction of labour probabilities for non-diabetic women [11] (Supplementary Table 2).

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 gestational diabetes and were taken directly from a recently updated systematic review described above [5]. The probabilities for shoulder dystocia in infants of women with T2D and non-diabetic women were taken from a population-based study of 11,000 deliveries in Israel [21]. National Women's Health reports were used to derive shoulder dystocia probabilities for the undiagnosed T2D group using the proportional difference in large for gestational age infants between these groups.

Perinatal death/still birth 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 non-diabetic women were derived from National Women's reports [11].

Baseline probabilities for neonatal intensive care admission in infants of women with gestational diabetes were taken directly from a metformin in gestational diabetes prospective study [19]. National Women's data was used to provide neonatal intensive care admission probabilities in infants of women with T2D and non-diabetic women [11]. (Supplementary Table 2)

Costs

All costs are in 2013 New Zealand dollars. The cost of most health outcomes were based on the average cost determined using weighted inlier equivalent separation data [24]. Prices were inflated to 2013 according to CPI tables from Statistics New Zealand. We did not apply discounting because the time horizon of the analysis was

less than one 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 [25]. 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. [26] The estimated cost of shoulder dystocia amounted to NZD$1,350. 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 hour GCT and the 2 hour OGTT were prices obtained from the Ministry of Health and an Auckland based laboratory [27] Full details of the methods for deriving costs are given in Supplementary Table 2.

Results

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

The total screening cost was $2.35m for the 2-step strategy versus $1.83m for the 3-step strategy, a marginal cost difference of $515,845. The total cost of treatment was $17m for the 2-step strategy versus $16m for the 3-step strategy, a marginal cost difference of $957,251. The total cost of health outcomes was $250.57m versus $250.66m for the 3-step strategy, a marginal cost difference of $88,423.

Sensitivity analysis

The model was examined at different gestational diabetes prevalence rates. A higher overall prevalence of gestational diabetes was found to favour the 2-step screening strategy. If the prevalence of gestational diabetes is increased to 10% the additional cost per case detected is reduced to NZD$5,161. If the overall prevalence of

gestational diabetes is reduced to 5% the additional cost per case detected is increased to NZD$42,022. We also assessed the effect of changing the sensitivity and specificity of the oral glucose tolerance test (Table 4). The baseline model assumed that the 2 hour 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 NZD$695,281, making the cost per additional case detected NZD$5,919. 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 gestational diabetes. 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 gestational diabetes in pregnancy. A two step strategy of an HbA1c followed by an OGTT was compared with a three 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 gestational diabetes in pregnancy being identified but would also incur significant costs to the New Zealand health care system. If the prevalence of gestational diabetes were higher than predicted then the costs would decrease.

We consider that our cost effectiveness model has merit. We have taken a whole of 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 type 2 diabetes. These women will most likely (90%) undertake further screening tests during the course of their pregnancy. Similarly, we could not find data reporting the sensitivity and specificity of the GCT test 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 to 49 mmol/L) that have not been diagnosed with gestational diabetes as women with an HbA1c below 40mmol/L (normal glucose tolerance). This may have underestimated the cost of treatment and affected the reliability 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 timeframe 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 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 gestational diabetes [28]. Universal screening will identify more women with gestational diabetes than risk-factor based screening but the effect of subsequent management on health outcomes are 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 [29].

The Guideline Development Team took into consideration the high prevalence of previously undiagnosed diabetes and gestational diabetes 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 United States the lifetime cost effectiveness of three strategies to identify gestational diabetes was analysed - no screening, current screening practice (1 hour 50 g GCT followed by 3 hour 100 g OGTT when indicated),

or screening practice proposed by the IADPSG [30]. 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 United States investigated the cost effectiveness of gestational diabetes screening using the IADPSG guidelines from a societal perspective [31]. This model compared routine screening with a 2 hour OGTT versus the 1 hour GCT. Screening at 24 to 28 weeks gestational age under the new IADPSG guidelines with the 2 hour 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 gestational diabetes [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 one 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 one 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 per cent 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 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 gestational diabetes 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 publshed in 2014) was an additional NZD$12,460 per case. The prevalence of gestational diabetes 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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Footnotes

Contributors CC is the guarantor. All the authors were involved in preparing this manuscript. CC was responsible for the overall study design, data analysis and interpretation of data, and wrote the initial draft of the manuscript. All other authors contributed to the study design, analysis and interpretation of data, and critical revision of the manuscript. RE, JB, and CF also provided supervision.

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Competing interests None.

Ethics There were no human subjects involved in this study.

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Competing interest declaration

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that (1) [initials of relevant authors] have support from [name of company] for the submitted work; (2) [initials of relevant authors] have [no or specified] relationships with [name of companies] that might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners, or children have [specified] financial relationships that may be relevant to the submitted work; and (4) [initials of relevant authors] have no [or specified] non-financial interests that may be relevant to the submitted work.

Transparency declaration

The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

*The manuscript's guarantor.

Table 1: Screening and diagnostic strategies

Strategy	Screening test – first booking	Screening test	Diagnostic test	Type 2 postnatal screening test
2-step	HbA1c	-	OGTT	HbA1c
3-step	HbA1c	GCT	OGTT	HbA1c

HbA1c – glycated haemoglobin, GCT- 1 hour 50g glucose challenge test, OGTT – 2 hour 75g oral glucose tolerance test

Table 2: Probabilities, costs and outcomes used in the model. All costs are expressed as $0.00k

Parameter	Costs	FN PD/GDM		TP PD/GDM		FN T2D		TP T2D		TN ALL		FP PD/GDM	
GDM Treatment		Treatment		No treatment		Treatment		No treatment		No treatment		Treatment	
Diabetes clinic	$300 per clinic	$-		$1200		$-		$3000		$-		$ 600	
Insulin	$3 per day	$-		$ 135		$-		$ 798		$-		$-	
Blood glucose monitor	$20	$-		$ 20		$-		$ 20		$-		$-	
Test strips	$11 per 50	$-		$ 77		$-		$ 231		$-		$-	
Metformin	$0.06 per day	$-		$ 2		$-		$ 16		$-		$-	
Ultrasound	$140 per U/S	$ 140		$ 280		$ 140		$ 280		$ 140		$ 140	
Total cost of treatment		$ 140		$1714		$ 140		$4345		$ 140		$ 740	
		Prob	**Cost**	**Prob**	**Cost**	**Prob**	**Cost**	**Prob**	**Cost**	**Prob**	**Cost**	**Prob**	**Cost**
Health Outcomes													
Preeclampsia	$8,144	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 (excl preeclampsia)	$6,398	0.27	$1727	0.25	$1600	0.40	$2559	0.11	$ 711	0.21	$1344	0.21	$1344
Vaginal delivery (excl preeclampsia)	$2,260	0.63	$1424	0.71	$1593	0.60	$1356	0.89	$2011	0.76	$1718	0.76	$1718
Shoulder dystocia	$1,351	0.04	$ 49	0.01	$ 18	0.15	$ 209	0.15	$ 203	0.06	$ 81	0.06	$81
Perinatal death/stillbirth	$7,383	0.005	$ 34	0.00	$ -	0.13	$ 984	0.00	$ -	0.00	$ -	0.00	$ -
Hyperbilirubinaemia/phototherapy	$1,125	0.10	$ 116	0.08	$ 86	0.09	$ 105	0.05	$ 61	0.12	$ 135	0.12	$135
Admitted to NICU	$5,010	0.14	$ 701	0.16	$ 782	0.21	$1068	0.24	$1190	0.09	$ 465	0.09	$465

FN – false negative, PD – prediabetes, GDM – gestational diabetes, TP – true positive, TN – true negative, T2D – type 2 diabetes, FP – false positive, U/S – ultrasound, Prob – probabilities, NICU – neonatal intensive care,

Table 3: Baseline results. All 62,000 annual births are represented. All costs expressed as $0.000m

	2-step					3-step				
Costs:	**TP**	**FP**	**FN**	**TN**	**Total**	**TP**	**FP**	**FN**	**TN**	**Total**
Screening	0.218	0.097	0.009	2.025	**2.351**	0.218	0.044	0.011	1.560	**1.835**
Treatment	7.596	1.759	0.065	7.731	**17.151**	7.354	0.856	0.082	7.902	**16.194**
Health outcomes	18.289	9.484	2.440	220.358	**250.571**	17.717	4.616	3.100	225.226	**250.660**
Total	26.103	11.341	2.514	230.114	**270.074**	25.289	5.516	3.193	234.688	**268.689**
Outcomes (number of women):										
New T2D diagnoses	322	0	33	0	355	310	0	45	0	355
Missed T2D diagnoses	0	0	409	0	409	0	0	409	0	409
Hyperglycaemia (prediabetes & gestational diabetes)	3616	2377	429	55223	61645	3505	1157	540	56443	61645

TP – true positive, FP – false positive, FN – false negative, TN – true negative, T2D - type 2 diabetes.

Table 4: Sensitivity analysis. Gestational diabetes prevalence and diagnostic accuracy of the oral glucose tolerance test. All costs are expressed as $0.000m

GDM diagnoses (numbers of women)		Total cost	Total cost	Cost difference (per case detected)	Cost difference (total cost)
2-step	3-step	2-step	3-step		
6.5% GDM prevalence (Baseline)					
3616	3505	$270.074	$268.689	$0.012	-$1.384
5% GDM prevalence					
2818	2788	$268.097	$266.851	$0.042	-$1.245
10% GDM prevalence					
5271	4969	$274.351	$272.792	$0.005	-$1.558
OGTT S & S 90%					
3440	3340	$271.247	$268.714	$0.025	-$2.533
OGTT S & S 98%					
3721	3604	$269.369	$268.674	$0.005	-$0.695
OGTT S & S 100%					
3792	3670	$268.900	$268.664	$0.001	-$0.235

GDM – gestational diabetes, OGTT – oral glucose tolerance test, S & S = sensitivity and specificity

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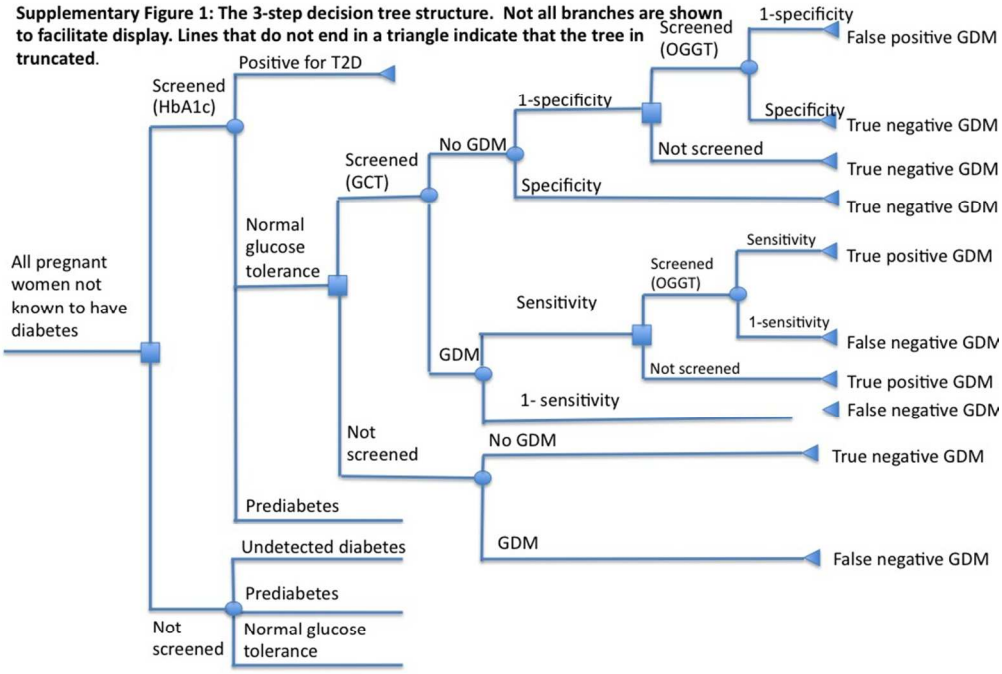
Supplementary Figure 1: The 3-step decision tree structure. Not all branches are shown to facilitate display. Lines that do not end in a triangle indicate that the tree in truncated.



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

352x264mm (72 x 72 DPI)

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 comordibity $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)

CHEERS Checklist
Items to include when reporting economic evaluations of health interventions

The CHEERS checklist is part of the CHEERS statement, as well as the ISPOR CHEERS explanation and elaboration task force report.

Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement please see:
http://download.journals.elsevierhealth.com/pdfs/journals/1098-3015/PIIS109830151300065X.pdf

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 evaluations publication guidelines good reporting practices task force. Value Health 2013;16:231-50.
http://www.ispor.org/ValueInHealth/ShowValueInHealth.aspx?issue=3D35FDBC-D569-431D-8C27-378B8F99EC67

CHEERS checklist—Items to include when reporting economic evaluations of health interventions

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	P1 Title
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Abstract
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	P1 & 2
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	3/13-15
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	2/12 & 3/ 7
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	3/11
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	1/49 & 4/11-26
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	3/5
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	7/50

Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	3/46
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	n/a
	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	3/48-55
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	n/a
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	n/a
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	7/4 &43
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	7/46
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	4/34
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	4/55 & 5/31
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	8/35
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly	Supp Table 1

BMJ Open

Cost effectiveness of the New Zealand Diabetes in Pregnancy guideline screening recommendations

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

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

Abstract

Objective To compare the cost effectiveness of two possible screening strategies for gestational diabetes 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 (HbA1c test at first booking and a 2 hour 75g OGTT as a single test at 24-28 weeks) with 3-step screening (HbA1c test at first booking and a 1 hour GCT followed by a 2 hour 75g OGTT when indicated from 24 to 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 (NZD$ 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 NZD$1.38m more than the 3-step screening strategy overall. The additional cost per case detected was NZD$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 hour 75g OGTT has a sensitivity and specificity of 95%. The 2-step strategy becomes more cost effective when the diagnostic accuracy measures are improved.

Conclusion 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 two different approaches would be welcome.

Article summary

Strengths and limitations of this study

- This study used a whole of 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.

Background

Gestational diabetes mellitus (GDM) is a form of diabetes that occurs in pregnancy. Although the condition usually resolves 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 gestational diabetes 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 later in life [3 4]. There is strong evidence suggesting a clear benefit in maternal and infant outcomes when women with gestational diabetes 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].

Gestational diabetes is a growing problem in New Zealand with increasing rates over the past five years [6]. Data presented at the New Zealand Society for the Study of Diabetes Conference reported that the number of pregnancies associated with gestational diabetes has increased from 1.3% in 2001 to 2% in 2006 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 gestational diabetes 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 mmol/L 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 hour, 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 mmol/L, 10.0 mmol/L and 8.5 mmol/L for fasting, one-hour and 2 hour post-glucose load glucose values respectively) rather than the standard 2-step approach widely used in New Zealand. Women are usually offered a 50 g, 1 hour oral glucose challenge test (GCT) at 24-28 weeks followed by a 75 g, 2 hour oral glucose

tolerance test (OGTT) for those who have had a positive result (plasma glucose ≥ 7.8 mmol/L 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 gestational diabetes, potentially adding to the cost of care for diagnosed pregnant women.

New Zealand Gestational Diabetes Guideline

Increasing gestational diabetes prevalence, 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 gestational diabetes 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 type 2 diabetes (HbA1c > 50 mmol/L) and prediabetes (HbA1c 41 to 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 gestational diabetes (HbA1c 41 to 49,) a 2 hour, 75 g oral glucose tolerance test
    - If fasting glucose ≥ 5.5 mmol/L or 2 hour value ≥ 9 mmol/L refer to diabetes in pregnancy clinic
- Offer all other women a 1 hour, 50 g, oral glucose challenge test
    - If glucose ≥ 11.1 mmol/L refer directly to diabetes in pregnancy clinic without further testing
    - If glucose ≥ 7.8mmol/L to < 11.0 mmol/L then arrange a 75 g, 2 hour oral glucose tolerance test 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

analytic 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 of 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 gestational diabetes.
- True Positive (T2D): Women correctly tested positive for type 2 diabetes.
- True Negative (non-GDM/non-T2D): Women correctly tested negative for gestational diabetes and previously undiagnosed type 2 diabetes.
- False Positive (non-GDM/non-T2D): Women without gestational diabetes and type 2 diabetes who incorrectly test positive.
- False Negative (GDM): Women with gestational diabetes who incorrectly test negative or who are not tested.
- False Negative (T2D): Women with type 2 diabetes 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 gestational diabetes, has a higher risk of complications than a true positive woman being treated for gestational diabetes. 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, hyperbilirubinanaemia, 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 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 type 2 diabetes (≥50 mmol/L) and prediabetes (41 to 49 mmol/L).

2-step screening strategy

At 24-28 weeks, the 2-step strategy offers all women a 2 hour oral glucose tolerance test (OGTT) as a single test (cut-off values - Fasting 5.5 mmol/L or 2 hour value ≥9.0 mmol/L).

3-step screening strategy

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

Both strategies offer all women with gestational diabetes an HbA1c test 12 weeks postnatally to identify women with undiagnosed type 2 diabetes.

Decision Tree

The basic structure of the 2-step decision tree used in developing the model is shown in Supplementary Figure 1. Women with previously undiagnosed type 2 diabetes (≥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 gestational diabetes, prediabetes, and type 2 diabetes. 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 gestational diabetes and prediabetes varies within different regions of New Zealand and the prevalence rate is also affected by local screening practices. Prevalence of gestational diabetes 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 gestational diabetes was assumed. Data published in 2013 used information from the 2008/9 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 gestational diabetes [13]. As a result of this high rate of gestational diabetes diagnosis amongst women with prediabetes, the remaining cohort of women with normal glucose tolerance were left with an estimated gestational diabetes diagnosis rate of 1%. The prevalence of previously undiagnosed type 2 diabetes 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 type 2 diabetes. This was considered to be an acceptably small number that was unlikely to substantially affect the validity of the model. (See Supplementary Table 1 for full details of diagnostic accuracy and prevalence estimates)

Screening and treatment assumptions

A recent New Zealand report found that 61% of women would accept the 1 hour glucose challenge test [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 glucose challenge test screening would be higher (80% test acceptance). Women receiving a positive result from the 1 hour GCT were also expected to be more willing to undertake the 2 hour OGTT test (90% test acceptance). The rate of postnatal glucose tolerance testing among women with gestational diabetes 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 gestational diabetes diagnosis. Women diagnosed with type 2 diabetes as a result of the HbA1c screening test or the 1 hour GCT, were also

assumed not to need any further testing. The proportion of women that were estimated not to undertake any gestational diabetes 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 gestational diabetes. We assume the 2 hour 75 g oral glucose tolerance test 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 gestational diabetes would need four multidisciplinary clinic visits after diagnosis and women with type 2 diabetes would require ten [19]. 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 a metformin in gestational diabetes cohort study [20]. Fifty per cent of the women diagnosed with gestational diabetes were estimated to require insulin and 38% metformin. It was assumed that all of the women with type 2 diabetes would be treated with insulin at an average of 100 international units per day. The cost of one pregnancy ultrasound (NZD$140) was included for all women. Women with type 2 diabetes and gestational diabetes were assumed to have two ultrasounds (Supplementary Table 2).

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 gestational diabetes were derived directly from a recently updated systematic review of combined diet and lifestyle interventions for gestational diabetes [5]. The interventions include any treatment package for gestational diabetes 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 [21]. Data from a recently published New Zealand Maternity Report were used to obtain caesarean section and vaginal delivery rates for non-diabetic women [10]. All probability rates for caesarean section and vaginal delivery were adjusted to avoid double counting the cost of these outcomes for women with preeclampsia.

National Women's data was used to provide induction of labour probabilities for women treated with type 2 diabetes (True Positive T2D) [11]. Induction of labour probabilities for women with untreated type 2 diabetes (False negative T2D) was difficult to source resulting in the use of National Women's data reporting on women postnatally diagnosed with type 2 diabetes [11]. These women were most likely treated for gestational diabetes. National Women's data was also used to provide preeclampsia and induction of labour probabilities for non-diabetic women [11] (Supplementary Table 2).

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 gestational diabetes and were taken directly from a recently updated systematic review described above [5]. The probabilities for shoulder dystocia in infants of women with T2D and non-diabetic women were taken from a population-based study of 11,000 deliveries in Israel [22]. National Women's Health reports were used to derive shoulder dystocia probabilities for the undiagnosed T2D group using the proportional difference in large for gestational age infants between these groups.

Perinatal death/still birth 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 [21].The remaining perinatal death probabilities were obtained from a New Zealand perinatal mortality report [23].

The baseline probabilities for hyperbilirubinaemia in infants of women with T2D were taken from RCT data from New Zealand and Australian women [24]. The hyperbilirubinaemia rates for infants of non-diabetic women were derived from National Women's reports [11].

Baseline probabilities for neonatal intensive care admission in infants of women with gestational diabetes were taken directly from a metformin in gestational diabetes prospective study [20]. National Women's data was used to provide neonatal intensive care admission probabilities in infants of women with T2D and non-diabetic women [11]. (Supplementary Table 2)

Costs

All costs are in 2013 New Zealand dollars. The cost of most health outcomes were based on the average cost determined using weighted inlier equivalent separation data [25]. Prices were inflated to 2013 according to CPI tables from Statistics New Zealand. We did not apply discounting because the time horizon of the analysis was

less than one 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 [26]. 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. [27] The estimated cost of shoulder dystocia amounted to NZD$1,350. 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 hour GCT and the 2 hour OGTT were prices obtained from the Ministry of Health and an Auckland based laboratory [28] Full details of the methods for deriving costs are given in Supplementary Table 2.

Results

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

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

Sensitivity analysis

The model was examined at different gestational diabetes prevalence rates. A higher overall prevalence of gestational diabetes was found to favour the 2-step screening strategy. If the prevalence of gestational diabetes is increased to 10% the additional cost per case detected is reduced to NZD$5,161. If the overall prevalence of

gestational diabetes is reduced to 5% the additional cost per case detected is increased to NZD$233,616. We also assessed the effect of changing the sensitivity and specificity of the oral glucose tolerance test (Table 4). The baseline model assumed that the 2 hour 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 NZD$695,281, making the cost per additional case detected NZD$5,919. 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 gestational diabetes. 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 gestational diabetes in pregnancy. A two step strategy of an HbA1c followed by an OGTT was compared with a three 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 gestational diabetes in pregnancy being identified but would also incur significant costs to the New Zealand health care system. If the prevalence of gestational diabetes were higher than predicted then the costs would decrease.

We consider that our cost effectiveness model has merit. We have taken a whole of 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 type 2 diabetes. These women will most likely (90%) undertake further screening tests during the course of their pregnancy. Similarly, we could not find data reporting the sensitivity and specificity of the GCT test 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 to 49 mmol/L) that have not been diagnosed with gestational diabetes as women with an HbA1c below 40mmol/L (normal glucose tolerance). This may have underestimated the cost of treatment and affected the reliability 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 timeframe 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 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 gestational diabetes [29]. Universal screening will identify more women with gestational diabetes than risk-factor based screening but the effect of subsequent management on health outcomes are 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 [30].

The Guideline Development Team took into consideration the high prevalence of previously undiagnosed diabetes and gestational diabetes 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 United States the lifetime cost effectiveness of three strategies to identify gestational diabetes was analysed - no screening, current screening practice (1 hour 50 g GCT followed by 3 hour 100 g OGTT when indicated),

or screening practice proposed by the IADPSG [31]. 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 United States investigated the cost effectiveness of gestational diabetes screening using the IADPSG guidelines from a societal perspective [32]. This model compared routine screening with a 2 hour OGTT versus the 1 hour GCT. Screening at 24 to 28 weeks gestational age under the new IADPSG guidelines with the 2 hour 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 gestational diabetes [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 one 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 one 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 per cent 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 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 gestational diabetes 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 NZD$12,460 per case. The prevalence of gestational diabetes 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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Footnotes

Contributors CC is the guarantor. All the authors were involved in preparing this manuscript. CC was responsible for the overall study design, data analysis and interpretation of data, and wrote the initial draft of the manuscript. All other authors contributed to the study design, analysis and interpretation of data, and critical revision of the manuscript. RE, JB, and CF also provided supervision.

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Competing interests None.

Ethics There were no human subjects involved in this study.

Data sharing statement The results from further sensitivity analyses are available by emailing Catherine Coop, catherinecoop6@gmail.com.

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Competing interest declaration

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that (1) [initials of relevant authors] have support from [name of company] for the submitted work; (2) [initials of relevant authors] have [no or specified] relationships with [name of companies] that might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners, or children have [specified] financial relationships that may be relevant to the submitted work; and (4) [initials of relevant authors] have no [or specified] non-financial interests that may be relevant to the submitted work.

Transparency declaration

The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.
*The manuscript's guarantor.

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 to 49 mmol/L	HbA1c

HbA1c – glycated haemoglobin, GCT- 1 hour 50g glucose challenge test, OGTT – 2 hour 75g oral glucose tolerance test

Table 2: Probabilities, costs and outcomes used in the model. All costs are expressed as $0.00k												
Parameter	**Costs**											
		FN PD/GDM		**TP PD/GDM**		**FN T2D**		**TP T2D**		**TN ALL**		**FP PD/GDM**	
GDM Treatment		Treatment		No treatment		Treatment		No treatment		No treatment		Treatment	
Diabetes clinic	$300 per clinic	$-		$1200		$-		$3000		$-		$ 600	
Insulin	$3 per day	$-		$ 135		$-		$ 798		$-		$-	
Blood glucose monitor	$20	$-		$ 20		$-		$ 20		$-		$-	
Test strips	$11 per 50	$-		$ 77		$-		$ 231		$-		$-	
Metformin	$0.06 per day	$-		$ 2		$-		$ 16		$-		$-	
Ultrasound	$140 per U/S	$ 140		$ 280		$ 140		$ 280		$ 140		$ 140	
Total cost of treatment		$ 140		$1714		$ 140		$4345		$ 140		$ 740	
		Prob	**Cost**	**Prob**	**Cost**	**Prob**	**Cost**	**Prob**	**Cost**	**Prob**	**Cost**	**Prob**	**Cost**
Health Outcomes													
Preeclampsia	$8,144	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 (excl preeclampsia)	$6,398	0.27	$1727	0.25	$1600	0.40	$2559	0.11	$ 711	0.21	$1344	0.21	$1344
Vaginal delivery (excl preeclampsia)	$2,260	0.63	$1424	0.71	$1593	0.60	$1356	0.89	$2011	0.76	$1718	0.76	$1718
Shoulder dystocia	$1,351	0.04	$ 49	0.01	$ 18	0.15	$ 209	0.15	$ 203	0.06	$ 81	0.06	$81
Perinatal death/stillbirth	$7,383	0.005	$ 34	0.00	$ -	0.13	$ 984	0.00	$ -	0.00	$ -	0.00	$ -
Hyperbilirubinaemia/phototherapy	$1,125	0.10	$ 116	0.08	$ 86	0.09	$ 105	0.05	$ 61	0.12	$ 135	0.12	$135
Admitted to NICU	$5,010	0.14	$ 701	0.16	$ 782	0.21	$1068	0.24	$1190	0.09	$ 465	0.09	$465
FN – false negative, PD – prediabetes, GDM – gestational diabetes, TP – true positive, TN – true negative, T2D – type 2 diabetes, FP – false positive, U/S – ultrasound, Prob – probabilities, NICU – neonatal intensive care,													

Table 3: Baseline results. All 62,000 annual births are represented. All costs expressed as $0.000m

	2-step					3-step				
Costs:	**TP**	**FP**	**FN**	**TN**	**Total**	**TP**	**FP**	**FN**	**TN**	**Total**
Screening	0.213	0.096	0.012	2.025	**2.348**	0.212	0.043	0.014	1.561	**1.832**
Treatment	7.358	1.733	0.084	7.736	**16.911**	7.115	0.830	84.112	7.906	**15.954**
Health outcomes	17.640	9.346	3.146	220.496	**250.629**	17.069	4.477	3.805	225.364	**250.629**
Total	25.212	11.176	3.242	230.258	**269.889**	24.398	5.351	3.921	234.832	**268.504**
Outcomes (number of women):										
New T2D diagnoses	322	0	33	0	355	310	0	45	0	355
Missed T2D diagnoses	0	0	409	0	409	0	0	409	0	409
Hyperglycaemia (prediabetes & gestational diabetes)	3477	2342	568	55258	61645	3366	1122	679	56478	61645

TP – true positive, FP – false positive, FN – false negative, TN – true negative, T2D - type 2 diabetes.

Table 4: Sensitivity analysis. Gestational diabetes prevalence and diagnostic accuracy of the oral glucose tolerance test. All costs are expressed as $0.000m

GDM diagnoses (numbers of women)		Total cost	Total cost	Cost difference (per case detected)	Cost difference (total cost)
2-step	3-step	2-step	3-step		
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 & S 90%					
3301	3201	$271.063	$268.529	$0.025	-$2.533
OGTT S & S 98%					
3582	3465	$269.185	$268.490	$0.005	-$0.695
OGTT S & S 100%					
3653	3531	$268.715	$268.480	$0.001	-$0.235

GDM – gestational diabetes, OGTT – oral glucose tolerance test, S & S = sensitivity and specificity

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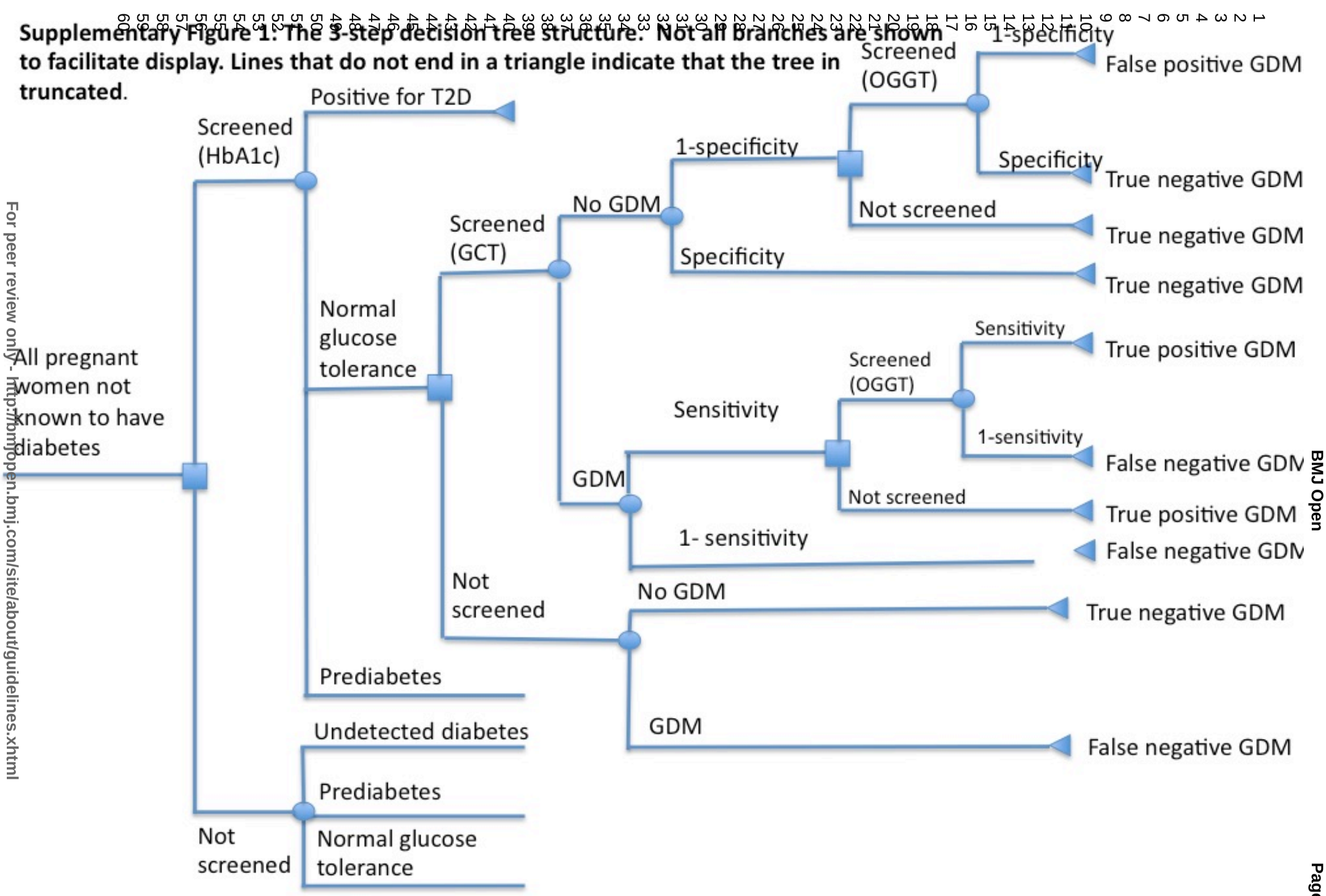
Supplementary Figure 1. The 3-step decision tree structure. Not all branches are shown to facilitate display. Lines that do not end in a triangle indicate that the tree in truncated.



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 comordibity $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)