Efficacy and cost of postpartum screening strategies for diabetes among women with histories of gestational diabetes

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Short running title: Screening strategies after gestational diabetes
Structured Abstract

Objective To compare the cost and time to diagnosis associated with several screening strategies for diabetes in women with histories of gestational diabetes mellitus (GDM)

Research Design and Methods We simulated screening for diabetes with fasting plasma glucose (FPG), a 2-hour oral glucose tolerance test (OGTT), and a hemoglobin A1c (HbA1c) annually, every 2 years, and every 3 years over a period of 12 years. We assumed that women had negative screening tests 6 weeks after delivery, progressed to diabetes at 8% per year, and that each positive FPG and HbA1c was followed by a confirmatory FPG. For each strategy, we calculated the cost per case detected, cost per woman screened, the percent of cases detected, and the time elapsed with undiagnosed diabetes. In sensitivity analyses, we considered inclusion of indirect costs, impact of imperfect adherence to screening strategies, exclusion of confirmatory tests, and lower rates of progression to diabetes.

Results When annual, biannual, or every 3 year screening strategies were employed, OGTT resulted in lower costs per case detected than FPG or HbA1c. Testing every 3 years resulted in lower costs per case detected than more frequent testing. These patterns persisted in sensitivity analyses, except FPG resulted in lower cost per case detected than OGTT assuming annual screening and inclusion of indirect costs, or assuming annual screening without a confirmatory FPG.

Conclusions Screening every 3 years with OGTT results in the lowest cost per case of diabetes detected.
Gestational diabetes (GDM), or glucose intolerance first recognized during pregnancy, affects 3-8% of pregnancies in the U.S.\(^1\) The incidence of GDM is increasing, fueled by maternal obesity and advancing maternal age.\(^2\)-\(^4\) While most women with GDM return to normal glucose tolerance after delivery, as many as 10-50% of women with GDM are diagnosed with diabetes within 5 years.\(^5\); \(^6\) Therefore, the 4\(^{th}\) International Workshop-Conference for Gestational Diabetes recommended that an oral glucose tolerance test (OGTT) be used to screen for diabetes at least 6 weeks after delivery, and if glucose levels were normal, glycemia be reassessed at a minimum of 3-year intervals with a screening test appropriate for the prevalence of diabetes in the population.\(^1\) A 2003 survey of American College of Obstetricians and Gynecologists (ACOG) fellows indicated that about three-quarters reported performing postpartum screening for diabetes in their patients with histories of GDM.\(^7\)

There are no long-term studies that compare the benefits of different screening strategies.\(^8\) Comparison of screening strategies for diabetes among women with histories of GDM is challenging for several reasons. First, a single screening strategy may not be appropriate across populations, as the performance and cost of screening strategies will vary with incidence of diabetes. A systematic review by Kim and colleagues found that the 8% per year conversion rate to diabetes did not apply to non-Hispanic white populations, where the cumulative incidence could be as low as 10% at 10 years.\(^6\) Second, to our knowledge, no data exist on the incidence of complications or the cost-effectiveness of treatment for diabetes in women with histories of GDM. Such women are up to 2 decades younger than those modeled in other cost-effectiveness studies.\(^9\) Third, the benefit of interventions to prevent diabetes in women with impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) has been demonstrated,\(^10\); \(^11\) but the availability of these interventions and the cost-effectiveness estimates vary.\(^12\); \(^13\) Finally, the frequency of screening for diabetes after delivery in women with histories of GDM has been reported to be low.\(^14\); \(^15\) Presumably, adoption of strategies requiring fasting or more than a single blood draw might be optimal but less applicable in practice.

Despite these obstacles, it is possible to compare the yield and costs associated with alternative screening strategies. Such “cost per diabetes case detected” analyses have been used in the assessment of other diabetes screening strategies.\(^16\) In these analyses, we sought to identify the screening strategy that would provide good case yield, sufficient protection from false negative and false-positive results, and acceptable cost.

**Research Design and Methods**

**Study Population**

The study population for our simulation was a cohort representing women with histories of GDM who had normal 6 week postpartum OGTTs. Since not all women have glucose levels before pregnancy, GDM may be diagnosed in women with undiagnosed diabetes before pregnancy and in women who develop glucose intolerance during pregnancy. The OGTT performed 6 weeks postpartum primarily identifies women with undiagnosed diabetes that preceded pregnancy. We therefore chose to exclude this population.\(^17\)

**Screening and Diagnostic Strategies**

We examined several screening strategies. After the 6 week postpartum OGTT, we assumed that women could undergo: 1) an
annual, biannual, or every 3-year 2 hour 75 gram oral glucose tolerance test, with a positive test defined as $\geq 126$ mg/dl on the fasting level or $\geq 200$ mg/dl on the 2 hour level with a sensitivity of 1.0 and specificity of 1.0; 2) an annual, biannual, or every 3-year FPG with a cut point of 126 mg/dl with a sensitivity of 0.5 and a specificity of 0.98; or 3) an annual, biannual, or every 3-year HbA1c with a cut-point of 6.3%, with a sensitivity of 0.48 and a specificity of 1.0.(18) In the base analysis, we assumed that women would be referred for their initial test at an annual gynecological health maintenance visit, and therefore would only be charged for the test and not for an entire additional physician visit, and would not incur time lost from work. We assumed that a positive FPG or HbA1c was followed by confirmatory testing with an FPG and an additional physician visit and we assumed that women with negative confirmatory tests would re-enter the population available for testing. We assumed that women with an initial positive OGTT did not undergo another OGTT. In the scenarios requiring confirmatory testing, the false positive was assumed to have minimal impact beyond the requirement for a follow-up test. Women were assumed to progress to diabetes at a rate of 8% per year.(6) We then estimated the number of cases detected for each strategy after 12 years, the percent of cases detected, the time spent with undiagnosed diabetes, and the number of false positives per strategy.

Cost analysis
The resources used for each strategy and associated costs are illustrated in Table 1. For all strategies, we considered the direct medical cost of screening to include costs incurred at the time of the initial test, including the cost of the screening test (FPG vs. OGTT vs. HbA1c), the cost of $\frac{3}{4}$ of the physician visit for the initial visit,(19) and administrative cost for scheduling the visit.(19) Administrative costs were estimated by assuming a secretarial wage of $13.13 per hour and estimating that the secretarial time used was approximately 1/12 of an hour.(19) Direct medical costs also included costs incurred at the time of the follow-up visit, if warranted, except the cost of an entire physician visit was charged. Laboratory costs were based in 2005 Medicare reimbursement CPT codes(20); physician visit charges were obtained from 2000 estimates(19) then adjusted for inflation to 2005.(21) Cost estimates for secretarial wages were obtained from Bureau of Labor Statistics data from 2005.(22) (19) We then estimated the cost for each woman after 12 years and the cost per case detected.

Sensitivity Analyses
We conducted multiple sensitivity analyses examining different screening scenarios. First, we calculated indirect costs in addition to the direct costs noted above. Indirect costs included the cost of lost work hours (0.75 hours for an FPG or HbA1c and 3.25 hours for an OGTT); the lost time was valued based on median wages from 2005 Bureau of Labor Statistics data.(22) We also included costs of travel ($7.00 per trip) based on a prior analysis.(19) Second, we examined a scenario where women referred for OGTTs actually underwent testing only 50% of the time, where women referred for FPGs actually underwent testing only about 75% of the time, and where women referred for HbA1cs underwent testing all of the time.(19) The rationale for 100% adherence for the HbA1c was that this test does not have to be done fasting and can be performed in the office. We did assume that the repeat FPG after an initial positive screen would have an adherence of 100% due to the concern caused by the first positive test result. Third, we examined a scenario that accounted for both indirect costs and differential adherence. Fourth, we examined a scenario that did not
require a confirmatory FPG for a positive FPG and the associated false positive rate. In these scenarios, we did not estimate any further effects of the false positive due to the nature of the cost per case calculation, which limits estimation of downstream effects. Fifth, we examined a scenario where some women underwent screening for other causes, such as symptoms. We varied this “background detection” screening between 0 and 7.5% of cases detected per year. Sixth, we examined confirmation of an initial positive HbA1c or FPG using an OGTT instead of an FPG. Seventh, we removed the costs for administrative charges from the base case and reduced the lost productivity hours associated with an OGTT to 2 hours. Finally, we decreased the rate of progression of diabetes from 8% to 2% in order to reflect the lower rates of progression reported in predominantly white populations.(6) We extrapolated the base-case results to a cohort of 1000 women and calculated incremental cost per case for annual, biannual, and every 3-year OGTT screening. (23)

**Results**

**Base Case**

The cost per person, cost per case of diabetes detected, the percent of cases detected, and time with undiagnosed diabetes for each screening interval for each strategy are illustrated in Table 2. OGTT resulted in a lower cost per case of diabetes detected than FPG, but slightly higher cost per woman screened than FPG, whether annual, biannual, or every 3-year testing was employed. In general, the longer the screening interval, the lower the cost per case of diabetes detected and the lower the cost per woman screened, with only a 6- to 14-month increase in the duration of undiagnosed diabetes. Testing with HbA1c was inferior to OGTT at every screening interval both in terms of cost per case detected and in cost per woman screened.

**Sensitivity Analyses**

In most sensitivity analyses, OGTT still resulted in lower costs per case detected than either FPG or HbA1c (Table 3). When adherence to OGTT testing was assumed to be 50%, adherence to FPG was assumed to be 75%, and adherence to HbA1c was assumed to be 100%, OGTT still resulted in lower cost per case detected at each screening interval. When we combined indirect costs and differential adherence to tests, a scenario that may more closely mimic the “real-world” situation, the results were similar. When the administrative charges were removed from the base case and the lost productivity associated with OGTT was reduced to 2 hours rather than 3.25 hours, OGTT was still favored. When we varied the rate of progression to diabetes by assuming a 2% progression per year rather than an 8% progression per year, the cost per diabetes case detected was higher than in the base case analyses, but similar patterns of lower costs with longer screening intervals were observed, and the OGTT still led to lower cost per case detected at each screening interval (Figure 1). Varying the background detection rate between 0 and 7.5% of cases still resulted in lower costs per case detected for OGTT compared to FPG and HbA1c (results not shown). Substituting an OGTT as a confirmatory test instead of the FPG did not significantly alter the results (results not shown).

FPG testing led to a lower cost per case detected in 2 scenarios. The first scenario included indirect costs and assumed annual testing. However, with longer screening intervals, OGTT testing resulting in lower cost per case detected (Table 2, sensitivity analysis 1). The second scenario was where a confirmatory FPG was not required and annual testing was assumed. Again, with longer screening intervals, OGTT testing
resulted in lower cost per case detected (Table 2, sensitivity analysis 4). When a confirmatory FPG was not required, false positive rates increased dramatically over the 12 year period; the false positive rate for annual FPG testing was 17%; biannual FPG testing was 9.5%; and every 3-year testing was 6.7%.

**Discussion**
Women with histories of GDM represent a unique population, in that screening for type 2 DM is already generally endorsed due to their high risk.(8; 24) Therefore, screening is already recommended, if not performed.(14) Current recommendations for screening for type 2 diabetes in women with histories of GDM have been guided by considerations of the increased cost and inconvenience of the OGTT, balanced by the concern for the sequelae of undiagnosed diabetes. In this analysis, we found that the increased sensitivity and specificity of the OGTT led to lower cost per diabetes case detected compared to other diagnostic tests. Moreover, we found that less frequent testing led to lower cost per case detected, with relatively small increments in the time spent with undiagnosed diabetes. These findings persisted despite assumptions of lower rates of progression, increased indirect costs for OGTT-based screening strategies, and decreased adherence to OGTT due to its need for multiple blood draws and increased patient time. FPG was a superior testing strategy only when annual testing was performed and indirect costs were included or when annual testing was performed and there was no confirmatory testing.

We considered multiple testing scenarios in our construction of these models. The base case results favored OGTT, so we tried to construct sensitivity analyses with assumptions that would favor FPG or HbA1c. Therefore, sensitivity analyses favored FPG and HbA1c by lower adherence for OGTT (resulting in fewer cases detected for OGTT strategies) and confirmatory tests using FPG rather than OGTT (resulting in lower costs for FPG and HbA1c strategies). However, cost per case detected patterns remained fairly consistent. Moreover, lack of confirmatory testing for FPG led to high false positive rates. Although not calculable in our cost-per case approach, the false positive rates likely have significant downstream effects. In a standard cost-effectiveness analysis, the false positive results would incur multiple repeat glucose measurements and physician visits, as well as testing for other cardiovascular risk factors.

Our report examines the optimal method and frequency of screening, but does not establish the benefit of screening itself. Our report is also limited by the fact that we did not examine all potential screening tests of strategies, but instead tried to target the ones that are recommended or performed most frequently. Finally, we did not attempt to incorporate prevention strategies for glucose intolerance. Although one cost-effectiveness analysis found that such interventions could be cost-saving,(12) another cost-effectiveness analysis did not.(13) These assessments differed primarily because of their different assumptions of the rate of progression from glucose intolerance to diabetes. It is possible that such programs would be cost-effective in populations that rapidly progressed but less effective in populations that progressed more slowly. In addition, using other diabetes disease management programs as a proxy, the availability and cost of such programs probably varies dramatically. Given these variations, it may not be possible to calculate a single cost-effectiveness estimate for the entire population of women with GDM.

We conclude that testing strategies utilizing OGTTs at three-year intervals may yield the lowest cost per diabetes case detected. Such
analyses should guide future recommendations about optimal diabetes screening strategies among women with GDM. More detailed, long-term assessments of the cardiovascular complications among women with a history GDM and their compliance with treatment, as well as the benefits of early treatment, are needed.

Acknowledgments
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References
Table 1. Cost estimates for resources used.

<table>
<thead>
<tr>
<th>Cost Categories</th>
<th>OGGT</th>
<th>FPG</th>
<th>HbA1c</th>
<th>Costs per unit</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physician time</strong></td>
<td>3/4 visit for initial visit</td>
<td>3/4 visit for initial visit</td>
<td>3/4 visit for initial visit</td>
<td>$51.00/visit</td>
<td>(19) (21)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 visit for follow-up if needed</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Secretary time</strong></td>
<td>1/12 hour per visit</td>
<td>1/12 hour per visit</td>
<td>1/12 hour per visit</td>
<td>$15.96/hour</td>
<td>(22)</td>
</tr>
<tr>
<td><strong>Laboratory tests</strong></td>
<td>1 OGGT</td>
<td>1 FPG; if (+), another FPG</td>
<td>1 HbA1c; if (+), an FPG</td>
<td>OGTT: $17.99 per test</td>
<td>(20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>FPG: $6.64 per test</td>
<td>(20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HbA1c: $13.56 per test</td>
<td>(20)</td>
</tr>
<tr>
<td><strong>Mailings</strong></td>
<td>1 for initial visit</td>
<td>1 for initial visit</td>
<td>1 for initial visit</td>
<td>$1.00/mailing</td>
<td>(19)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 for follow-up if needed</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Patient time</strong></td>
<td>3.25 hours</td>
<td>0.75 hours; if (+), another</td>
<td>0.75 hours; if (+), another</td>
<td>$16.24/hour</td>
<td>(22)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.75 hours</td>
<td>0.75 hours</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Comparison of screening strategies for diabetes among women with histories of gestational diabetes mellitus.

**Base case assumptions:** costs include cost of tests and visit but not time lost from work; tests are obtained whenever ordered, rate of progression to diabetes is 8% per year.

<table>
<thead>
<tr>
<th></th>
<th>OGTT every year</th>
<th>FPG every year</th>
<th>HbA1c every year</th>
<th>OGTT every 2 years</th>
<th>FPG every 2 years</th>
<th>HbA1c every 2 years</th>
<th>OGTT every 3 years</th>
<th>FPG every 3 years</th>
<th>HbA1c every 3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost per case detected</td>
<td>$860</td>
<td>$1145</td>
<td>$1288</td>
<td>$502</td>
<td>$924</td>
<td>$1047</td>
<td>$388</td>
<td>$895</td>
<td>$1018</td>
</tr>
<tr>
<td>Cost per person screened</td>
<td>$513</td>
<td>$543</td>
<td>$603</td>
<td>$283</td>
<td>$310</td>
<td>$342</td>
<td>$205</td>
<td>$219</td>
<td>$241</td>
</tr>
<tr>
<td>Percent of cases detected</td>
<td>97.5%</td>
<td>77.4%</td>
<td>76.5%</td>
<td>92.1%</td>
<td>54.8%</td>
<td>53.4%</td>
<td>86.2%</td>
<td>39.9%</td>
<td>38.6%</td>
</tr>
<tr>
<td>Duration (years) of undiagnosed diabetes</td>
<td>0.29</td>
<td>1.73</td>
<td>1.79</td>
<td>0.58</td>
<td>2.51</td>
<td>2.57</td>
<td>0.88</td>
<td>2.95</td>
<td>2.99</td>
</tr>
</tbody>
</table>

*FPG=fasting plasma glucose; OGTT = 2 hour glucose tolerance test with 75 gram challenge*
Table 3. Sensitivity analyses of base case assumptions.

1) Sensitivity analysis assumptions: costs include base case costs and costs of time lost from work; otherwise similar to base case.

<table>
<thead>
<tr>
<th></th>
<th>OGTT every year</th>
<th>FPG every year</th>
<th>HbA1c every year</th>
<th>OGTT every 2 years</th>
<th>FPG every 2 years</th>
<th>HbA1c every 2 years</th>
<th>OGTT every 3 years</th>
<th>FPG every 3 years</th>
<th>HbA1c every 3 years</th>
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</thead>
<tbody>
<tr>
<td>Cost per case detected</td>
<td>$1771</td>
<td>$1621</td>
<td>$1764</td>
<td>$1033</td>
<td>$1308</td>
<td>$1435</td>
<td>$799</td>
<td>$1267</td>
<td>$1395</td>
</tr>
<tr>
<td>Cost per person screened</td>
<td>$1057</td>
<td>$768</td>
<td>$826</td>
<td>$583</td>
<td>$439</td>
<td>$469</td>
<td>$422</td>
<td>$309</td>
<td>$330</td>
</tr>
</tbody>
</table>

2) Sensitivity analysis assumptions: OGTT obtained only 50% after ordering and FPG obtained 75% after ordering; otherwise similar to base case.

<table>
<thead>
<tr>
<th></th>
<th>OGTT every year</th>
<th>FPG every year</th>
<th>HbA1c every year</th>
<th>OGTT every 2 years</th>
<th>FPG every 2 years</th>
<th>HbA1c every 2 years</th>
<th>OGTT every 3 years</th>
<th>FPG every 3 years</th>
<th>HbA1c every 3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost per case detected</td>
<td>$487</td>
<td>$1013</td>
<td>$1288</td>
<td>$321</td>
<td>$870</td>
<td>$1047</td>
<td>$279</td>
<td>$865</td>
<td>$1018</td>
</tr>
<tr>
<td>Cost per person screened</td>
<td>$272</td>
<td>$428</td>
<td>$603</td>
<td>$154</td>
<td>$240</td>
<td>$342</td>
<td>$111</td>
<td>$167</td>
<td>$241</td>
</tr>
<tr>
<td>Percent of cases detected</td>
<td>91.5%</td>
<td>69.0%</td>
<td>76.5%</td>
<td>78.1%</td>
<td>45.0%</td>
<td>53.4%</td>
<td>64.7%</td>
<td>31.5%</td>
<td>38.6%</td>
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</table>

3) Sensitivity analysis assumptions: indirect costs (sensitivity analysis 1) and imperfect adherence to tests (sensitivity analysis 2).

<table>
<thead>
<tr>
<th></th>
<th>OGTT every year</th>
<th>FPG every year</th>
<th>HbA1c every year</th>
<th>OGTT every 2 years</th>
<th>FPG every 2 years</th>
<th>HbA1c every 2 years</th>
<th>OGTT every 3 years</th>
<th>FPG every 3 years</th>
<th>HbA1c every 3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost per case detected</td>
<td>$1003</td>
<td>$1434</td>
<td>$1764</td>
<td>$662</td>
<td>$1232</td>
<td>$1435</td>
<td>$575</td>
<td>$1224</td>
<td>$1395</td>
</tr>
<tr>
<td>Cost per person screened</td>
<td>$562</td>
<td>$605</td>
<td>$826</td>
<td>$316</td>
<td>$339</td>
<td>$469</td>
<td>$228</td>
<td>$236</td>
<td>$330</td>
</tr>
</tbody>
</table>

4) Sensitivity analysis assumptions: no confirmatory test needed for a positive FPG; otherwise similar to base case.

<table>
<thead>
<tr>
<th></th>
<th>OGTT every year</th>
<th>FPG every year</th>
<th>HbA1c every year</th>
<th>OGTT every 2 years</th>
<th>FPG every 2 years</th>
<th>HbA1c every 2 years</th>
<th>OGTT every 3 years</th>
<th>FPG every 3 years</th>
<th>HbA1c every 3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost per case detected</td>
<td>$860</td>
<td>$798</td>
<td>$1288</td>
<td>$502</td>
<td>$528</td>
<td>$1047</td>
<td>$388</td>
<td>$460</td>
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</tr>
<tr>
<td>Cost per person screened</td>
<td>$513</td>
<td>$399</td>
<td>$603</td>
<td>$283</td>
<td>$239</td>
<td>$342</td>
<td>$205</td>
<td>$175</td>
<td>$241</td>
</tr>
<tr>
<td>Percent of cases detected</td>
<td>97.5%</td>
<td>81.8%</td>
<td>76.5%</td>
<td>92.1%</td>
<td>73.8%</td>
<td>53.4%</td>
<td>86.2%</td>
<td>62.2%</td>
<td>38.6%</td>
</tr>
</tbody>
</table>

Duration (years) of undiagnosed diabetes: 0.29, 0.81, 1.79, 0.58, 1.44, 2.57, 0.88, 1.93, 2.99

*FPG=fasting plasma glucose; OGTT = 2 hour glucose tolerance test with 75 gram challenge*
Figure 1. Cost per case detected by annual rate of progression to diabetes, assuming screening every 3 years.