JOURNAL CLUB

Cost-effectiveness of Screening Strategies for Identifying Pediatric Diabetes Mellitus and Dysglycemia

En-Ling Wu, BA; Nayla G. Kazzi, BA; Joyce M. Lee, MD, MPH

Objective: To conduct a cost-effectiveness analysis of screening strategies for identifying children with type 2 diabetes mellitus and dysglycemia (prediabetes/diabetes).

Design: Cost simulation study.

Setting: A one-time US screening program.

Study Participants: A total of 2.5 million children aged 10 to 17 years.

Intervention: Screening strategies for identifying diabetes and dysglycemia.

Main Outcome Measures: Effectiveness (proportion of cases identified), total costs (direct and indirect), and efficiency (cost per case identified) of each screening strategy based on test performance data from a pediatric cohort and cost data from Medicare and the US Bureau of Labor Statistics.

Results: In the base-case model, 500 and 400 000 US adolescents had diabetes and dysglycemia, respectively. For diabetes, the cost per case was extremely high ($312 000-$831 000 per case identified) because of the low prevalence of disease. For dysglycemia, the cost per case was in a more reasonable range. For dysglycemia, preferred strategies were the 2-hour oral glucose tolerance test (100% effectiveness; $390 per case), 1-hour glucose challenge test (63% effectiveness; $571), random glucose test (55% effectiveness; $498), or a hemoglobin A_{1c} threshold of 5.5% (45% effectiveness; $763). Hemoglobin A_{1c} thresholds of 5.7% and 6.5% were the least effective and least efficient (ranges, 7%-32% and $938-$3370) of all strategies evaluated. Sensitivity analyses for diabetes revealed that disease prevalence was a major driver of cost-effectiveness. Sensitivity analyses for dysglycemia did not lead to appreciable changes in overall rankings among tests.

Conclusions: For diabetes, the cost per case is extremely high because of the low prevalence of the disease in the pediatric population. Screening for diabetes could become more cost-effective if dysglycemia is explicitly considered as a screening outcome.

JAMA Pediatr. 2013;167(1):32-39.
Published online November 19, 2012.
doi:10.1001/jamapediatrics.2013.419

Author Affiliations: Division of Pediatric Endocrinology, Child Health Evaluation and Research Unit, University of Michigan Medical School (Mr Wu and Ms Kazzi), and Divisions of General Pediatrics (Dr Lee) and Pediatric Endocrinology (Dr Lee), University of Michigan, Ann Arbor.

GIVEN REPORTS OF INCREASING levels of type 2 diabetes mellitus (T2D) in children and adolescents during the late 1990s, the American Diabetes Association (ADA) established population-based pediatric screening guidelines for T2D in 2000, which were also endorsed by the American Academy of Pediatrics (AAP).[1] The ADA guidelines were based on the best evidence available at the time, recommending that asymptomatic high-risk adolescents (ie, those with a body mass index ≥85th percentile for age and sex and 2 additional risk factors, including positive family history of T2D, nonwhite ethnic origin, signs of insulin resistance, or maternal history of diabetes or gestational diabetes) be screened for T2D with either a fasting plasma glucose test or a fasting 2-hour oral glucose tolerance test (OGTT).

Despite the guidelines, only a fraction of pediatric health care professionals (4%-21%) in the primary care setting report screening practices consistent with ADA guidelines, in large part due to the inconvenience of the fasting requirement.[2,3] As part of an effort to lower screening barriers, the ADA updated its diabetes diagnostic guidelines in 2010, advocating the use of hemoglobin A_{1c} (HbA_{1c}) for the diagnosis of diabetes and prediabetes for adults and children, which could lead to increased uptake of this test for screening purposes.[4]

Journal Club slides available at www.jamapeds.com

CME available online at www.jamanetworkcme.com and questions on page 6

One-third of the US pediatric population is classified as overweight or obese,[5] and the Centers for Disease Control and Prevention has estimated that up to 2.5 million US adolescents potentially qualify for T2D screening.[6] Ideally, screening strategies should be valid and reliable, and their overall costs and cost-effectiveness are also important considerations,[7,8] particularly given the low prevalence of undiagnosed diabetes in the pediatric population (0.02%).[9-11] Although previous investigators have reported on the cost-effectiveness of various screening strategies for identifying diabetes and dysglycemia (prediabetes or diabetes) in adults,[12,13] we are unaware of similar studies in children. Therefore, our objective was to examine the total costs, effectiveness, and efficiency of different screening strategies for identifying children with diabetes and dysglycemia. We considered dysglycemia as an outcome given that it has a relatively high prevalence in the US pediatric population (16%-23%)[14,15] and its early detection could lead to prevention or delay of the development of diabetes.[16]

METHODS

STUDY POPULATION

On the basis of estimates of the number of overweight or obese US children eligible for diabetes screening,[6] our study population consisted of a hypothetical cohort of 2.5 million children aged 10 to 17 years.[6] For our base-case analyses, we assumed a 16% prevalence of dysglycemia and a 0.02% prevalence of diabetes based on national estimates.[11,15,17] We assumed 100% adherence to the screening strategies, including the initial and confirmatory screens.

COST-EFFECTIVENESS ANALYSIS

We evaluated a variety of different screening strategies for identifying children with diabetes and dysglycemia.

Identifying Diabetes

The initial strategy we considered was the 2-hour OGTT, with the assumption that all eligible participants were tested. No confirmatory screen was required for this strategy because it is considered the criterion standard and has been used to define diabetes and prediabetes in landmark trials, such as the Diabetes Prevention Program.[4,16] We assumed a test performance of 100% sensitivity and specificity, similar to previous studies.[12,18] We then tested 3 additional strategies using HbA_{1c}, including thresholds of 6.5% (ADA definition of diabetes), 5.7% (ADA definition of prediabetes),[19] and 5.5% (a threshold suggested as an optimal cutoff for detecting prediabetes in children).[20] For all the HbA_{1c} strategies, we assumed a 2-step screening strategy in which only individuals with a positive initial test result (ie, above the defined threshold) receive a confirmatory 2-hour OGTT. Assumptions of test performance for HbA_{1c} for the base case were based on a previously studied clinical cohort of children for whom the outcome of dysglycemia was studied.[21] Because the diabetes test performance data were not previously published in that study, we conducted the analyses with the same pediatric cohort for the outcome of diabetes (see test performance results in the eTable; http://www.jamapeds.com), for which 3 children were identified as having diabetes.

Table 1. Test Performance Assumptions for Various Screening Strategies (at Selected Thresholds) for Identifying Children With Diabetes Mellitus and Dysglycemia for the Base-Case Analysis and Sensitivity Analyses

Screening Strategy and Cutoff Value	Sensitivity, %	Specificity, %
Base-Case Analysis		
Diabetes mellitus		
2-h OGTT (200 mg/dL)	100	100
HbA_{1c}		
5.5%	33	56
5.7%	33	71
6.5%	33	96
Dysglycemia (prediabetes and diabetes)		
2-h OGTT (140 mg/dL)	100	100
Random glucose test		
100 mg/dL	55	67
110 mg/dL	30	88
HbA_{1c}		
5.5%	45	57
5.7%	32	74
6.5%	7	98
1-h Glucose challenge test		
110 mg/dL	63	63
120 mg/dL	44	81
Sensitivity Analyses		
Diabetes mellitus		
HbA_{1c}		
5.7%	71	79
6.5%	32	99
Dysglycemia (prediabetes and diabetes)		
HbA_{1c}		
5.7%	34	83
6.5%	4	100

Abbreviations: HbA_{1c} hemoglobin A_{1c}; OGTT, oral glucose tolerance test.

Identifying Prediabetes

For prediabetes, we also evaluated a 2-hour OGTT, assuming 100% sensitivity and specificity. For the additional strategies, we assumed a 2-step screening strategy (confirmatory 2-hour OGTT after a positive initial test result) to evaluate HbA_{1c} at thresholds of 5.5%, 5.7%, and 6.5%; random glucose test results (blood glucose level in a nonfasting state) at thresholds of 100 and 110 mg/dL (to convert to millimoles per liter, multiply by 0.0555); and a 1-hour glucose challenge test (GCT) result (blood glucose measurement 1 hour after ingestion of 50 g of Glucola in a nonfasting state) at thresholds of 110 and 120 mg/dL. We acknowledge that the random glucose test and the 1-hour GCT are not endorsed by the ADA; however, we thought that cost-effectiveness evaluation of these strategies was warranted given their improved test performance over HbA_{1c} in a previously published study.[21]

Our analyses were conducted from the health care system perspective (direct costs) and the societal perspective (direct plus indirect costs). **Table 1** gives the test performance assumptions used for the base-case analysis and sensitivity analyses. The direct and indirect cost assumptions for each screening strategy are listed in **Table 2**. Direct costs were calculated using Medicare reimbursement rates[22] and included costs of the initial screening test, the follow-up 2-hour OGTT, and health care provider time.

Table 2. Cost Assumptions for the Base-Case Analysis[a]

Screening Strategy	Cost Per Screen, $	Additional Time for Testing, min
2-h OGTT	18.44	135
Random glucose test	5.62	15
HbA_{1c}	13.90	15
1-h Glucose challenge test	6.80	75

Abbreviations: HbA_{1c} hemoglobin A_{1c}; OGTT, oral glucose tolerance test.
[a]The half mean hourly wage for all occupations in 2010 was $10.68 per hour. Provider time was one-fifth the cost of a primary care visit ($20).

Provider time for identification of high-risk patients and interpretation of laboratory results was valued at one-fifth the cost ($20) of a full primary care visit (25 minutes of face-to-face time) for all screening strategies. Indirect costs were calculated using wage data from the US Bureau of Labor Statistics[23] and accounted for the value of the patients' time, which was calculated as the lost wages of the parent/guardian (who must accompany their child to the screening). As a conservative estimate, parent/guardian time was valued at half the mean hourly wage for all occupations in 2010.[24] All cost data were expressed in 2010 US dollars.

We conducted sensitivity analyses to assess the effect of differing levels of (1) adherence (75% adherence to the nonfasting screening strategies and 75% and 50% adherence to the 2-hour OGTT), (2) changes in the prevalence of dysglycemia or diabetes (±25% and adult prevalence estimates), (3) costs (doubling of provider time costs and reduction in HbA_{1c} costs by half), and (4) alternate estimates of test performance for HbA_{1c} from an additional pediatric study.[20]

OUTCOME VARIABLES

Our main outcome of interest was the *cost per identified case of diabetes or dysglycemia* (efficiency) from the health care (direct medical costs associated with testing) and societal (direct medical costs plus indirect costs associated with parent/guardian time) perspectives. To derive this estimate, we had to assess total costs from the health care and societal perspectives and the percentage of cases of diabetes and dysglycemia identified (effectiveness). All analyses were conducted using Excel 2010 (Microsoft Inc). Results for the sensitivity analyses from the health care system perspective are available on request.

RESULTS

Table 3 gives the results of the base-case analysis from the societal and health care system perspectives. In the base-case model, there were 500 adolescents with diabetes and 400 000 adolescents with dysglycemia.

Total costs for a one-time screening were in a similar range for dysglycemia and diabetes, between 94 million and 156 million US dollars, because the same pool of eligible children would need to be screened regardless of the disease prevalence. Total costs were highest for the 2-hour OGTT for both dysglycemia and diabetes, in part due to higher test costs and the patient time costs associated with a longer test (2½ hours).

For diabetes, the 2-hour OGTT had the highest test effectiveness, detecting 100% of cases vs 33% for the HbA_{1c} strategies. The cost per case was extremely high for all strategies because of the small number of children with diabetes: $312 000 per case for the 2-hour OGTT and $571 000 to $831 000 per case for the HbA_{1c} strategies.

Figure 1A shows effectiveness and efficiency for the base-case diabetes analysis from the societal perspective. The figure illustrates tradeoffs between 2 competing goals of screening efforts: identifying a greater proportion of cases and minimizing the cost per case identified. Preferred screening strategies are in the upper left, maximizing the percentage of cases identified and minimizing the total costs per case. In contrast, least preferred screening strategies are in the bottom right. On the basis of these criteria, the 2-hour OGTT was the most desirable strategy for diabetes. Effectiveness was similar across the various HbA_{1c} thresholds; however, the cost per case was lowest for the HbA_{1c} threshold of 6.5%.

For dysglycemia, the 2-hour OGTT strategy had the highest test effectiveness (100%) followed by a 1-hour GCT threshold of 110 mg/dL (63%), a random glucose threshold of 100 mg/dL (55%), and an HbA_{1c} threshold of 5.5% (45%). The HbA_{1c} thresholds of 5.7% and 6.5% had lower levels of effectiveness (32% and 7%, respectively).The 2-hour OGTT had the lowest total costs per case identified ($390), followed by a random glucose threshold of 100 mg/dL ($498), a 1-hour GCT threshold of 110 mg/dL ($571), and an HbA_{1c} threshold of 5.5% ($763). In contrast, HbA_{1c} thresholds of 5.7% and 6.5% had the highest costs per case identified, ranging from $938 to $3370.

Figure 2A shows effectiveness plotted against efficiency for dysglycemia from the societal perspective. The 2-hour OGTT was the most desirable strategy, followed by a 1-hour GCT, a random glucose test, and an HbA_{1c} level of 5.5%. The HbA_{1c} thresholds of 5.7% and 6.5% were the least desirable strategies.

In our sensitivity analyses, similar trends were seen for diabetes and dysglycemia. Lower adherence to the nonfasting strategies and to the 2-hour OGTT decreased total costs and screening effectiveness (**Table 4**). Cost per case identified was unchanged for the 2-hour OGTT but increased for the nonfasting strategies given an increasing number of missed cases.

A higher prevalence of disease slightly increased total costs but resulted in a lower cost per case, whereas a lower prevalence slightly decreased total costs and resulted in a higher cost per case (**Table 5**). When we assumed a population prevalence of diabetes and dysglycemia similar to adult levels, the cost per case decreased markedly for both outcomes but particularly for diabetes, which decreased from $312 000 to $831 000 per case to $781 to $2064 per case.

Doubling of provider time resulted in higher total costs and higher cost per case identified (**Table 6**), and halving the price of HbA_{1c} resulted in slightly lower total costs and lower cost per case, with no changes in the effectiveness estimates for either sensitivity analysis.

Finally, when we assumed alternate test performance characteristics for HbA_{1c} for diabetes,[20] the cost per case identified was lower ($320 000-$578 000) compared with the base case ($571 000-$831 000) due to improved test performance but still remained quite high (Figure 1B). For dysglycemia, the cost per case was lower

Table 3. Proportion of Cases and Costs Identified for the Different Screening Strategies for the Base-Case Analysis

Screening Strategy and Cutoff Value	Cases Identified, %	Total Costs (Direct), $	Total Costs (Direct and Indirect), $	Cost per Case Identified (Direct), $	Cost per Case Identified (Direct and Indirect), $
Diabetes mellitus					
2-h OGTT (200 mg/dL)	100	96 065 001	156 111 876	192 130	312 224
HbA_{1c}					
5.5%	33	105 182 379	138 513 737	631 157	831 166
5.7%	33	97 992 217	121 958 136	588 012	731 822
6.5%	33	86 377 340	95 214 473	518 316	571 344
Dysglycemia (prediabetes and diabetes)					
2-h OGTT (140 mg/dL)	100	96 065 001	156 111 876	240	390
Random glucose test					
100 mg/dL	55	80 850 720	109 451 714	368	498
110 mg/dL	30	70 874 680	86 481 530	591	721
HbA_{1c}					
5.5%	45	104 685 520	137 369 701	582	763
5.7%	32	97 143 559	120 004 072	759	938
6.5%	7	86 005 799	94 358 987	3072	3370
1-h Glucose challenge test					
110 mg/dL	63	85 939 761	144 014 430	341	571
120 mg/dL	44	77 568 001	124 738 157	441	709

Abbreviations: HbA_{1c} hemoglobin A_{1c}; OGTT, oral glucose tolerance test.

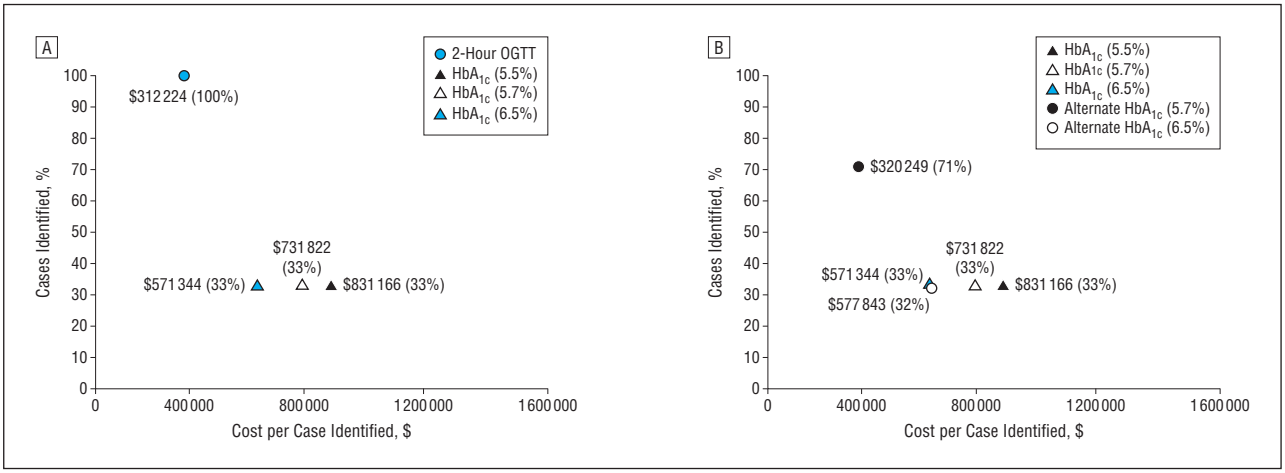

Figure 1. Screening effectiveness for diabetes (percentage of cases identified) plotted against screening efficiency (costs per case identified) from a societal perspective. A, Base-case analysis; B, alternative estimates of hemoglobin A_{1c} (HbA_{1c}) test performance. OGTT indicates oral glucose tolerance test.

for a threshold of 5.7% ($826 vs $938) because of improved test performance, and the cost per case was higher for a threshold of 6.5% ($5754 vs $3370) because of lower test performance (Figure 2B).

Across the multiple sensitivity analyses for dysglycemia, the relative rankings of efficiency and effectiveness for the various screening strategies for dysglycemia were similar to the base case.

COMMENT

This study evaluated the total costs, effectiveness, and efficiency (cost per case identified) of a number of different screening strategies for identifying children with diabetes and dysglycemia. One of the most striking findings of our study was the very high cost per case of screening for T2D in adolescents regardless of test type, ranging from $312 000 to $831 000 per case identified. This finding is due to the low prevalence of T2D in the US pediatric population.[11]

The ADA formulated the first screening guidelines for T2D in children in 2000 in response to an epidemic of obesity and increasing reports of a T2D phenotype in tertiary care clinics[25] and high-risk populations.[26] At the time that the recommendations were made, empirical data on screening efficacy and costs for T2D were not available; therefore, the recommendations were based on expert opinion. Since that time, a number of population-based studies[9-11,27] evaluating the epidemiology of pediatric diabetes have been conducted and suggest that the overall burden of T2D in children is still low, particularly compared with the burden among adults.

A similar study[13] conducted in adults reported a cost per case identified of T2D, ranging from $600 to $850

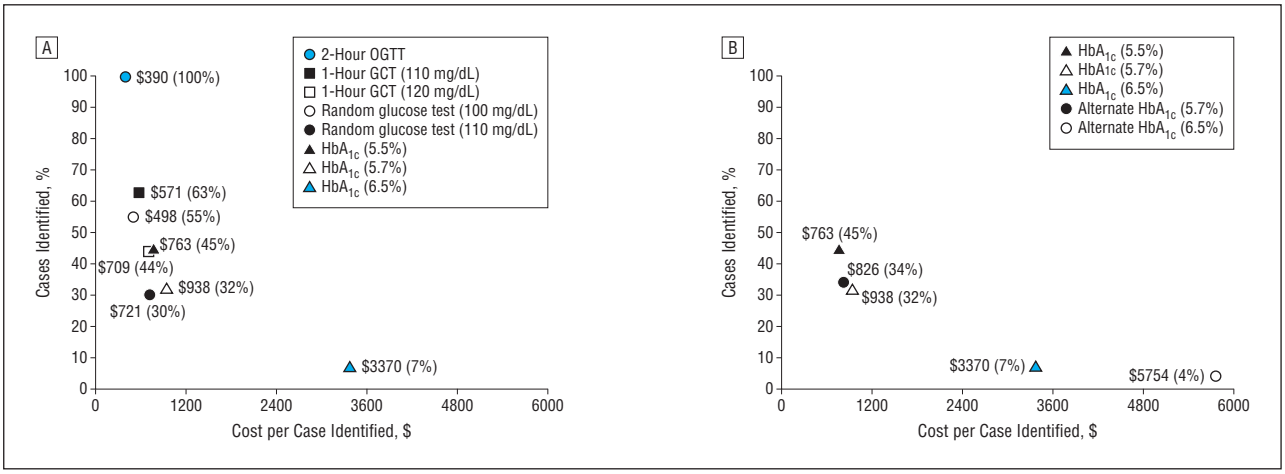

Figure 2. Screening effectiveness for dysglycemia (percentage of cases identified) plotted against screening efficiency (costs per case identified) from a societal perspective. A, Base-case analysis; B, alternative estimates of hemoglobin A_{1c} (HbA_{1c}) test performance. GCT indicates glucose challenge test; and OGTT, oral glucose tolerance test.

Table 4. Proportion of Cases and Costs Identified for the Different Screening Strategies for 75% Adherence to Initial Nonfasting Screening Strategies and 75% or 50% Adherence to 2-Hour OGTT

	75% Adherence to Nonfasting Screening and 75% Adherence to 2-Hour OGTT			75% Adherence to Nonfasting Screening and 50% Adherence to 2-Hour OGTT		
Screening Strategy and Cutoff Value	Cases Identified, %	Total Costs (Direct and Indirect), $	Cost per Case Identified (Direct and Indirect), $	Cases Identified, %	Total Costs (Direct and Indirect), $	Cost per Case Identified (Direct and Indirect), $
Diabetes mellitus						
2-h OGTT (200 mg/dL)	75	117 083 907	312 224	50	78 055 938	312 224
HbA_{1c}						
5.5%	19	94 810 233	1 011 410	12	86 053 541	1 376 994
5.7%	19	85 855 882	915 888	12	80 083 973	1 281 472
6.5%	19	70 931 963	756 683	12	70 134 694	1 122 267
Dysglycemia (prediabetes and diabetes)						
2-h OGTT (140 mg/dL)	75	117 083 907	390	50	78 055 938	390
Random glucose test						
100 mg/dL	31	74 820 378	605	21	67 551 971	819
110 mg/dL	17	61 899 650	917	11	58 938 152	1310
HbA_{1c}						
5.5%	25	94 405 496	932	17	85 783 716	1271
5.7%	18	84 637 329	1176	12	79 271 605	1651
6.5%	4	70 211 969	4458	3	69 654 698	6634
1-h Glucose challenge test						
110 mg/dL	35	99 818 937	704	24	91 627 052	970
120 mg/dL	25	88 976 034	899	17	84 398 450	1279

Abbreviations: HbA_{1c} hemoglobin A_{1c}; OGTT, oral glucose tolerance test.

per case across a variety of HbA_{1c} thresholds and assuming a national T2D prevalence of 8%. When we assumed a similar prevalence for our pediatric population, the cost per case for children was reduced markedly, closer to the range reported in adults, suggesting that disease prevalence is the major determinant of cost-effectiveness for diabetes screening in children.

We did not explicitly calculate costs per quality-adjusted life-year for our analysis, which makes determination of cost-effectiveness difficult, but the extremely high cost per case values would suggest that screening for T2D in children may not fall into the cost-effective range. In contrast, our analyses for identification of dysglycemia resulted in much more reasonable cost-per-case ratios. A screening program for glucose abnormalities could therefore be considered more cost-effective if dysglycemia were explicitly considered as a screening outcome. However, the ADA and AAP guidelines are focused on screening for diabetes as the primary outcome.

Screening for dysglycemia could be endorsed by the ADA and AAP because studies[28,29] such as the Diabetes Prevention Program in adults have demonstrated that early identification and treatment of individuals with prediabetes is both effective and cost-effective for reducing the rates of diabetes. However, it is unclear whether these conclusions could be extrapolated to the pediatric population, especially given the accelerated progression of dis-

Table 5. Proportion of Cases and Costs Identified for the Different Screening Strategies for a 25% Increase in Prevalence, a 25% Decrease in Prevalence, or Adult Prevalence Assumptions

Screening Strategy and Cutoff Value	Cases Identified, %	25% Increase in Prevalence		25% Decrease in Prevalence		Adult Prevalence Assumptions (8% for Diabetes and 37% for Prediabetes)	
		Total Costs (Direct and Indirect), $	Cost per Case Identified (Direct and Indirect), $	Total Costs (Direct and Indirect), $	Cost per Case Identified (Direct and Indirect), $	Total Costs (Direct and Indirect), $	Cost per Case Identified (Direct and Indirect), $
Diabetes mellitus							
2-h OGTT (200 mg/dL)	100	156 111 876	249 779	156 111 876	416 298	156 111 876	781
HbA_{1c}							
5.5%	33	138 513 150	664 930	138 514 325	1 108 225	137 576 050	2064
5.7%	33	121 958 377	585 459	121 957 896	975 761	122 341 851	1835
6.5%	33	95 216 051	457 083	95 212 895	761 779	97 732 759	1466
Dysglycemia (prediabetes and diabetes)							
2-h OGTT (140 mg/dL)	100	156 111 876	312	156 111 876	520	156 111 876	169
Random glucose test							
100 mg/dL	55	110 385 806	401	108 517 621	658	114 355 700	225
110 mg/dL	30	87 245 787	582	85 717 272	952	90 493 882	326
HbA_{1c}							
5.5%	45	137 454 618	611	137 284 783	1017	137 815 518	331
5.7%	32	120 258 824	752	119 749 319	1247	121 341 523	410
6.5%	7	94 571 280	2702	94 146 693	4483	95 473 529	1474
1-h Glucose challenge test							
110 mg/dL	63	145 118 357	461	142 910 502	756	149 810 049	257
120 mg/dL	44	125 799 626	572	123 676 688	937	130 310 868	326

Abbreviations: HbA_{1c} hemoglobin A_{1c}; OGTT, oral glucose tolerance test.

Table 6. Proportion of Cases and Costs Identified for the Different Screening Strategies for Doubling the Provider Costs or Cutting the HbA_{1c} Test Costs in Half

Screening Strategy and Cutoff Value	Cases Identified, %	Double Provider Costs, $		50% HbA_{1c} Test Costs, $	
		Total Costs (Direct and Indirect)	Cost per Case Identified (Direct and Indirect)	Total Costs (Direct and Indirect)	Cost per Case Identified (Direct and Indirect)
Diabetes mellitus					
2-h OGTT (200 mg/dL0	100	206 076 8 76	412 154		
HbA_{1c}					
5.5%	33	188 478 737	1 130 986	121 138 738	726 905
5.7%	33	171 923 136	1 031 642	104 583 137	627 562
6.5%	33	145 179 473	871 164	77 839 474	467 084
Dysglycemia (prediabetes and diabetes)					
2-h OGTT (140 mg/dL)	100	206 076 876	515		
Random glucose test					
100 mg/dL	55	159 416 714	725		
110 mg/dL	30	136 446 530	1137		
HbA_{1c}					
5.5%	45	187 334 701	1041	119 994 702	667
5.7%	32	169 969 072	1328	102 629 073	802
6.5%	7	144 323 987	5154	76 983 988	2749
1-h Glucose challenge test					
110 mg/dL	63	193 979 430	770		
120 mg/dL	44	174 703 157	993		

Abbreviations: HbA_{1c} hemoglobin A_{1c}; OGTT, oral glucose tolerance test.

ease reported in adolescents vs adults[30] and the fact that the benefits of early detection of dysglycemia in children are currently unknown.[31]

When comparing our cost-per-case ratios for identifying dysglycemia with adult studies,[13] the cost-per-case ratios were in a similar range but were higher for our pediatric population ($390-$3000 per case) compared with adults ($150-$500 per case). Again, this finding was likely in part due to the lower prevalence of prediabetes as shown by the results of our sensitivity analysis when we assumed a prevalence similar to the adult population (37%).

When comparing screening strategies for dysglycemia, the 2-hour OGTT (a fasting test) was the preferred strategy. However, previous studies[2,3,32] have shown remarkably low adherence with ADA-recommended screening tests among providers (4%-21%) in pediatric settings, most likely due to their onerous fasting requirement and associated increase in nonadherence rates among patients. Given these findings, the nonfasting 1-hour GCT and random glucose test may represent convenient and preferred screening alternatives for health care professionals. If efficiency (lower cost per case) were prioritized, then the random glucose test (100 mg/dL) would be a preferred strategy. Alternatively, if effectiveness (percentage of cases identified) were prioritized, then the 1-hour GCT (110 mg/dL) would be preferred.

The HbA_{1c} thresholds of 5.7% and 6.5% were the least preferred strategies because they had the highest cost per case and the highest proportion of cases missed—a finding that has important policy implications given the recent ADA guidelines recommending the exclusive use of HbA_{1c} for the diagnosis of prediabetes and diabetes in children. The guidelines will likely lead to increased use of HbA_{1c} as a screening test. Given our findings, reconsideration of the new HbA_{1c} guidelines or a lowering of the HbA_{1c} threshold to 5.5% may be warranted.

We are unaware of previous studies that have compared the cost-effectiveness of different nonfasting screening strategies for identifying diabetes and dysglycemia in children. Previous studies[13] have focused exclusively on adults for whom there are notable differences in test performance and disease prevalence.[33] Strengths of our study include the fact that our model simulation was based on empiric screening data in overweight and obese children[20,21] and the fact that our findings were robust to a variety of sensitivity analyses that explored changes in dysglycemia prevalence, testing adherence, provider time costs, lower test costs, and alternate test performance estimates for HbA_{1c}.

We acknowledge several limitations of our study. First, we assessed the cost-effectiveness of a one-time screening of the pediatric population, despite the ADA recommendation that children receive biannual screenings because of a lack of longitudinal data regarding pediatric screening outcomes. Second, we used Medicare estimates for our cost assumptions. Testing costs may vary by payer; however, our objective was to evaluate the relative costs of different screening strategies. Third, our analysis included only costs associated with the detection of diabetes and dysglycemia, which represents just one aspect of the total costs associated with screening programs and did not consider the costs associated with treatment, health care utilization, or downstream productivity costs. Fourth, we did not address the benefits of early detection, including improvements in length and quality of life. Last, our test performance data relied on a single 2-hour OGTT to classify children as having dysglycemia. Although most studies of children and adults with dysglycemia rely on this definition,[9,18,34,35] we acknowledge that some studies[36] have reported a lack of reproducibility of the 2-hour OGTT results in children.

We recognize that all overweight and obese children likely require aggressive lifestyle management, regardless of their glycemic status, to reduce the risk of comorbidities. However, given limited health care resources, early identification of children with dysglycemia may represent a reasonable strategy for targeting the children at highest risk.

Since the recent guidelines recommending HbA_{1c} for diagnosis of diabetes in children and adults, commentaries have highlighted testing costs as an important issue for determining which tests should be prioritized.[37] Total costs, efficiency (cost per case), and effectiveness (proportion of cases identified) of screening at-risk individuals are important criteria for determining optimal screening policy, and our findings highlight important tradeoffs to consider for the pediatric population. Future longitudinal studies are needed to evaluate the long-term outcomes (effectiveness and cost-effectiveness) of screening for pediatric glucose abnormalities, particularly for the most promising strategies (1-hour GCT and random glucose test).

The high cost per case of screening for diabetes should inform future pediatric screening policy. The low effectiveness and high cost per case of current recommended HbA_{1c} thresholds warrant reconsideration of the recent ADA guidelines recommending HbA_{1c} measurement for the diagnosis of diabetes and dysglycemia in adolescents.

Accepted for Publication: June 21, 2012.
Published Online: November 19, 2012. doi:10.1001/jamapediatrics.2013.419
Correspondence: Joyce Lee, MD, MPH, Division of Pediatric Endocrinology, Child Health Evaluation and Research Unit, Child Health Evaluation and Research Unit, University of Michigan, 300 NIB, Room 6E18, Campus Box 5456, Ann Arbor, MI 48109-5456 (joyclee@umich.edu).
Author Contributions: *Acquisition of data:* Wu, Kazzi, and Lee. *Analysis and interpretation of data:* Wu, Kazzi, and Lee. *Drafting of the manuscript:* Wu, Kazzi, and Lee. *Critical revision of the manuscript for important intellectual content:* Kazzi and Lee. *Statistical analysis:* Wu, Kazzi, and Lee. *Obtained funding:* Lee. *Administrative, technical, and material support:* Kazzi and Lee. *Study supervision:* Lee.
Conflict of Interest Disclosures: None reported.
Funding/Support: Dr Lee was supported by grant K08 DK082386 from the National Institute of Diabetes and Digestive and Kidney Disorders and the Clinical Sciences Scholars Program at the University of Michigan. This project was supported by the following: grant UL1RR024986 from the Michigan Clinical Research Unit, Michigan Institute for Clinical and Health Research Pilot and Collaborative Grant UL1RR024986, Blue Cross Blue Shield Foundation of Michigan Investigator Initiated Research Grant, and grants from the University of Michigan (Elizabeth Kennedy Award, Elizabeth Crosby Funds, and Office of the Vice President for Research). This work used the laboratory core(s) of the Michigan Diabetes Research and Training Center funded by grant 5P60 DK20572 from the National Institute of Diabetes and Digestive and Kidney Disorders, National Institutes of Health.
Online-Only Material: The eTable is available at http://www.jamapeds.com.

Additional Contributions: We thank Courtney Nelson, BS, for her assistance with the manuscript.

REFERENCES

1. American Diabetes Association. Type 2 diabetes in children and adolescents. *Pediatrics*. 2000;105(3, pt 1):671-680.
2. Rhodes ET, Finkelstein JA, Marshall R, Allen C, Gillman MW, Ludwig DS. Screening for type 2 diabetes mellitus in children and adolescents: attitudes, barriers, and practices among pediatric clinicians. *Ambul Pediatr*. 2006;6(2):110-114.
3. Anand SG, Mehta SD, Adams WG. Diabetes mellitus screening in pediatric primary care. *Pediatrics*. 2006;118(5):1888-1895.
4. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2010;33(suppl 1):S62-S69.
5. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity in the United States, 2009-2010. *NCHS Data Brief*. 2012;(82):1-8.
6. Fagot-Campagna A, Saaddine JB, Engelgau MM. Is testing children for type 2 diabetes a lost battle? *Diabetes Care*. 2000;23(9):1442-1443.
7. Edgell C. Costs of screening are important. *BMJ*. 1993;306(6880):797.
8. Grimes DA, Schulz KF. Uses and abuses of screening tests. *Lancet*. 2002;359(9309): 881-884.
9. Dolan LM, Bean J, D'Alessio D, et al. Frequency of abnormal carbohydrate metabolism and diabetes in a population-based screening of adolescents. *J Pediatr*. 2005;146(6):751-758.
10. Lee JM. Why young adults hold the key to assessing the obesity epidemic in children. *Arch Pediatr Adolesc Med*. 2008;162(7):682-687.
11. Liese AD, D'Agostino RB Jr, Hamman RF, et al; SEARCH for Diabetes in Youth Study Group. The burden of diabetes mellitus among US youth: prevalence estimates from the SEARCH for Diabetes in Youth Study. *Pediatrics*. 2006;118 (4):1510-1518.
12. Zhang P, Engelgau MM, Valdez R, Benjamin SM, Cadwell B, Narayan KM. Costs of screening for pre-diabetes among US adults: a comparison of different screening strategies. *Diabetes Care*. 2003;26(9):2536-2542.
13. Zhang P, Engelgau MM, Valdez R, Cadwell B, Benjamin SM, Narayan KM. Efficient cutoff points for three screening tests for detecting undiagnosed diabetes and pre-diabetes: an economic analysis. *Diabetes Care*. 2005;28(6):1321-1325.
14. May AL, Kuklina EV, Yoon PW. Prevalence of cardiovascular disease risk factors among US adolescents, 1999-2008. *Pediatrics*. 2012;129(6):1035-1041.
15. Cowie CC, Rust KF, Ford ES, et al. Full accounting of diabetes and pre-diabetes in the U.S. population in 1988-1994 and 2005-2006. *Diabetes Care*. 2009;32 (2):287-294.
16. Knowler WC, Barrett-Connor E, Fowler SE, et al; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346(6):393-403.
17. Li C, Ford ES, Zhao G, Mokdad AH. Prevalence of pre-diabetes and its association with clustering of cardiometabolic risk factors and hyperinsulinemia among U.S. adolescents: National Health and Nutrition Examination Survey 2005-2006. *Diabetes Care*. 2009;32(2):342-347.
18. Johnson SL, Tabaei BP, Herman WH. The efficacy and cost of alternative strategies for systematic screening for type 2 diabetes in the U.S. population 45-74 years of age. *Diabetes Care*. 2005;28(2):307-311.
19. American Diabetes Association. Standards of medical care in diabetes—2010. *Diabetes Care*. 2010;33(suppl 1):S11-S61.
20. Nowicka P, Santoro N, Liu H, et al. Utility of hemoglobin A_{1c} for diagnosing prediabetes and diabetes in obese children and adolescents. *Diabetes Care*. 2011; 34(6):1306-1311.
21. Lee JM, Gebremariam A, Wu EL, LaRose J, Gurney JG. Evaluation of nonfasting tests to screen for childhood and adolescent dysglycemia. *Diabetes Care*. 2011; 34(12):2597-2602.
22. Physician fee schedule. Centers for Medicare & Medicaid Services website. 2011. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/index.html?redirect=/PhysicianFeeSched/. Accessed October 13, 2011.
23. US Department of Labor. Occupational employment statistics. Bureau of Labor Statistics website. 2011. http://bls.gov/oes/. Accessed September 22, 2011.
24. Chatterjee R, Narayan KM, Lipscomb J, Phillips LS. Screening adults for prediabetes and diabetes may be cost-saving. *Diabetes Care*. 2010;33(7):1484-1490.
25. Pinhas-Hamiel O, Dolan LM, Daniels SR, Standiford D, Khoury PR, Zeitler P. Increased incidence of non-insulin-dependent diabetes mellitus among adolescents. *J Pediatr*. 1996;128(5, pt 1):608-615.
26. Pavkov ME, Hanson RL, Knowler WC, Bennett PH, Krakoff J, Nelson RG. Changing patterns of type 2 diabetes incidence among Pima Indians. *Diabetes Care*. 2007;30(7):1758-1763.
27. Goran MI, Davis J, Kelly L, et al. Low prevalence of pediatric type 2 diabetes: where's the epidemic? *J Pediatr*. 2008;152(6):753-755.
28. Diabetes Prevention Program Research Group. Within-trial cost-effectiveness of lifestyle intervention or metformin for the primary prevention of type 2 diabetes. *Diabetes Care*. 2003;26(9):2518-2523.
29. Diabetes Prevention Program Research Group. The 10-year cost-effectiveness of lifestyle intervention or metformin for diabetes prevention: an intent-to-treat analysis of the DPP/DPPOS. *Diabetes Care*. 2012;35(4):723-730.
30. Zeitler P, Hirst K, Pyle L, et al; TODAY Study Group. A clinical trial to maintain glycemic control in youth with type 2 diabetes. *N Engl J Med*. 2012;366(24): 2247-2256.
31. Gillman MW. Predicting prediabetes and diabetes: can we do it? Is it worth it? *Arch Pediatr Adolesc Med*. 2010;164(2):198-199.
32. Benson LJ, Baer HJ, Kaelber DC. Screening for obesity-related complications among obese children and adolescents: 1999-2008. *Obesity (Silver Spring)*. 2011; 19(5):1077-1082.
33. Lee JM, Wu EL, Tarini B, Herman WH, Yoon E. Diagnosis of diabetes using hemoglobin A1c: should recommendations in adults be extrapolated to adolescents? *J Pediatr*. 2011;158(6):947-952.
34. Phillips LS, Ziemer DC, Kolm P, et al. Glucose challenge test screening for prediabetes and undiagnosed diabetes. *Diabetologia*. 2009;52(9):1798-1807.
35. Sinha R, Fisch G, Teague B, et al. Prevalence of impaired glucose tolerance among children and adolescents with marked obesity (published correction appears in *N Engl J Med*. 2002;30:346[22]:1756). *N Engl J Med*. 2002;346(11):802-810.
36. Libman IM, Barinas-Mitchell E, Bartucci A, Robertson R, Arslanian S. Reproducibility of the oral glucose tolerance test in overweight children. *J Clin Endocrinol Metab*. 2008;93(11):4231-4237.
37. Shaw JE, d'Emden MC, Goodall I. Is Australia ready to use glycated haemoglobin for the diagnosis of diabetes? *Med J Aust*. 2011;195(1):7-8.