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Developing a screening algorithm for type II diabetes in the resource-limited setting of rural Tanzania

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Abstract

Background—Non-communicable diseases are on pace to outnumber infectious disease as the leading cause of death in sub-Saharan Africa, yet many questions remain unanswered with concern towards effective methods of screening for type II diabetes (DM) in this resource-limited setting. We aim to design a screening algorithm for type II diabetes that optimizes sensitivity and specificity of identifying individuals with undiagnosed DM, as well as affordability to health systems and individuals.

Methods—Baseline demographic and clinical data, including HbA1c, were collected on 713 participants using probability sampling of the general population. We used these data, along with model parameters obtained from the literature, to mathematically model 8 purposed DM screening algorithms, while optimizing the sensitivity and specificity using Monte Carlo and Latin Hypercube simulation.

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The abstract for this submission was presented at the 14th Annual SSCI Nephrology Young Investigators Forum in February 2015, MUSC Student Research Day 2014, and MUSC Department of Medicine Research Day in 2015.

Results—An algorithm that combines risk assessment and measurement of fasting blood glucose was found to be superior for the most resource-limited settings (sensitivity 68%, sensitivity 99%, cost per DM patient identified \$2.94). Incorporating HbA1c testing improves the sensitivity to 75.62%, but raises the cost per DM case identified to \$6.04. The preferred algorithms are heavily biased to diagnose those with more severe cases of DM.

Conclusions—Using basic risk assessment tools and fasting blood sugar testing in lieu of HbA1c testing in resource-limited settings could allow for significantly more feasible DM screening programs with reasonable sensitivity and specificity.

Keywords

type II diabetes mellitus; non-communicable disease; sub-Saharan Africa; Tanzania

INTRODUCTION

There exists a growing body of research indicating that the global epidemic of non-communicable diseases does not spare sub-Saharan Africa (1). According to data collected by the International Diabetes Federation (IDF), non-communicable diseases are expected to outnumber infectious disease as the leading cause of death in sub-Saharan Africa in the next 20 year (2). That same report predicts that the prevalence of type II diabetes in Africa will rise from 19.8 million in 2013 to 41.4 million in 2035. The IDF estimates that in Tanzania the prevalence of type II diabetes is approximately 9%. Health systems in sub-Saharan Africa are already facing many of the known complications of diabetes, including macrovascular complications, like cardiovascular disease (3–5), and microvascular complications, like blindness (6) and foot ulcers (7, 8). According to data reported by IDF (2), 6.1% of all deaths in Africa are attributed to diabetes. More concerning, 72.8% of these deaths occur in people under the age of 60.

Type II diabetes mellitus fits the criteria of diseases appropriate for widespread screening, primarily because of the long asymptomatic period and availability of effective and relatively inexpensive interventions like lifestyle modifications and metformin (9). With the growing burden of hyperglycemia on health systems, research continues to recommend public policy support of widespread screening for pre-diabetes and diabetes in sub-Saharan Africa. (10). Several important questions have emerged in the literature concerning screening strategies for diabetes in developing countries, including the effectiveness of specific screening tests, the cost-effectiveness of widespread screening, and which of multiple public health screening strategies is most appropriate to adopt in this unique setting. Screening tests, including risk assessment tools and biochemical tests like urinalysis, fasting and casual blood glucose, and hemoglobin A1c, have each been found to have advantages and disadvantages in the context of screening in developing countries, but none prevail as ideal (11). Various combinations of these tests, in series and in parallel, have been explored as options for implementation, but the vast majority of these tests have not been validated on their population-specific performance.

While systemic literature review has indicated much progress in the field of screening for hyperglycemia, there is a little research concerning modeling screening strategies based on

actual biochemical data from individuals in developing countries. This study aims to contribute more information to this ongoing discussion by defining a screening algorithm for type II diabetes that optimizes sensitivity and specificity of identifying individuals with undiagnosed type II diabetes in rural Tanzania, as well as affordability to health systems and individuals in a very resource limited setting.

METHODS

The current study was conducted in concert with a 3-year phase II randomized control trial designed to reduce population-level HIV incidence in a rural developing country setting with sub-studies to determine prevalence of hypertension, diabetes, and chronic kidney disease in the general population.

Algorithm Design

We identified 5 possible screening tests for type II diabetes, namely Risk Assessment Questionnaire (RA), Urinalysis for glucose using a dipstick (UA), Casual Blood Glucose (CBG), Fasting Blood Glucose (FBG), and Hemoglobin A1c (HbA1c). Through literature review, each test was assessed on a number of statistical performance indicators, including sensitivity, specificity, and positive predictive value. We averaged the results across relevant studies. The results of this literature review are summarized in Table 1.

To establish a definitive diagnosis of diabetes, we used cut-off points set by the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (28), namely a positive result for any of the following: (1) CBG greater than or equal to 200 mg/dl with symptoms of hyperglycemia, (2) FBG greater than or equal to 126 mg/dl, or (3) HbA1C score greater than or equal to 6.5%. We also used cut-off points set by the Expert Committee to identify individuals with a high risk of developing type II diabetes in the future, namely (1) FBG between 100–125 mg/dl (Impaired Fasting Glucose) or (2) an HbA1c of 5.7–6.5%. The cut-off point for high-risk using CBG is contested in the literature (9), and we chose the most widely supported value of 140 mg/dl.

To our knowledge, there is no commonly used risk assessment tool that is validated for a community comparable to our research population, though there is work in progress to explore this issue (29). For the risk assessment tool used in our screening algorithms, we modeled the Finnish Diabetes Risk Score (30), a widely used questionnaire supported by the IDF as a basis on which questionnaires for specific communities can be developed. This questionnaire could be adapted for the setting of rural Tanzania and includes patient characteristics such as age, gender, weight, height, history of or current hypertension, and level of physical activity.

The 5 individual screening tests were combined in a variety of series to develop 8 algorithms based on potential supply availability, clinical knowledge, and feasibility in the field.

Data Collection

We collected behavioral data and biochemical data on 713 participants within 2 communities in the rural district of Kisarawe, Tanzania. Trained data collection workers travelled to

randomly selected family homes in this district, which had been extensively mapped in previous studies in the region, to collect qualitative and demographic data (31). At each selected household, we randomly selected a household member between the ages of 18 and 55 years, and after informed consent, performed a detailed interview and conducted a point-of-care HbA1c test concurrent with blood specimen collection for laboratory testing for the larger study (HIV, syphilis, creatinine, and Herpes Simplex Virus 2).

Creating a dataset

The values for HbA1c collected in the baseline data population were used to back-calculate the predicted results of the other 4 screening tests to create a synthetic dataset representing 10,000 individuals. To conduct sensitivity analyses, triangular distribution functions were applied, which specify low, most likely, and high values. These values were assigned based on literature review, and typically were the average of the lower bound of the 95% confidence interval (CI), point estimate, and upper bound of the 95% CI from extant studies. In any given iteration of the model, each input parameter was assigned a value using Monte Carlo simulation, but constrained by the likelihood of occurring as specified by the probability distribution function. The resulting model output was calculated, and the inputs and outputs were saved. Convergence was set to occur when the addition of model iterations changed the average and standard deviation of the output by less than 1.5%. Additionally, in any single iteration of the model, the random generation of constrained input values can result in nonsensical combinations of input values. To correct for this, we used literature review to generate a matrix of correlation values between model parameters (Table 2). The ultimate result of this process was a dataset of inputs (varied across the distribution function constraints) and associated outputs. In this way, we generated a dataset to represent 10,000 individuals with a proportional variation of HbA1c values true to our population.

Analysis of algorithm performance

In Phase I of modeling, we used the generated dataset of 10,000 individuals to conduct multivariate regression analysis of each algorithm and to identify the independent relationship between changes in model parameters and the outcome of interest for each alternative algorithm. We used Monte Carlo and Latin Hypercube simulation techniques with correlation analysis to both optimize the model options and to examine the affectability of model parameters with sensitivity analyses. We subjected the dataset to a best-fit analysis to identify the optimal probability distribution function. As well, and importantly, the output could then be conveyed as a distribution rather than a single value, which helps express the uncertainty inherent in the model, and the likelihood of different outcomes occurring. At each branch point of each algorithm, we calculated the percentage of individuals with an HbA1c greater than or equal to 6.5% who were “caught” by the algorithm and identified as diabetic, who were identified as high risk and thus moved onto the next screening test in the algorithm, or who were “missed” by the algorithm and falsely not identified as diabetic. This output data represents the sensitivity and specificity of each competing algorithm in identifying individuals with an HbA1c greater than or equal to 6.5%. This is the “algorithm sensitivity”, or the ability of the screening algorithm to identify individuals with diabetes, not to be confused with the model sensitivities previously described. Additionally, by dividing the total cost of screening for each algorithm by the sum of the number of diabetic

individuals identified at each branch point, the relative cost per diagnostic test by each algorithm was estimated.

Any algorithm that includes a measurement of FBG would require the patient to leave the health clinic and return at some point in the future after having fasted for 8 hours. In rural Tanzania, it can take a tremendous effort to come to the health clinic, a task that often requires individuals to stop work, make decisions about childcare, and walk several miles on roads that are often in poor condition. Because of this significant effort, we must take into account loss to follow-up rate for individuals asked to return to the health clinic on a subsequent day. In Phase II Modeling, we applied triangular distribution function with a point estimate of 10% for the percentage of loss to follow-up at any point in an algorithm that included FBG.

Finally, we qualitatively assessed the feasibility of each screening algorithm within the context of the Kisarawe district health centers in rural Tanzania based on our first-hand knowledge and experience working in the area.

RESULTS

The results of the algorithm design are displayed in Table 3 under “Series of Tests”. Statistical analysis of each algorithm using our synthetic population of 10,000 individuals generated the sensitivity and specificity of each algorithm in the identification of individuals with an HbA1c greater than or equal to 6.5%. The sensitivities of each algorithm were compared in an attempt to determine which algorithm had the least number of individuals with an HbA1c greater than or equal to 6.5% that were not identified at any point in that algorithm. Total cost is defined as the cost of all the tests performed for 10,000 individuals in each algorithm and is based on prices of individual point-of-care tests that would need to be purchased. Cost effectiveness is represented by the cost of identifying an individual with an HbA1c of greater than or equal to 6.5% (Cost/DM). The results of the modeling and cost calculations are also reported in Table 3.

Modeling of the algorithms resulted in specificities all above 99%, indicating that it is unlikely that individuals in this setting would be falsely identified as having diabetes when they did not have an HbA1c of 6.5% or greater. The “control” group represents the hypothetical scenario in which all 10,000 individuals received an HbA1c test as the first and only screening test.

The sensitivity, specificity, and cost calculations after incorporating loss to follow-up rates (Phase II Modeling) are also found in Table 3. Algorithms 5 and 7 did not involve a FBG measurement; therefore participants dropping out of the screening process would not affect sensitivity, specificity, and cost calculations of those algorithms.

Multivariate regression modeling was performed to determine which inputs of the model most strongly impacted the Cost per Diagnostic Test output for each competing algorithm. The higher the coefficient value, the more strongly that input impacted the cost effectiveness of the algorithm (Table 4). Modeling of each algorithm to determine sensitivity generated a division between the individuals with an HbA1c greater than or equal to 6.5%: those who

were identified by the algorithm (True Positives) and those who were not identified by the algorithm (False Negatives). The average HbA1c of the individuals in those two groups of each algorithm are found in Table 5.

Phase I Modeling

Phase I modeling did not incorporate loss to follow-up rates when comparing sensitivity and cost effectiveness of each competing model. While Algorithm 1 is the most cost effective, it is also the least sensitive. Adding more tests does not necessarily lead to an algorithm identifying more individuals with an HbA1c greater than or equal to 6.5% (compare Algorithm 2 to Algorithm 3), while it does increase the cost per diagnostic test. Adding HbA1c to an algorithm (Algorithm 4, 5, and 7) significantly increases the total cost and cost per diagnostic test, but also contributes a relative increase in sensitivity when compared to the more cost effective algorithms. With the elimination of risk assessment in Algorithm 8, the results showed it was most sensitive at identifying individuals with an HbA1c greater than or equal to 6.5% and it was more cost effective than any test that involved HbA1c.

Phase II Modeling and Model Sensitivities

Incorporating loss to follow-up did not change the relative cost effectiveness when comparing algorithms, but did decrease the total cost and increase the cost per diagnostic test for all algorithms that include FBG except Algorithm 4. The effect of decreasing total costs while increasing the cost per diagnostic test is exaggerated if loss to follow-up rates are adjusted above the estimated 10%. The sensitivity of the algorithms changed depending on how many individuals were required to return at a later date, which itself depended on the order of the tests in the algorithm. If more individuals required a FBG, more individuals would be lost to follow-up, and the sensitivity of the algorithm overall would be impacted negatively. For example, Algorithm 1, 2, and 8 were all strongly affected by loss to follow-up because the FBG is offered to a larger proportion of people in these algorithms.

Algorithm 4 is unique in that the cost per diagnostic test decreased in Phase II modeling. This indicates that the high price of HbA1c is such that if more people were lost to follow-up in the previous step, the algorithm would in fact be more cost effective. The cost prohibitive nature of HbA1c is again emphasized when looking at the model sensitivities, or the driving factors for the cost per diagnostic test for each algorithm, found in Table 4. In this table, the closer the value to 1.0, the more impact that factor had on increasing the cost per diagnostic test. The model sensitivities of Algorithms 4, 5, and 7 demonstrate that when HbA1c is included in the screening algorithm, the individual material costs of using HbA1c drives the cost of the entire screening process.

In all of the algorithms that include FBG, loss to follow-up does not affect the cost effectiveness as strongly as the cost of the individual testing modalities that make up that algorithm. Interestingly, the cost of the Risk Assessment is the most important factor in all algorithms that do not include HbA1c. Even though the Risk Assessment is the least expensive individual test when compared to the other testing modalities, far more individuals receive this test (n=10,000) compared to tests further along in the algorithm. Thus for algorithms without HbA1c, the cost effectiveness is driven by the cost of paper and printing

needed to provide a Risk Assessment Questionnaire for each individual presenting for screening.

Algorithm Sensitivity

For ideal widespread screening processes, specificity and sensitivity of the algorithms would both be close to 100%. While testing for diabetes in this population would not likely lead to significant numbers of individuals falsely identified as diabetic when they are not (as indicated by the high specificities), the algorithms do not catch every individual with elevated an HbA1c (as indicated by the lower sensitivities). However, using less sensitive modalities with higher cut-off values for diagnosis identifies the individuals with more pronounced disease, in this case, higher HbA1c scores. As shown in Table 5, individuals with HbA1c of 6.5% or greater who were identified by the algorithm as diabetic (True Positives) have a higher average HbA1c when compared to individuals who had an HbA1c of 6.5% or greater but for whom the algorithm failed to identify as diabetic (False Negatives). Thus, despite low sensitivities of the algorithms, those with more severe disease are potentially identified preferentially over those with more severe disease.

DISCUSSION

Screening strategies using Risk Assessment

The existing risk assessment tools available, including the Finnish Diabetes Risk Score used in this study, are not validated in sub-Saharan Africa, and thus introduce a concern in the applicability of these non-invasive tools in the setting of rural Tanzania (36). However, beginning the screening process with risk assessment, for example in Algorithm1 and 2, provides an opportunity for patient education about risk factors and represents a cost effective step towards identifying those at higher risk for disease that would then go on to more specific biochemical tests. Additionally, assessment of risk would provide a natural opportunity to screen individuals for hypertension, as history of hypertension and objective measurement of blood pressure are included as a component in the risk assessment. Thus, Algorithm 8 may be less ideal in this context when compared to the other algorithms that begin with a validated risk assessment, despite the higher sensitivity and relative cost effectiveness suggested by the modeling. The need for validation of a specific risk assessment tool for this population is emphasized by this research as an essential step in development of an appropriate widespread screening strategy. Additionally, the modeling of algorithm sensitivities demonstrated that the material costs of assessing risk is the driving factor for the overall cost effectiveness of any widespread screening strategy that involved using a risk assessment tool for every individual. Decreasing the material costs of a risk assessment tool, perhaps through use of one large informative poster for the triage room compared to the price of individual paper and printing for thousands of patients, or, in the future, software on a tablet for a clinic, would make overall screening algorithms more cost effective.

Screening strategies using Urine Analysis

Urine dipstick analysis has low sensitivity for identifying type II diabetes, as many individuals with hyperglycemia do not yet glycosuria tested for on urinalysis (37). It has

largely been determined that urinalysis is not appropriate for widespread screening as many individuals would remain undiagnosed (38). On the other hand, our modeling revealed Algorithm 1 (RA→UA→FBG) to be the most cost effective. While this algorithm has a modest sensitivity (56.6% after loss to follow up), the algorithm would preferentially identify those with more progressed disease as indicated previously in Table 4. Using urine dipsticks requires no batteries, no electricity, and, in our experience, we found that many health care workers in Tanzania are already trained in their use. While not ideal, it is not infeasible to think that incorporating UA in a screening algorithm followed by a more diagnostic biochemical test, like in Algorithm 1, would be a cost effective option for communities with very little healthcare resources where no previous screening for hyperglycemia has taken place.

Screening strategies using CBG/FBG

Algorithm 2, which simplifies the screening process to RA followed by FBG, was slightly more sensitive and slightly less cost effective than Algorithm 1, representing another possible cost effective screening strategy with reasonable sensitivity for identifying undiagnosed individuals. While CBG is not as clinically useful as FBG due to its wide variability in an individual, this was not reflected in the algorithms that directly compare the two tests (Algorithms 4 and 5).

Measuring FBG over CBG shifts the burden to the patient, as they would be responsible for returning to the health clinic after fasting for 8 hours. One argument for including FBG despite lower retention rates for follow up may be to select for those individuals most invested in their health, and thus would be more likely to commit to lifestyle changes needed to decrease morbidity and mortality of the disease. Our model sensitivities showed that loss to follow-up, while it does negatively impact the sensitivity of screening algorithms overall, is not a major driving factor for cost per diagnostic test. However, using CBG and FBG in screening algorithms is not without major complications. Glucometers and test strips are not widely available in sub-Saharan Africa, and are nearly non-existent outside of major urban areas (39), an issue our research team frequently observed when visiting rural health clinics in the two rural villages participating in this study. Implementing algorithms with blood glucose measurements would require shipping materials great distances and training staff members in their proper use. This research emphasizes a need for a more universal and technologically appropriate glucometer for use in widespread screening strategies in resource-limited settings.

Screening strategies using HbA1c

Using screening algorithms that include an HbA1c have the highest sensitivities in our modeling, but not without significant decreases in cost effectiveness. Even when combining the HbA1c test in series with previous, less sensitive tests in the algorithms to decrease the number of people requiring an HbA1c, it is still likely infeasible to introduce this modality in a widespread screening algorithm in this setting. The current study faced major obstacles to include point-of-care HbA1c in the baseline data collection, namely shipping difficulties, temperature fluctuations, the need for refrigerators and coolers, as well as expense. Additionally, a disparity between HbA1c and FBG in identifying individuals with diabetes

has been reported in sub-Saharan Africa, in part explained by the fact that HbA1c testing has not been fully validated in this setting (40). One reason could be that individuals of African descent have differences in baseline levels of glycosylated hemoglobin (41) or that HbA1c is affected by various hemolytic processes, some common medications, and dyslipidemias (42). Based on our experience with infeasibility of widespread use of HbA1c in the field, as well as the cost prohibitive nature revealed by the modeling of algorithms featuring this testing modality, we do not recommend widespread use of point-of-care HbA1c testing at this time.

Limitations

While we feel the analyses conducted have a high degree of validity, the study is not without limitations. One potential limitation is the fact that the estimated correlation values and statistical parameters used for the algorithms primarily came from sources in high-income countries, with populations much different than the study population in Kisarawe. Tests like RA and HbA1c are potentially varied in their correlation with the other testing modalities depending on the population in question. Ideally, the correlation values would be drawn from our own baseline data. However, the baseline data did not include collection of all testing modalities, thus consistent correlations between HbA1c and the other tests could not be calculated. One of the biggest limitations of this research is the necessity to use back-calculation to create a hypothetical dataset using HbA1c values from baseline data collection, a testing modality that is not yet validated with specific cut-off points in this community. Again, a dataset with a full range of biochemical labs and risk factor information from individuals in our research population would have been ideal to statistically analyze the relative effectiveness of the screening algorithms. We did not include screening strategies that involved tests in parallel in our analyses, though this strategy is of interest to our research community. Additionally, we did not incorporate Oral Glucose Tolerance Test into the algorithms because it is far too infeasible to consider this as an option in this environment, though it does represent a gold standard in screening and diagnosis of type II diabetes in developed countries, especially in the prenatal population (11). The baseline data collection took place in two rural communities, thus excluding analysis and discussions on variations in screening strategies between urban and rural populations. An urban population, with more availability of testing resources and treatment, would potentially benefit from a more sensitive algorithm, despite higher costs. While relative cost effectiveness is reflected in the basic cost calculations, we did not incorporate the cost of shipping, training of health care workers, and lost test kits to temperature sensitivities or malfunction. Regardless, we feel that the veracity of the analyses presented is strong enough to inform strategies for type II diabetes screening in low-resource settings.

CONCLUSIONS AND RECOMMENDATIONS

This study provides statistical modeling of various screening algorithms based on biochemical data collected in the field to suggest that in very resource poor settings, the most basic of screening algorithms including non-invasive RA and FBG offer a cost effective option with reasonable sensitivity for identifying undiagnosed individuals with type II diabetes. Additionally, though UA alone is the least sensitive testing modality,

incorporating UA into screening algorithms with RA and subsequent diagnostic biochemical tests, like FBG, improves cost effectiveness with comparable sensitivity in identifying previously undiagnosed individuals with more progressed hyperglycemia. Though point-of-care HbA1c has been suggested as a more sensitive screening test, this study demonstrates the cost-prohibitive drawback of their widespread use. Screening strategies leading to diagnosis of individuals allows for a more accurate grasp of the burden of disease in developing countries and paves the way for public policy to require basic treatment for hyperglycemia in rural medical dispensaries and pharmacies. Future directions of this research include validating risk assessment tools on their population-specific performance and working with colleagues in biomedical engineering to re-think diabetes screening technology in the setting of developing nations.

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Abbreviations

CBG	Casual Blood Glucose
DM	Type II diabetes mellitus
FBG	Fasting Blood Glucose
HbA1c	Hemoglobin A1c
HIV	Human Immunodeficiency Virus
IDF	International Diabetes Federation
IFG	Impaired Fasting Glucose
NCDs	Non-communicable diseases
RA	Risk Assessment questionnaire
UA	Urinalysis

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Summary of statistical performance indicators found through literature review of selected screening tests

Table 1

Screening Test	Study	Cut-off Point	N=	Sensitivity	Specificity	PPV ^a	Country/ Population
RA ^b	Heikes (12)	Varied	7092	88	75	14	US
	Herman (13)	Varied	3384	79	65	10	US
	Heianza (14)	Varied	7477	72.7	68.1	9.6	Japan
	Griffin (15)	Varied	1077	77	72	11	UK
UA ^c	Andersson (16)	>Trace	3201	23	99	48	Sweden
	Davies (17)	>Trace	10348	43	98	53	UK
	Hanson (18)	>Trace	2092	64	99	36	Pima Indians
	Andersson (16)	>144 mg/dl	3268	73	95	29	Sweden
CBG ^d	Rolka (19)	>140 mg/dl	1471	56–65	95–96	30	US
	Somannavar (20)	>140 mg/dl	185	86.5	80.7	42	India
	Blunt (21)	>126 mg/dl	1851	40–60	>90	60–80	US
	Chang (22)	>126 mg/dl	5303	40	99	26	Taiwan
FBG ^e	Wiener (23)	>126 mg/dl	233	59	96	27	Netherlands
	Kramer(24)	>6.5%	2107	44	79	60–80	US
	Kharroubi (25)	>6.5%	1370	57	97	77	Palestine
	Simon (26)	>6.0%	333	60	91	35	France
FBG, HbA1c	Ko (27)	100–140 mg/dl, 5.5%–6.1%	2250	69–83	96	30	China

a= Positive Predictive Value;

b= Risk Assessment;

c= Urinalysis;

d= Casual Blood Glucose;

e= Fasting Blood Glucose;

f= Hemoglobin A1c

Table 2

Correlation values for HbA1c and other screening tests

Test	Correlation values from literature comparing HbA1C to other tests	Estimated correlation value used in the algorithm
RA	0.75–0.83 (32)	0.80
UA	0.64 – 0.704 (33)	0.65
CBG	0.54– 0.76 (34)	0.60
FBG	0.74 (35)	0.75
HbA1c	-	1.00

Table 3

Results

	Series of Tests	Phase I: Without Loss to Follow-Up				Phase II: With Loss to Follow-up			
		Sensitivity	SPC ^a	Total Cost	Cost/DM ^b	Sensitivity	SPC	Total Cost	Cost/DM
Algorithm 1	RA ^c → UA ^d → FBG ^e	63.6% (61.2%–65.8%)	>99%	\$3,129	\$2.84	56.6% (50.9%–61.7%)	>99%	\$2,957	\$3.01
Algorithm 2	RA → FBG	68.2% (66.0%–70.4%)	>99%	\$3,474	\$2.94	60.7% (54.6%–66.1%)	>99%	\$3,221	\$3.06
Algorithm 3	RA → UA → CBG ^f → FBG	67.9% (65.7%–70.1%)	>99%	\$3,708	\$3.10	67.2% (65.8%–68.4%)	>99%	\$3,648	\$3.13
Algorithm 4	RA → FBG → HbA1c ^g	76.0% (74.0%–78.0%)	>99%	\$7,984	\$6.05	75.2% (74.5%–75.8%)	>99%	\$7,238	\$5.55
Algorithm 5	RA → CBG → HbA1c	76.5% (74.5%–78.5%)	>99%	\$13,720	\$10.32	No change	>99%	No change	No change
Algorithm 6	RA → CBG → FBG	72.6% (70.5%–74.7%)	>99%	\$4,444	\$3.52	70.8% (69.0%–72.3%)	>99%	\$4,341	\$3.54
Algorithm 7	RA → HbA1c	77.3% (75.3%–79.3%)	>99%	\$26,376	\$19.68	No change	>99%	No change	No change
Algorithm 8	UA → FBG	81.4% (79.5%–83.2%)	>99%	\$4,594	\$3.25	72.5% (65.25%–79.0%)	>99%	\$4,298	\$3.42
Control	HbA1c	100%	100%	\$120,000	\$80	No change	No change	No change	No change

a= Specificity;

b= Cost per diabetic patient identified;

c= Risk Assessment;

d= Urinalysis,

e= Fasting Blood Glucose;

f= Casual Blood Glucose;

g= Hemoglobin A1c

Table 4

Model Sensitivities for Cost per Diagnostic Test

	RA ^a cost	UA ^b cost	FBG ^c cost	CBG ^d cost	HbA1c ^e cost	Loss to follow-up
Algorithm 1	0.91	0.13	0.32	-	-	0.18
Algorithm 2	0.87	-	0.47	-	-	0.13
Algorithm 3	0.91	0.13	0.12	0.37	-	0.03
Algorithm 4	0.60	-	0.32	-	0.62	-0.40
Algorithm 5	0.34	-	-	0.21	0.92	-
Algorithm 6	0.85	-	0.19	0.51	-	0.024
Algorithm 7	0.15	-	-	-	0.99	-
Algorithm 8	-	0.74	0.68	-	-	0.25

a= Risk Assessment;

b= Urinalysis;

c= Fasting Blood Glucose;

d= Casual Blood Glucose;

e= Hemoglobin A1c

Table 5

Average HbA1c values for True Positives and False Negatives

	Average HbA1c (%) for True Positives	Average HbA1c (%) for False Negatives
Algorithm 1	7.34	6.82
Algorithm 2	7.32	6.79
Algorithm 3	7.31	6.82
Algorithm 4	7.28	6.76
Algorithm 5	7.27	6.76
Algorithm 6	7.30	6.76
Algorithm 7	7.27	6.75
Algorithm 8	7.22	6.87