Validation of Prediction of Diabetes by Archimedes and Comparison with Other Predicting Models

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**Objective:** To validate the ability of the Archimedes Model to accurately predict the risk of developing diabetes in individuals.

**Research Design and Methods:** Subjects were randomly selected from the San Antonio Heart Study population. The area under the Receiver Operator Characteristic (aROC) curve derived from the Archimedes Model was calculated and also compared to the aROCs from two published multiple logistic regression models designed to estimate diabetes risk.

**Results:** The aROC (95% CI) for the Archimedes Model was 0.818 (0.739,0.899) compared to aROCs of 0.869 (0.801,0.936) and 0.870 (0.802,0.937) for the two logistic regression models, respectively. Risk estimates from the logistic models were highly correlated with the estimates derived from the Archimedes Model.

**Conclusions:** The Archimedes Model predicts individual diabetes risk with a high level of sensitivity and specificity, comparable to that of models designed specifically for that purpose. Unlike the latter models, Archimedes also predicts the risk of numerous other health outcomes.
The Archimedes Model is a large-scale simulation model of human physiology and health care systems (1). It has been extensively validated by its ability to replicate quite closely a wide variety of aggregate health outcomes in populations (1). The ability of Archimedes to make accurate predictions for individuals, however, has thus far not been validated. Using data from the San Antonio Heart Study (SAHS), we attempted such a validation. We also compared the area under the Receiver Operating Characteristic curves (aROC) derived from Archimedes to those derived from two other diabetes predicting models, namely, the SAHS Predicting Model (2) and the Atherosclerosis Risk in Communities (ARIC) Predicting Model (3).

RESEARCH DESIGN AND METHODS

The SAHS is a prospective cohort study (62% Mexican Americans and 38% non-Hispanic whites) consisting of 3682 individuals followed for 7-8 years (4). The SAHS Predicting Model is a multiple logistic regression model with incident diabetes as the dependent variable and a panel of baseline characteristics that are ordinarily available in a routine clinical setting as independent variables (2). The ARIC Predicting Model is a similarly constructed logistic regression model (3).

The Archimedes Model is built from underlying anatomy and physiology and uses scores of ordinary and differential equations to represent metabolic pathways, occurrence and progression of diseases, signs and symptoms, treatments and outcomes. A practical, free, readily available tool derived from the Archimedes Model is the “Diabetes Personal Health Decisions (PHD)” (5). The PHD can simultaneously predict the risk of diabetes, numerous other outcomes and the effects of a wide variety of treatments in many different populations (e.g. those with diabetes). It was used here to provide external validation of its prediction of the incidence of diabetes.

Among the 3228 individuals in the SAHS who were non-diabetic at baseline, 295 developed diabetes over the 7-8 years of follow-up. All the required elements for the Archimedes risk estimation were available in the subjects selected for the present analyses. The present analyses were restricted to the recent cohort 2 of SAHS with 1734 non-diabetic individuals of whom 195 developed diabetes in follow-up. Within the SAHS database, we selected 100 individuals at random, 50 of whom had developed diabetes at follow-up and 50 who remained free of diabetes at follow-up. This sample size would provide 80% power to detect an aROC significantly (p<0.05) greater than 0.70, the low end of acceptable discrimination (6), if the true aROC was >0.80, and 90% power if the true aROC=0.83 (benchmark values near that of other established models) (2,3).

The risk of developing diabetes for each individual was determined according to the years of follow-up for that individual (rounded to the nearest year), which ranged from 6-9 with a mean of 7.5. Data from each individual was entered into the PHD and the results obtained from the graphical output displayed on the computer screen. A second person confirmed the accuracy of the input and in a random sample of 20 forms also confirmed the output from PHD.

We also estimated the risk of diabetes for the same 100 individuals using both the SAHS Diabetes Predicting Model and the ARIC Predicting Model. The aROC’s and confidence intervals for all three models were computed and compared (7). Finally, we computed the Spearman correlation coefficients between the risk estimates obtained from each pair of predicting models.

RESULTS
The aROC (95%CI) for the PHD was 0.818 (0.739,0.899) and was not statistically different than the aROC of the SAHS Model (0.869 (0.801, 0.936) or the ARIC Model 0.870 (0.802, 0.937)(Figure 1). The risk estimates from the SAHS Model and ARIC Model were highly correlated (r=0.962), and both correlated well with the PHD (r=0.834 and 0.842, respectively).

**CONCLUSIONS**

With an aROC of 0.818 it is evident that the accuracy of the PHD (i.e. Archimedes) to predict an individual’s risk of diabetes is excellent, almost as high as models specifically designed and used only for that purpose. The SAHS Model may have had an unfair advantage over Archimedes since it was designed and optimized using the SAHS database and could be overfitted to the subset of SAHS cases selected for this analysis. It was for that reason that we used the ARIC Predicting Model, since the latter was developed in an entirely independent data set, and it performed as well as the SAHS model.

Both the SAHS and ARIC Models were built from person-specific data and optimized specifically for predicting incident diabetes. In contrast, Archimedes was designed to be used for a very wide range of purposes, calculates many different outcomes, was not built from person-specific data, and was not calibrated to determine the incidence of diabetes. Also, several of the variables Archimedes uses that may have enhanced its predictive capability were not included in this analysis.

This report extends the validation of Archimedes, and demonstrates its excellent ability to discriminate between individuals who will or will not develop diabetes. Its utility is comparable to models developed solely for that purpose. Because the PHD, derived from Archimedes, is freely available on the internet and calculates many additional outcomes, it is a powerful tool that can reliably be used for comprehensive risk assessment and decision-making. PHD is now widely accessed (about 80,000 users/yr) for comprehensive risk assessment of cardiometabolic disease over a 30 year period, and to appreciate better the likely benefits of risk factor reduction. Although the tool currently uses complex distributive computing which limits its speed and capacity, a much more rapid version will soon become available with unlimited capacity. This will allow for widespread promotion.

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Figure 1. Areas under the Receiver Operator Characteristic curves for the PHD (filled in squares), the SAHS Predicting Model (open triangles) and the ARIC Predicting Model (x’s).