

DiaSys: Computerized Decision Support to Improve Diabetes Management in Primary Care

A. Background and Specific Aims

Inadequate control of type 2 diabetes is a leading cause of morbidity, mortality, and costs for the American healthcare system.^{1,2} While national guidelines call for intensification when blood glucose levels are high, such guidelines are neither specific nor individualized. There are multiple choices of drugs, dosages are not specified, and there is no consideration of blood glucose patterns. Primary care providers (PCPs), who deliver the bulk of diabetes care, often have difficulty navigating these guidelines.^{12,13} The result is **delays in initiating and intensifying therapy compared to endocrinologists,^{3,4} contributing to inadequate glucose control among millions of patients.**^{5,6}

Endocrinologist support of PCPs can improve care. We showed in a randomized, controlled trial at Grady Memorial Hospital that PCPs' care improved and was more consistent with national guidelines when endocrinologists gave the PCPs feedback on their performance.⁷ However, that approach is labor-intensive and expensive, and would be difficult to generalize across the U.S.

The use of decision support by PCPs could reduce the need for endocrinologist assistance and improve diabetes management. However, currently available decision support tools are focused on process measures (e.g. such as whether a patient is referred for a foot exam) rather than to help PCPs make timely, evidence-based, and individualized decisions. To address this gap, we have collaborated with researchers at the Georgia Institute of Technology to develop a prototype of a novel decision-support tool (DiaSys) to assist PCPs in diabetes management (See Preliminary Data). DiaSys uses algorithms based on the pattern of fingerstick home blood glucose monitoring values obtained by patients, can be used during office visits or telephone calls to guide therapeutic recommendations that are timely, has little risk of hypoglycemia, and improves blood glucose levels. Through the incorporation of machine learning technologies, user-testing, and validation, as we are proposing in this application, DiaSys could help PCPs make diabetes management decisions that are highly individualized, evidence-based, quick, and convenient. Ultimately, we envision that decision support will facilitate diabetes management decisions by non-physician providers and patients themselves, potentially leading to large decreases in the cost and efficiency of diabetes management.

Achieving this vision will be a collaborative effort involving Georgia Tech and Emory, spanning the disciplines of computer science, endocrinology, primary care, and nursing. Our HIP team has expertise in the development of machine learning and predictive algorithms, management of diabetes, quality improvement and clinical informatics.^{3,4,7-21} The team will use this experience to refine the software, validate the management recommendations, and test feasibility, safety, and effectiveness in a clinical trial.

A.1. Hypotheses

- (i) Decision support technology will provide primary care providers with individualized treatment recommendations, and the underlying rationale.
- (ii) Decision support recommendations for changes in therapy will be considered valid by endocrinologists.
- (iii) Use of glucose monitoring-based computerized decision support by PCPs and their nursing staff will be feasible, safe, and effective.

A.2. Aims

(i) To develop a computerized, decision support tool, the Georgia Tech team will integrate DiaSys with machine learning technologies developed by Dr. Eva Lee to provide both individualized diabetes treatment recommendations, and an explanation of the basis for the recommendations.

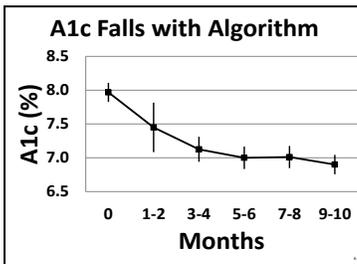
(ii) To assess the internal and external validity of the treatment recommendations, they will be compared with recommendations made by Board-certified endocrinologists – allowing fine-tuning of the approach.

(iii) To assess the feasibility, safety, and effectiveness of computerized decision support, we will conduct a pilot study in a PCP setting.

B. Preliminary Data

The team has extensive experience in 1) the management of diabetes, 2) use of algorithms in diabetes management, and 3) the development of machine learning and predictive technologies. In addition, the team has worked with researchers at Georgia Tech to develop a prototype of the decision-support technology. Through the integration of machine learning this software will be able to provide PCPs with highly individualized recommendations.

Our use of algorithms in clinical practice, which underlie DiaSys, has led to significant improvements in clinical practice. In an ongoing pilot study, clinic staff at the Atlanta VAMC teaches patients with diabetes to do structured glucose monitoring – initially daily “fasting” measurements before breakfast, and once a week, a “7 point profile”, before and 90 minutes after each meal, and at bedtime. Patients report the glucose values at office visits and via telephone calls. The mid-level provider uses these and additional data – such as deviations from usual meals or physical activity – to make recommendations based on algorithms we have developed. These recommendations are reviewed by an endocrinologist and ultimately relayed to the patient.



Among 13 patients who would meet inclusion criteria for the proposed study, with usual management in primary care before use of the algorithm, there was little change in A1c – which remained about 8.0%. With use of the algorithm, A1c improved from 8.0 ± 0.1% to 6.9 ± 0.1% over 9-10 months (mean ± SEM, p < 0.001). Adherence to the protocol was excellent, with patients reporting blood glucose values more than 80% of the time. There were few problems from hypoglycemia, because adjustments in therapy are made simultaneously – increased to lower high glucose, and decreased to raise low glucose.

Hypoglycemia averaged less than one episode per patient per month (symptoms and/or fingerstick glucose <70 mg/dl) – despite the fall in A1c. Moreover, no values were below 60 mg/dl and there was no severe hypoglycemia. Despite their effectiveness, these algorithms are difficult to use in clinical practice, requiring clinical staff with advanced training.

To overcome this limitation we have collaborated with colleagues at Georgia Tech in PHP to develop a prototype of the decision support technology (shown on the right). The prototype decision support tool provides recommendations for initiation and titration of 1) metformin, 2) glipizide and 3) basal insulin. Such a strategy is likely to be cost-effective.²² In addition, these drugs are widely used,²³ are recommended in guidelines,²⁴ have a relatively low risk of hypoglycemia,²⁵ and are inexpensive.²⁶ Recommendations for use of the complete range of diabetes medications – including thiazolidinediones, dipeptidyl peptidase-4 inhibitors, and meal-time insulin – can be incorporated in the future.

The software is internet-based, but could eventually be integrated into electronic health records; use does not require personal health information (PHI). A user inputs medications and glucose monitoring values, along with structured, qualitative information, i.e., whether glucose levels might have been affected by meal size or physical activity, non-adherence, or new medications. Ultimately, we envision integration with a patient’s glucose monitor. The software provides individualized treatment recommendations and rationales based on algorithms we have developed. By integrating the prototype software with machine learning technologies, we will be able to “predict” the impact of medication changes on glucose levels and better respond to glucose variability, thus permitting the delivery of more tailored recommendations and enhancing the safety and

Fasting Glucose Levels		Additional Comments			
Date	Blood Sugar Level	Meal Size		Physical Activity	
Day 1	120	<input type="checkbox"/> Small	<input type="checkbox"/> Big	<input type="checkbox"/> Low	<input type="checkbox"/> High
Day 2	130	<input type="checkbox"/> Small	<input type="checkbox"/> Big	<input type="checkbox"/> Low	<input type="checkbox"/> High
Day 3	125	<input type="checkbox"/> Small	<input type="checkbox"/> Big	<input type="checkbox"/> Low	<input type="checkbox"/> High
Day 4	140	<input type="checkbox"/> Small	<input type="checkbox"/> Big	<input type="checkbox"/> Low	<input type="checkbox"/> High
Day 5	132	<input type="checkbox"/> Small	<input type="checkbox"/> Big	<input type="checkbox"/> Low	<input type="checkbox"/> High
Day 6	125	<input type="checkbox"/> Small	<input type="checkbox"/> Big	<input type="checkbox"/> Low	<input type="checkbox"/> High
Day 7	126	<input type="checkbox"/> Small	<input type="checkbox"/> Big	<input type="checkbox"/> Low	<input type="checkbox"/> High
Average	128	"Adjusted" Average (Accounted for Hypoglycemia & Variability)		128	

7-Point Glucose Profile							
	Breakfast		Lunch		Dinner		Bedtime
	Before	After	Before	After	Before	After	Bedtime
Blood Sugar Level	110	143	99	192	157	173	160
Original Glipizide (mg)	5		0		5		0
Recommended Glipizide (mg)	2.5		2.5		5		2.5
Original Glargine (units)					0		
Recommended Glargine (units)					0		

Final Recommendation	Dosage Change	Rationale
0 units of glargine at dinner	No change	Patient is currently on bedtime glipizide and insulin glargine is not necessary.
2.5 mg of glipizide at bedtime	Increase by 2.5 mg	Glucose is too high at breakfast-- so glipizide at bedtime needs to be increased.
2.5 mg of glipizide at breakfast	Decrease by 2.5 mg	Glucose is okay at lunch but expected to fall and might become too low because medication changes at bedtime will lower the lunch glucose below normal levels-- so glipizide at breakfast needs to be decreased.
2.5 mg of glipizide at lunch	Increase by 2.5 mg	Glucose is too high at dinner-- so glipizide at lunch needs to be increased.
5 mg of glipizide at dinner	No change	Glucose is too high at bedtime but expected to fall because medication changes at lunch will lower the bedtime glucose to normal levels-- so glipizide at dinner does not need to be changed.

efficacy of the software.

C. Research design

Software development will occur primarily at Georgia Tech in the laboratory of Professor Lee. Working along with the clinical investigators, Dr. Lee will integrate DiaSys with machine learning technologies. Validation will involve senior endocrinologists in the Division of Endocrinology at Emory, Grady, and the Atlanta VA. Clinical evaluation will involve patients, nursing staff, and PCPs at the Atlanta VA; all patient and staff involvement will include informed consent, and occur only after review and approval of protocols by the Emory University Institutional Review Board (IRB) and VA Research and Development (R&D) Committee. See Appendix 1 for project timeline.

C.1. Specific Aim #1 – development of the computerized decision support tool

Modifications to the DiaSys Prototype The prototype software described in Section B will be integrated with machine learning technologies. This will permit the provision of safer and more effective recommendations. In addition, modifications will be made to enhance the software's usability.

Usability Testing Once a revised version of DiaSys has been created, we will utilize the discount usability testing methodology²⁸ to quickly identify and then rectify weaknesses. For this, we will draw on volunteer students and faculty from GA Tech. Then we will begin end-user usability testing to assess issues with the system among clinic staff. Based on a series of tasks in a typical usage scenario, quantitative and qualitative performance measures will be collected. Quantitative measures include task completion times, number of errors and success rate. Qualitative measures will include different dimensions of usability and satisfaction. The measures will be compared to pre-defined goals. Iterative refinement and re-testing of the software will continue until goals are achieved (we expect 2 rounds involving a convenience sample of 4 participants each – different participants, to factor out learning that would negatively affect a within-user testing plan).

C.2. Specific Aim #2 – to assess the validity of the treatment recommendations

Validation and refinement of the decision support system will occur at the Atlanta VA. Participants will be 3 Board certified endocrinologists from Emory working in different practice settings. We will develop 50 cases abstracted from a data set of over 100 consecutive clinical encounters of patients with diabetes currently managed by Dr. Phillips. Each case scenario will include typical patient information gathered at outpatient office visits, such as age, body mass index, medications, A1c level (a measure of average blood glucose levels over the preceding 2-3 months), fingerstick glucose monitoring data, and qualitative information (meal size, physical activity, etc.). For each case scenario, Dr. Phillips will assign a recommended treatment recommendation using the management algorithm we have developed. A trained research coordinator will then enter the data into the decision support system to generate treatment recommendations and rationale. Study participants will be oriented to the diabetes management algorithm and will be asked to rate: 1) treatment recommendations on the basis of a) safety and b) effectiveness, and 2) rationale on the basis of appropriateness. Internal and external validity, descriptive statistics, sensitivity, specificity and kappa will be calculated using SAS 9.2 (Carey, NC). The software and underlying logic will be further modified as needed.

C.3. Specific Aim #3 – to assess the potential utility of the decision support approach

Participants Structured decision support will be evaluated in 24 patients with diabetes. In this “proof of concept” study, each patient will serve as his/her own control, and effectiveness will be assessed primarily by the decrease in A1c – the “gold standard” for diabetes control. Eligible patients will be recruited from VA Stockbridge Community Based Outpatient Clinic (CBOC) where care is provided via a “patient centered medical home” model.

We will initially target patients who: 1) are already using metformin and/or glipizide, but not insulin, 2) have glucose levels that are above goal ($A1c \geq 7.0\%$ and $\leq 10.0\%$), and 3) have consistent primary care (≥ 2 visits per year for 2 years in a row). Patients will be excluded if they do not have access to a telephone. Patients meeting study inclusion and exclusion criteria will be identified from the Atlanta VA database and their

appropriateness for study will be verified with their PCPs. Based on interviews with nursing leadership at the Atlanta VAMC, we anticipate 2-5 patients meeting eligibility criteria are seen each day. A Research Assistant will contact such patients prior to their scheduled clinic visits, and if they are interested in participating, obtain informed consent when they come to clinic, and administer the well-validated Diabetes Quality of Life (DQoL) questionnaire.²⁹ All subsequent management will be by primary care nursing staff and the PCPs. A single RN Care Manager will collect baseline data including current medications, body mass index, and A1c, and teach the patients structured home blood glucose monitoring (“fasting” and “7 point profile” measurements). Although patient data recording will ultimately be computerized, in this initial study, the patients will be given paper forms to facilitate recording of glucose values on different days and at different times of day.

Intervention All participating patients will receive the intervention. No diabetes medication changes will occur at the initial visit, but structured glucose monitoring will be initiated at that visit, and reinforced at a follow-up visit 2 weeks later. The RN Care Manager will call the patient on a weekly basis and collect 1) structured glucose monitoring data, 2) self-reported adherence to medications using the 4-item Morisky scale,³⁰ 3) adverse drug events³¹ and 4) episodes of hypoglycemia. The RN Care manager will also collect relevant patient-centric qualifying information (e.g. illness, changes in meals, etc.) that may affect treatment recommendations. Each week, the RN Care Manager will enter the information for each patient into the decision support tool, obtain management recommendations and rationale, and review these with each patient’s PCP. The PCP will be able to agree with or modify the treatment recommendation. The RN care manager will subsequently call the patient with a final treatment recommendation. Based on our experience, we expect that the process should take 5-10 minutes per patient per week. This process will be continued for 12 weeks, after which diabetes management will revert fully to the patient’s PCP. During the study, participation will not constitute a replacement for face-to-face visits with or telephone calls from the PCP for all aspects of primary care management.

Follow-up Data Collection, Outcome Assessment, Analysis, and Expected Results Upon completion of the 12-week study, patients will be asked to return for a clinic visit to repeat the A1c measurement, body weight measurement, and the DQoL. In addition, we will conduct in-depth, semi-structured interviews with the RN Care Manager and any PCP caring for study patients at 1 week and 12 weeks; the first interview should identify any problems with use the decision support tool, so that they can be corrected.

The primary analysis will be a pre-post comparison of changes in 1) A1c and 2) blood glucose levels. Secondary analyses will be performed to determine safety and feasibility of the intervention. Safety will be assessed through 1) frequency of hypoglycemia and 2) adverse drug events, the presence and severity of which will be ascertained through standard methodology.³¹ Feasibility will be determined through 1) patient satisfaction as determined by the DQoL, 2) provider and RN Care Manager satisfaction, 3) adherence to structured home blood glucose monitoring, and 4) the Morisky self-reported adherence scale. For the analyses, A1c, glucose levels, and changes in the DQoL will be treated as continuous variables, and paired t-tests will be used to compare baseline and end-of-study groups. If the data do not follow a normal distribution, we will use the Mann-Whitney test. Results for frequency of hypoglycemia and adverse drug events, Morisky self-reported adherence, and answers to questions pertaining to satisfaction will be summarized with descriptive statistics and frequencies.

The study is designed to have at least a 90% power to detect a change of 0.5% in A1c levels – widely accepted as predicting a clinically significant decrease in development of diabetes complications.^{32,33} Power and sample size assessments for the primary analysis are informed by our preliminary experience with 13 patients (see Appendix 1.E) where mean A1c at 12-20 weeks fell 0.92% with standard deviation of 0.59%. In the proposed study, we will have sufficient resources and clinic volume to enroll 24 patients. Allowing for a loss to follow-up of 20% and with an alpha of 0.05, we will have 90% power to detect a pre-post difference of 0.41%. Based on our preliminary experience we anticipate that the strategy will prove to be feasible, safe, convenient and effective - and that the findings will be publishable in a well-respected peer-review journal.