Developing a Recommendation-Based Application to Help Endocrinologists Treat Type II Diabetes Mellitus

By

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I. Introduction

Diabetes Mellitus type II is a disease characterized by abnormally high levels of glucose in the bloodstream (hyperglycemia) due to decreased insulin secretion, insulin resistance, or both. It affects approximately 425 million adults worldwide and is the 7th most common chronic condition according to the CDC (Figure 1).[1] Patients with this disease typically have increased urination, increased thirst, and fatigue and can even be vulnerable to many types of infections. Patients with type II diabetes see diabetes specialists and endocrinologists to effectively treat their disease. Currently, however, there is a massive shortage of endocrinologists in the United States due to a growing demand of chronic diseases such as diabetes and osteoporosis.[2] In one study, the majority of endocrinologists surveyed believed the process of treating diabetes is difficult for these four reasons: the shortage of physicians, constantly evolving diabetes research, rapidly changing medication guidelines, and the rate at which medications are being added to the market.[3] Another major problem in the diabetes community is the risk of potentially inappropriate medications (PIMs), which are defined as prescribing medications that have a greater risk of potentially severe adverse

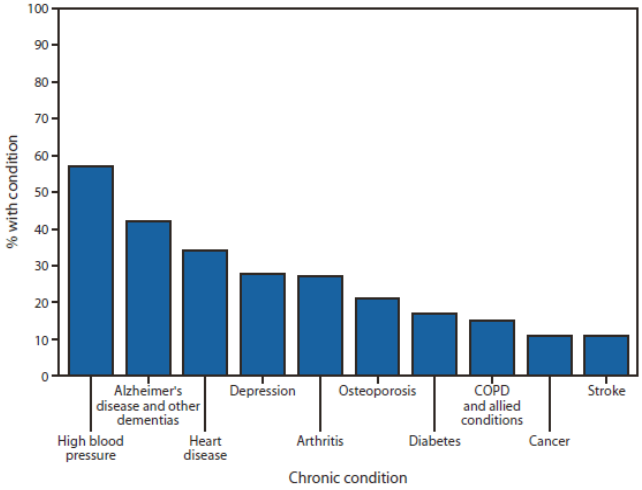

Figure 1: *Most common chronic conditions as per the CDC*

effects. 74% of elderly patients with type II diabetes are prescribed at least one PIM when hospitalized.[4]

The studies conducted by Healy et al. and Sharma et al. reveal that the process of treating type II diabetes is difficult because of 3 main reasons: The shortage of endocrinologists, rapidly evolving medication recommendations by diabetes associations, and the health risk to elderly diabetic patients due to PIMs. There is a growing need for technology that assists endocrinologists in prescribing medication based on factors that adjust to the evolving recommendations by the American Diabetes Association and uses patient biomarkers along with other factors to recommend appropriate medications for patients.

To characterize the patients and recommend appropriate medications, the application must evaluate patient features to assess risk factors associated with the most common diabetes medications. Typically, patients are evaluated on their Hemoglobin A1C levels, Glomerular Filtration Rate (GFR), age, BMI, blood pressure, heart disease, and kidney disease.[5-6] To assess all of these factors and to also take into consideration the patient's ability to afford medication, the patient characteristics within the app will include: patient GFR levels, polyuria/polydipsia/HbA1C levels, obesity, and insurance status as well as if the patient has any history of atherosclerotic cardiovascular disease (ASCVD), heart failure, or chronic kidney disease (CKD).

This research will use guidelines from the American Diabetes Association and literature to develop an application that physicians can use to treat patients with type II diabetes. The main aspect of this research is correlating patient characteristics with either viable or non-viable drugs. This will be done using a point system in which positive points

will be assigned to drug classes when the patient characteristics indicate the drug should be used. Negative point values will be assigned when the drug class is not recommended based on patient characteristics. The magnitude of point values will reflect how recommended the drug is (highly positive), or how contraindicated the drug is (low negative). This way, if a patient exhibits multiple characteristics, such as chronic kidney disease and heart failure, drugs that have positive values for both will be summed so that the drug will have an even higher positive value. Similarly, drugs that do not work well for both, i.e. a drug has negative values for both CKD and heart failure, the negative values will be summed to get an even lower negative value. Finally, all the drugs will be ranked and the drugs with the highest positive values will be recommended. All of these point values will be stored in a decision matrix that the application can access to make recommendations.

With this app, physicians will be able to quickly diagnose patients with type II diabetes accurately and effectively. The application addresses the 3 main issues in treating type II diabetes. The application will aim to reduce patient visit times while ensuring the patients receive proper care as recommended by the American Diabetes Association to assist with the shortage of endocrinologists. The application will also be constantly updated whenever new medication guidelines are released to ensure the physicians are up-to-date on the best medication to prescribe based on patient characteristics. Lastly, by developing a standard prescription process for patients (especially the elderly), the application will reduce the risk of PIMs due to human error or oversight. The initial application’s effectiveness will be evaluated quantitatively by assessing the number of times the algorithm outputs the correct recommendation and the

amount of time it saves endocrinologists during patient visits. The application will also be assessed qualitatively by interviewing physicians and asking them how they believe the application is useful as well as where they believe improvements can be made.

II. Literature Review

Challenges

Developing this technology of course comes with many obstacles. Increasingly, when prescribing medication to patients with diabetes mellitus type II, physicians often choose the name brand medication to increase their own profit margins. This increases the chances of medication nonadherence by the patient, in which patients ignore medication perhaps due to the financial burden of treatment.[7] So the question then arises, should the algorithm always output the cheapest option for treating the patient, in which case the treatment may not be as effective, or should the algorithm always output the best medication regardless of cost, and thereby increase the odds of patient medication nonadherence? To address this issue, the application will factor in a patient's insurance status and only recommend drug classes, rather than specific drugs, to allow the physician to choose a suitable drug within the class recommended or perhaps allow the patient to find the cheapest option within the drug class. Also, due to supply chain issues around the United States, some specific drugs are not available in parts of the country.[8] Providing a drug class recommendation makes it easier for the patient to find the medication they need, wherever they are.

Patient Factors and Drug Classes

An important factor to consider when recommending diabetes medication is the patient's estimated glomerular filtration rate (eGFR) which can be measured using a simple blood test to check for creatinine levels. Patients with type II diabetes often experience elevated GFR levels which can lead to nephron damage and eventual kidney disease. GFR levels must be controlled in diabetic patients to stop the onset/progression of kidney disease.[9] GFR is widely monitored in patients and is an important factor in recommending the appropriate medication for treatment.

The most common drug classes used to treat type II diabetes mellitus are Metformin, DPP-4 Inhibitors, GLP-1 Receptor agonists, SGLT-2 Inhibitors, Sulfonylureas, Thiazolidinediones (TZD), and various insulin types.[10] These drug classes are used for initiating therapy, the drugs used to initiate treatment for patients, and combination therapy to be used in tandem with one another for multiple treatment approaches. These drug classes will be used in the application (Figure 2) and initiating therapy will be recommended based on eGFR levels, history of polyuria/polydipsia, blood glucose levels, insurance status, age, history of atherosclerotic cardiovascular disease/heart

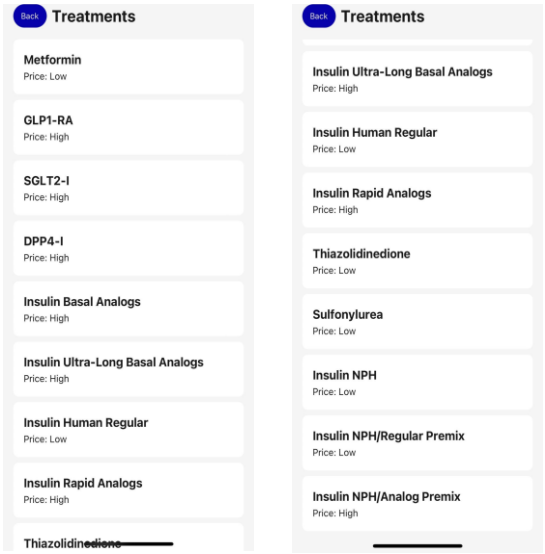

Figure 2: *Screenshots of the drug classes listed within the application. These are the most common medications used to treat type II diabetes mellitus. Each drug class has associated point values for every patient characteristic*

failure/chronic kidney disease/hypoglycemia unawareness, and BMI based on recommendations from Dr. Guillermo Umpierrez, President of the American Diabetes Association.[11] Combination therapy will use all the factors listed above and take into consideration the drugs currently being used by the patient to provide extra medication to meet treatment goals, avoid contraindications, and address the issues highlighted by the papers by Sharma et al. and Flegel et al. Patient Characteristics will be used to determine initiating therapy and combination therapy (Figure 3).

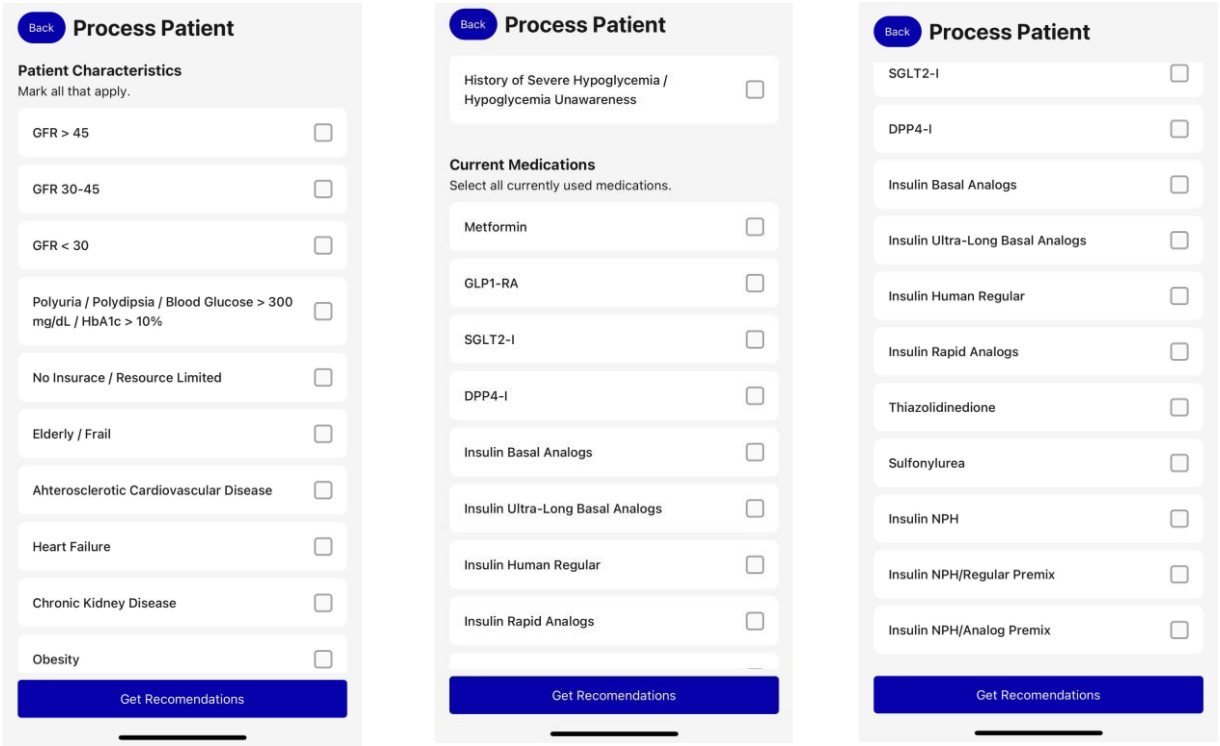

Figure 3: *Screenshots of the patient characteristic checklist that will be used to determine the best drug classes for both initiating therapy and combination therapy. Physicians will click the characteristics for patients as well as the patient's current medications, and the next page provides a detailed list of recommended drugs*

Metformin is a biguanide drug and widely prescribed as an initiating therapy because of price, safety, and efficacy in lowering blood glucose levels.[12] Metformin also has great cardiovascular protective effects, which is beneficial to patients who may be at

risk of developing cardiac issues. Additional benefits such as antitumor effects, anti-aging effects, cost, and neuroprotective effects makes Metformin a great initiating therapy option. However, Metformin is not recommended when patients already have severe cardiac or renal complications such as atherosclerotic cardiovascular disease/heart failure, or chronic kidney disease. [13-14] Metformin is contraindicated when a patient's estimated glomerular filtration rate is below 30 mL/min/1.73 m^2. [15] Metformin works very well in combination therapy as well and can be used alongside almost all drug classes to further decrease blood glucose levels.[16]

GLP-1 Receptor Agonists work to decrease hyperglycemia by increasing insulin secretion and decreasing glucagon secretion based on available glucose. Insulin is known to reduce blood sugar levels and glucagon works to increase blood sugar levels. Between the different drugs within the GLP-1 RA class, all that are approved have been shown to reduce HbA1C levels. However, these drugs differ in terms of magnitude of effectiveness and the gravity of side effects. GLP-1 RAs have been known to work very well with Metformin to decrease A1C levels as well as decrease weight.[17] GLP1-RAs should not be used with patients who are pregnant or have severe gastrointestinal diseases.[18] Additionally, GLP1-RAs have been known to cause adverse effects in patients who have a history of pancreatitis.[19]

SGLT-2 Inhibitors are a class of drugs that work to reduce A1C levels by stopping glucose uptake from the proximal tube of the kidney to increase sugar levels in urine. This drug class is known primarily for its benefits on body weight, blood pressure, lipid profile, arterial stiffness and endothelial function. SGLT-2 Inhibitors (as well as GLP-1 RA) have shown great macrovascular benefits including lowering the risk of adverse cardiovascular

effects overall. SGLT-2 is a great secondary drug to be used alongside Metformin if patients exhibit cardiovascular diseases (CV) or chronic kidney disease (CKD). Although a promising and widely used drug class, the study mentions that it is unclear if the CV/CKD benefits of SGLT2 Inhibitors can be generalized to entire diabetic populations or are restricted to groups with cardiac and renal issues.[20] Because the efficacy of SGLT-2 Inhibitors is dependent on glucose filtration in the kidneys, this drug class is heavily contraindicated in patients who have impaired renal functions (GFR < 30 mL/min/1.73 m^2).[21]

DPP-4 Inhibitors work by increasing insulin secretion and reducing glucagon secretion (similar to how GLP1-RAs work). Typically, DPP4-Inhibitors can reduce A1C levels by about 0.5-1%. Metformin and DPP-4 Inhibitors used in tandem help reach A1C goals of <7% along with no body weight gain. This makes DPP-4 Inhibitors a suitable option to be used alongside metformin for patients struggling with weight gain. The adverse effects of DPP4-I are most notably nasopharyngitis and skin lesions, but in most cases, these are not serious enough to discontinue treatment. DPP4-I is contraindicated in patients that take GLP1-RAs and it is not recommended to combine them, but patients on GLP1-RAs can replace it with DPP-4 Inhibitors because of the similar mechanisms of action.[22]

TZDs target the body's insulin resistance and work on adipose tissue to increase the uptake of fatty acids which in turn improves insulin sensitivity. TZDs are known to benefit certain cardiac markers but it remains to be seen whether it truly decreases the risk of cardiovascular events. TZD is not widely used because of its adverse effects such

as weight gain, fluid retention, and increasing bone fragility.[23] Because of the risk of fluid retention, TZD is contraindicated in patients who have a history or risk of heart failure.[24]

Sulfonylureas (SU) work by increasing plasma insulin levels. It does this by attaching to a receptor on β-cells to secrete more insulin. This drug class shows similar levels of reducing blood glucose levels and A1C levels (20% and 1-2% respectively) as Metformin but poses a greater risk of hypoglycemia and weight gain. Physicians recommend that patients taking Sulfonylureas are cautioned about their risk of hypoglycemia, especially after exercise or a long period of time without food. Also, the use of this drug is cautioned in patients who are undernourished, long-time alcohol abusers, or have impaired renal or cardiac function. This means that Sulfonylureas can be used as initial therapy treatment, but metformin is still preferred as there are fewer risks involved. If the drug must be used, it should be recommended at a low dose first.[25] Additionally, physicians should not prescribe sulfonylureas if the patient can control blood sugar levels with a proper diet, otherwise the patient could suffer from hypoglycemia.[26]

The last drug category is Insulin. Insulin is a naturally occurring hormone within the body that regulates glucose levels and is important for many other aspects of human growth, development, and regulation of homeostasis. Regular insulin is a drug class that is a synthetic version of insulin and is taken via injection usually 30-40 mins before each meal. There are various types of insulin to treat Diabetes mellitus type II such as Insulin Basal Analogs, Insulin Ultra-Long Basal Analogs, Insulin Human Regular, Insulin Rapid Analogs, Insulin NPH/Regular Premix, and Insulin NPH/Analog Premix that will be included as separate drug classes within the application. Insulin is associated with many adverse side effects such as weight gain, potential anaphylaxis because of

hypersensitivity, and hypoglycemia.[27] Recommending insulin comes at a risk and should only be recommended primarily to lower A1C levels if other medication options are not available or contraindicated.

III. Methods

The process behind developing SMARTDM2 was split into 4 parts: 1. decision matrix design, 2. app development, 3. quantitative testing and 4. qualitative testing. The development process was sectioned to ensure that rigorous detail was given to developing and testing the application before and after posting it on iOS and Android platforms. Dr. Guillermo Umpierrez from the Emory University of Medicine assisted every part of the process to help cater the user interface to better suit clinicians that deal with diabetes patients daily. He also provided extensive insight on medication indications/contraindications and advice on combination therapy treatments based on his expertise and guidance from the Emory Healthcare Council.

Decision Matrix Design

The goal of the application was to receive patient characteristics, and current medications to display the best possible drugs for that particular patient. To combat the issue of sorting and ranking with every decision, the idea of a decision matrix was implemented to use summative measures to quickly find the best drug from patient characteristics. The 1x1 cell on the table was left blank, drug classes were put on a table in the first column, and patient characteristics were put on the first row. The complete list

of patient characteristics and drug classes has been mentioned previously. Then, through literature research and insight from Dr. Guillermo Umpierrez, points were assigned - moving from column to column - to both patient characteristics and drug classes. High values were given to the best drug class based on the specific patient markers, and low values were given to contraindicated drugs. For combination therapy, the same process was performed. Current patient medications (same as drug classes) were put in the first row, as an extension of the patient characteristics. Then, point values were assigned to the drug classes based on the medications the patient currently uses. High point values were assigned to drug classes that interact well with the specific medication and factors such as cardiac protectiveness, and cardiac/renal protectiveness were heavily considered. Low point values were assigned to drug classes that were either contraindicative to the specific medication or repetitive to specific medication (e.g. metformin would not be recommended if the patient was already on it). Negative values mean the drug is contraindicated with the patient characteristic, and a value of -99 designates severe contraindication. The process of the decision matrix can be seen in table 1. If a patient does not exhibit a characteristic, the respective point values of that column do not contribute to the sum.

	PC 1	PC 2	PC 3	Sum	Ranking
Drug 1	3	4	-1	6	Drug 1
Drug 2	2	-1	-3	-2	Drug 4
Drug 3	-99	2	0	-97	Drug 2
Drug 4	2	1	1	4	Drug 3

***Table 1**: Example of the decision matrix algorithm behind the application. PC stands for patient characteristic. In this scenario, drug 1 is the best medication for the patient.*

Application Development

The framework for the application was developed using React Native, for application use on both iOS and Android platforms. The application uses Firebase to store application data and can update the application with new decision matrix values from the cloud every time the physician opens the application. This is useful for collecting and storing application-use data, data analysis, receiving feedback from physicians, and correcting errors in the algorithm in real-time. Variables were created for the drug classes and patient characteristics (including current medications). The variables were assigned values from the decision matrix, and the application retrieves these values whenever its respective patient characteristic is selected. The application was designed to be fast and easy-to-use for physicians, so a quick “process a patient” button was included to begin the recommendation process as fast as possible. A color-coded recommended drugs page was added after the physician inputs patient information to visually show the drugs that are recommended (green), cautioned (yellow), and contraindicated (red). A disclaimer and FAQ/About section were incorporated on the home page to give more details about the application, and to emphasize that the application is solely a helpful adjunct and is not meant to be taken as professional medical advice. A feedback form was inserted after the recommendation page for physicians to enter a simple “thumbs up” or “thumbs down” to indicate if they felt the recommendations were correct or incorrect

respectively. If the physicians feel the recommendations are wrong, they can elaborate on what medications specifically are incorrect and why. The patient characteristics and recommendations are automatically captured to associate with the feedback form for later analysis. Figure 4 represents the feedback mechanism for improving the algorithm.

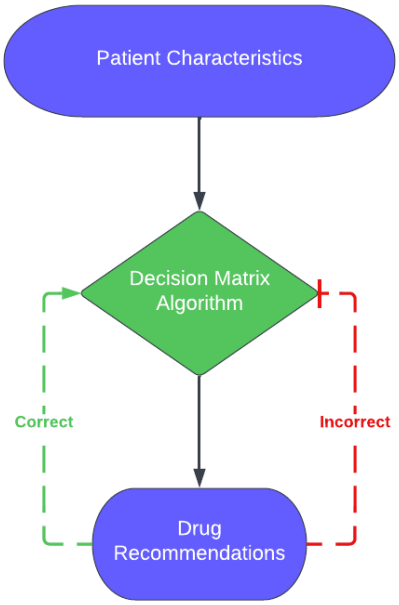

Figure 4: *Feedback mechanism for revising the decision matrix algorithm based on correct or incorrect recommendations*

Preliminary Testing

To eliminate any human error in transferring the values from the decision matrix into the application and any application errors in computing, the application recommendations were checked against a calculator run on Excel that used values directly from the finalized decision matrix. There are 3,145,725 possible combinations from the algorithm, found by using the sum of combinations equation $C_N = 3 \times \sum_{i=1}^{20} \frac{n!}{n!(n-i)!}$ in which n is the number of patient characteristics. In this case, n is equal to 20, the number of patient characteristics. The value was multiplied by 3, as there are 3 GFR classifications: GFR>45, GFR 30-45, and GFR<30. These are mutually exclusive events, so these 3 patient characteristics are excluded from summation of combinations. At first, it was proposed that the process of checking the results from excel and the application be automated, but the application cannot handle large data sets and continuous calculations due to the lack of processing power. Instead, the process was done manually by the

research team. The decision matrix was copied into a MATLAB program that put all the possible recommendations per combination into a CSV file. The CSV file with recommendations was cross-checked with the application recommendations by all members of the team. The team then noted any deviations into another spreadsheet, and the data was evaluated.

Quantitative Testing

The application is able to track application usage anonymously, and that data was used to identify the efficacy of the algorithm. Physicians were able to note if they felt that a recommendation was incorrect, and the accuracy of the recommendations were evaluated. The accuracy of the recommendations was tracked by the amount of times the physicians left a thumbs down (incorrect recommendation given) divided by the amount of times the physicians received a recommendation from the application. This equation can be represented as a simple accuracy percentage: $\frac{X_C}{X_T} \times 100 = P_A$, where X_C is the amount of correct recommendations, X_T is the total amount of recommendations, and P_A is the accuracy percentage. Similarly, the inaccuracy percentage was calculated with the equation: $\frac{X_{IC}}{X_T} \times 100 = P_I$, where X_{IC} is the amount of incorrect recommendations, X_T is the total amount of recommendations, and P_I is the inaccuracy percentage.

Qualitative Testing

The application was assessed qualitatively by asking physicians to rate how much they agreed or disagreed on a set of statements regarding the efficacy and usability of the application. The physicians that used the application were asked to fill out a survey in

Google Forms with questions on a scale of 1 to 10. A score of 1 meant the physician completely disagreed with the statement and 10 meant the physician completely agreed with the statement. The statements on the survey were:

1. *I feel the application is accurate at recommending medication for patients*
2. *I feel the application makes it easier to treat patients as a clinician*
3. *I feel the application reduces the time it takes to prescribe medication to patients*
4. *I feel the application is reliable and works well*
5. *I feel the application is easy to use*

The results were anonymized to allow the physicians to review the application truthfully.

IV. Results

Preliminary Testing

Out of the 3,145,725 possible combinations tested, 94.97% of the recommendations from the application matched the results from the original decision matrix (Table 2).

Total Possible Combinations (N_T)	Correct (N_C, %)		Human Error (N_{HE}, %)		Application Error (N_{AE}, %)	
3145725	2987642	94.97%	157,871	5.02%	212	0.007%

Table 2*: Accuracy rate of the application compared to decision matrix. 94.97% of the recommendations were "correct" or matched the recommendation based on the original decision matrix.*

The application deviated from the decision matrix a total of 158,083 times. The error that resulted in the most incorrect recommendations within the application was found to be

due to an improper data entry into the application code. This issue has been resolved by updating the application code. The error that resulted in 212 incorrect recommendations was the application missed certain values at times when the application loses internet connection mid-recommendation. This problem was fixed by allowing the application to access a stored offline matrix to eliminate network dependency. The offline matrix is auto-updated when the application is connected to an internet connection to ensure the physicians always use the most up-to-date algorithm.

Quantitative Results and Analysis

After two months of application testing by 17 physicians, there have been 918 recommendations given by the SMARTDM2 application. The number of correct recommendations were recorded as the amount of times the drug recommendations were given a thumbs up. The number of incorrect recommendations were recorded as the amount of times the drug recommendations were given a thumbs down. The results of this analysis are shown in table 3 and Figure 5.

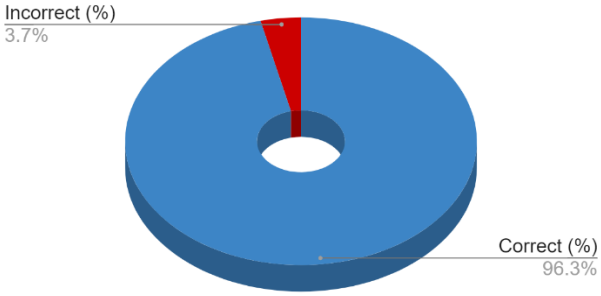

Figure 5: *Pie chart of the percentage of correct recommendations vs incorrect recommendations*

Recommendations Given (n)	Correct (n, %)		Incorrect (n, %)	
918	884	96.3%	34	3.7%

Table 3*: Number of correct recommendations and incorrect recommendations given out of total recommendations*

The results indicate the recommendations are correct majority of the time. 15 of 34 (44.1%) of the incorrect recommendations were supplemented with the physicians

input on why they believed the recommendations were incorrect. Relevant comments about why the recommendations were incorrect which influenced the changing of the algorithm will be explored later in this paper.

Qualitative Results and Analysis

Endocrinologists and diabetes physicians at Emory University were asked a series of qualitative questions to evaluate the application after using the application for 15 days. Most physicians found the application was both effective and easy to use. The physicians' (n=17) ratings are shown in Table 4. An aggregate analysis is shown in Figure 6 and Table 5.

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17
Q1	6	8	7	8	8	9	6	9	9	6	10	9	6	7	7	10	6
Q2	7	7	8	10	6	8	8	9	8	9	8	8	10	9	8	7	10
Q3	10	7	6	10	9	8	6	8	6	8	9	8	7	10	7	10	7
Q4	7	8	6	8	7	7	8	10	10	10	9	7	6	8	9	9	7
Q5	7	8	8	6	10	6	9	10	10	9	9	9	6	9	6	9	6

Table 4*: Individual physician responses to the qualitative analysis questions. P1 refers to physician 1, P2 refers to physician 2, and so on. Q1 refers to question 1 (referenced earlier), Q2 refers to question 2, etc. The lowest score by all the physicians was a 6*

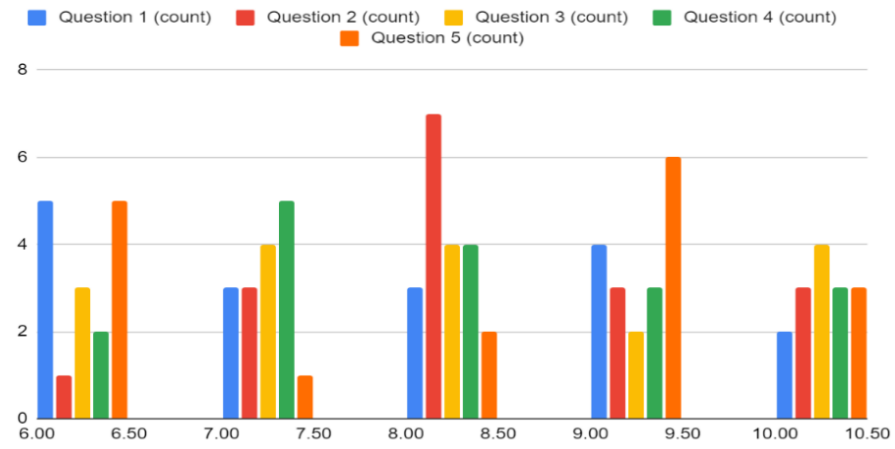

Figure 6: *Histogram chart showing frequency of physician responses to survey questions*.

Question	Response Mean ± SD	Range
Q1. I feel the application is accurate at recommending medication for patients	7.71 ± 1.45	1-10
Q2. I feel the application makes it easier to treat patients as a clinician	8.25 ± 1.15	1-10
Q3. I feel the application reduces the time it takes to prescribe medication to patients	8.00 ± 1.46	1-10
Q4. I feel the application is reliable and works well	8.00 ± 1.32	1-10
Q5. I feel the application is easy to use	7.79 ± 1.56	1-10

Table 5: *Aggregate analysis of the responses. The responses for each question are averaged plus or minus the standard deviation. All of the averages of the responses to individual questions were higher than 5*

V. Discussion

Recommendations and Feedback

Physicians indicated the application displayed correct recommendations greater than 96% of the time. Incorrect recommendations were largely based on incorrect drug interactions, and drugs that do not work well (but not contraindicated) were recommended before drugs that did work well with medication the patient was currently on. Some of the recommendations that were marked as incorrect did not have supplemental information. Some incorrect recommendations with supplementary comments that did lead to changes in the algorithm were:

1. *"[Sulfonylurea] should have a higher value for patients with a GFR between 30-45. [The drug] is cheaper and safer than insulin in patients with impaired kidney function"*

This recommendation was given in a scenario in which a patient had a GFR between 30-45 (moderately impaired renal function) and had no insurance. The recommendation originally recommended the various insulin types higher than sulfonylurea. Several

studies have shown that the use of sulfonylureas and insulin greatly increase the risk of hypoglycemia in patients and must be used with caution.[28] It is also true however, that sulfonylureas are more widely prescribed to patients due to availability of the drug and its low cost, even in patients with impaired renal function due to its efficacy at lowering HbA1c levels in relatively low doses with very few adverse effects (when compared to insulin).[11] The value of sulfonylurea was lowered for patients with moderately impaired renal function so that it would be recommended higher than insulin for these specific patients.

2. *"[Insulin] NPHs should be ranked very low when patients are over 65 and have a long history of cardiac issues. Regular [insulin] or [insulin] basal analogs would work slightly better here"*

The application was wrong here because Neutral Protamine Hagedorn insulin (Insulin NPH) had the same score as regular and insulin analogs in patients who were elderly and suffered from heart failure or atherosclerotic cardiovascular disease. In the *Outcome Reduction with an Initial Glargine Intervention* trial, insulin basal analogs and regular human insulin were shown to have neutral effects to the incidence of major cardiovascular effects in patients.[29] There have not been any major clinical studies to determine the incidence of major cardiovascular effects in patients taking insulin NPH, so the algorithm was altered to reflect the preference of regular insulin and insulin basal analogs over insulin NPH for these specific patient categories.

All qualitative feedback showed that all physicians surveyed at least somewhat agreed on all the statement provided (>5 to all questions). The physicians felt the application gave accurate recommendations, made it easier to treat patients, reduces patient visit times, and was reliable and easy to use. Therefore, the results of this study

highlight that this application is a viable tool for assisting endocrinologists suffering from patient overload while simultaneously reducing the risk of human error when prescribing medication. The application will be continuously improved and updated as further feedback from physicians are received.

Limitations

One limitation of this study was the inability to test all possible combinations (3.1 million) with every physician. There is no way to know, without a large number of physicians for testing and ample timeframe, whether all the individual recommendations are correct. Also, due to the nature of diabetes as a disease, some patient characteristics are more prevalent than others, leading to recommendations for the larger population being evaluated more by the physicians compared to rarer combinations of patient characteristics. Another limitation was the small and homogeneous sample size (Emory University physicians), which limits the generalization of results to other physicians across the country.

Implications and Future Work

This study implies that applications can be a useful tool to assist physicians not just in the diabetes space, but for other diseases in which physicians suffer from patient overload and confusion from rapidly evolving medication guidelines by governing bodies. In further studies, a decision matrix-based application could be used to assist physicians in prescribing medications for other widespread chronic diseases such as heart diseases and cancers. Shortcomings of the *SMARTDM2* application as noted by physicians have

already been fixed, and it remains to be seen whether these changes will improve the efficacy of recommendations.

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