

Precise Humane Diabetes Management: Synergy Of Physiological And Psychological Data In AI Based Diabetes

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Abstract: Artificial Intelligence (AI) is revolutionizing the healthcare industry. It has got the eloquence to provide globally accessible, improved diagnosis at affordable price. As, per Forbes report the investment in healthcare AI is expected to reach \$6.6 billion by 2021 portraying a compound annual growth rate of 34 percent. The market of AI in diabetes care alone is expected to reach \$626.3 million by 2022, as per Infoholic Research LLP. AI is seen as the most germane technology remodeling the diabetes care sector. Diabetes is anticipated to affect an approximate of 642M people by 2040. More funding are being poured into the research of using AI to provide the right diabetes treatment. This paper reviews the appropriateness of AI in providing right and timely diabetes treatment. It also highlights the impediments present in laundering successful accurate diagnosis. Currently, stress is laid upon considering only the physiological data of the patient with diabetes by AI. The human dimension, i.e. the psychological data of the patient is nowhere considered by the AI models. This certainly leads to absurdity. Psychological research has an important role to play in improving the prevention and care of diabetes. Disregardance of this aspect will lead to fallacious treatment being administered to a patient. Putting AI based diabetic care on the wrong track. Hence stressing upon the need to consider both physiological and psychological data of a patient, this review paper highlights the right kind of data to be examined and investigated while modeling the AI algorithms. This aids to administer personalized precise clinical diagnosis and quality diabetes care.

Index Terms: Artificial Intelligence, Cross Validation, Diabetes Management, Performance Parameters, Physiological and Psychological Data, Time Series

1. INTRODUCTION

Convergence of medical diagnosis and technology is made possible with the advent of Artificial Intelligence (AI) in healthcare. AI has the potential and covenant to improve the health outcome, due to its ability to provide personalized precise targeted clinical care for an individual. Ingraining AI into medical diagnosis curtails the momentousness of human error saving time and money improvident on wrong clinical diagnosis. AI based medical diagnosis helps healthcare professionals to craft improvised patient treatment care. And for patients, AI provides increased safety through real time continuous monitoring and alert system; it prevents recurrent hospitalization and curtails superfluous expenses incurred due to wrong diagnosis. Currently there is the "golden triangle" problem bothering the healthcare sector globally i.e. cost, precise diagnosis and access. Optimizing any one of these three parameters is feasible but with a tradeoff. AI capacitated healthcare sector is adept to play the pivotal role in deciphering this "golden triangle" quandary. AI has got the eloquence to provide globally accessible improved diagnosis at affordable price. This revolution brought by AI is wavering the global healthcare sector market. More than one third of the healthcare providers and drug manufacturers are investing in AI. As, per Forbes report [1] investment in healthcare AI is expected to reach \$6.6 billion by 2021 portraying a compound annual growth rate of 34 percent. The market of AI in diabetes management alone is expected to reach \$626.3 million by 2022, as per Infoholic Research LLP [2].

As per World Health Organization (WHO) records, nearly 422 million people globally have diabetes, and diabetes being a burgeoning pandemic epidemic, it is anticipated that an approximate of 642M people are expected to suffer from this metabolic disease by 2040 [2]. The comprehensive nature of diabetes data available in ease makes it a quintessential fit for applying AI and Machine Learning (ML) to improve diabetes care. Hence, AI can be seen as the most germane technology revolutionizing the diabetes care sector. This paper reviews the appropriateness of AI in providing right and timely diabetes treatment. It discusses the significant contributions made and the use of ML algorithms used to ensure the ascendancy of AI in diabetes care. It also highlights the impediments present in laundering successful accurate diagnosis. Currently, stress is laid upon considering only the physiological aspect of the diabetes data by ML algorithms in most of the research work reviewed in this paper [3-10]. The patient is being considered as an object; by sensing variation in the physiological data ML model predicts the blood glucose level and the treatment plan is laid out. The human dimension, of the patient not being considered certainly leads to absurdity. However, only meager amount of quality research papers are available focusing on the application of psychological data by ML algorithms. In a special issue [11] of American Psychologist entitled "Diabetes and Psychology," researchers review the impact of psychological factors to the well-being of people with or at risk of developing diabetes. The psychological factors includes: family and social connections, changing technology, behavioral intervention programs and identification and treatment of mental disorders associated with diabetes itself. It was concluded by many researchers [12-15] that psychological factor has an important role to play in improving the prevention and care of diabetes. Since psychology can optimize diabetes treatment, this current review paper examines the psychological needs of diabetic patients and emphasizes the need for considering psychological data in synergy with physiological data by Alaiding to administer personalized precise clinical diagnosis and quality diabetes

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2 Role of Machine Learning in Blood Glucose Level Prediction

Diabetes Mellitus (DM) is a metabolic disorder of chronic hyperglycemia due to either immune-mediated (Type 1), insulin resistive (Type 2), gestational or others (environment, genetic defects, infections, and certain drugs) [16]. The worldwide occurrence of diabetes has and will continue to increase drastically. However, diabetes is expected to show a steady rise in Asia and Africa, by 2030 [17]. The list of top five countries with the highest estimate of diabetic cases in-between 2000 and 2030 is tabulated in Table 1.

Table 1: Countries with Highest Estimate of Diabetic Cases [17].

Sl No	2000		2030	
	Country	No. of Diabetic Cases (in Millions)	Country	Estimated No. of Diabetic Cases (in Millions)
1	India	31.7	India	79.4
2	China	20.8	China	42.3
3	U.S	17.7	U.S	30.3
4	Indonesia	8.4	Indonesia	21.3
5	Japan	6.8	Japan	8.9

An upswing of diabetes at such a high rate imposes an unseen threat on both the healthcare system and diabetic patients. Impact can be seen on achieving affordable, accurate and accessible patient care. Importance of using technology towards the prevention and treatment of diabetes has risen to the zenith. Diabetes care has got a breakthrough with AI Technology. AI provides leading-edge analytics to educate, evaluate and update patients about their glucose levels continuously in real-time so that necessary adjustments w.r.t food, insulin dosage, exercise, and other factors can be made. This aids in self-diabetes care management fostering improved health outcomes. AI provides a real-time connect between the medical professional and the patient, this improves the tenacity of treatment administered thereby bridging gaps in therapy and reducing the potential for adverse clinical consequences otherwise. Compendium on the recent works of AI techniques used to assist in the management of diabetes, along with the associated challenges is presented in this section. Figure 1 illustrates the block diagram indicating

the various stages needed in implementing the “AI based Diabetes Management Model”.

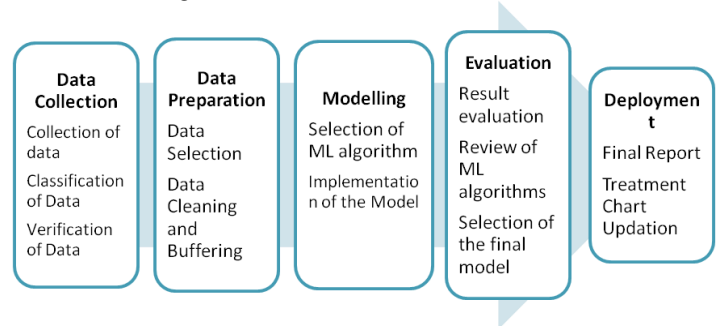


Fig 1: AI based Diabetes Management Model

We use the following proposed diabetes management steps to summarize the contributions, improvements and results described in the reviewed articles:

- Blood glucose data collection and classification
- Blood glucose data preparation
- ML algorithms based detection of adverse glycemic events.
- Performance parameters for evaluation of ML algorithms.
- Report on patient's risk factor, insulin calculator and other information.

2.1 Blood Glucose Data Collection and Classification

This step is necessary to collect, understand and clean the dataset. Classification and analysis of data to gain insight on its potential features is of prime importance. Riccardo Bellazzi, et.al [18], article suggest that diabetes data mining in two areas is of significant use to researchers and clinical practitioners, namely: analysis of (i) blood glucose home monitoring data of diabetes mellitus patients and (ii) blood glucose monitoring data from hospitalized intensive care unit patients. It is suggested that data should include administrative information, such as cost, physician's workload and patient's hospital admission history, as well as clinical variables, such as drug prescriptions and laboratory test results. As per, “CDISC Therapeutic Area Data Standards User Guide for Diabetes (Version 1.0)” released by Clinical Data Interchange Standards Consortium, Inc in 2014 [19], the various diabetes related markers is tabulated in Table 2.

Table 2. Diabetes Related Markers [19]

Common Test Abbreviation	Test Name	Description	Specimen
A1c HbA1c	Glycosylated Hemoglobin, Glycated Hemoglobin, Hemoglobin A1c, Glycosylated Hemoglobin A1c	Glycosylated hemoglobin is formed in a non-enzymatic glycation pathway by hemoglobin's exposure to plasma glucose. As the average amount of plasma glucose increases, the fraction of glycosylated hemoglobin increases in a predictable way. This serves as a marker for average blood glucose concentrations over the previous two to three months prior to the measurement.	Blood
	Glucose	Glucose is a carbohydrate and is the most important simple sugar in human metabolism. The body naturally tightly regulates the glucose concentrations as a part of metabolic homeostasis. Glucose is transported from the intestines or liver to body cells via the bloodstream and is made available for cell absorption via the hormone insulin. Diabetes mellitus is characterized by consistent hyperglycemia.	Serum, Plasma, Blood, Urine
	Insulin	Insulin is a peptide hormone produced by beta-cells of the pancreas that is central to regulating carbohydrate and fat metabolism. As glucose concentrations normally rise after a meal, insulin increases in the bloodstream and promotes use and storage of glucose. In diabetes, there is either an absolute or relative insulin deficiency, resulting in abnormal glucose homeostasis.	Serum, Plasma
C-peptide	Connecting Peptide	C-peptide is a peptide that connects the A-chain and B-chain of insulin in the pro	Serum, Plasma

		insulin molecule. When insulin is secreted from the pancreatic beta cells, equal amounts of C-peptide are released into the blood stream. Measuring the concentration of C-peptide reflects the amount of insulin being produced by beta cells. Measuring the concentration of C-peptide is sometimes useful to assess beta cell function.	Urine
GIP	Glucose-Dependent Insulinotropic Peptide, Gastric Inhibitory Peptide	GIP is a secretin hormone, meaning that it is produced by particular intestinal cells. It enhances the release of insulin in response to a meal. Subjects with diabetes are relatively unresponsive to GIP and their GIP concentrations after a meal are lower than normal.	Serum, Plasma

Glucose reading considered for ML algorithms is obtained either through Self-Monitoring Blood Glucose (SMBG), or through laboratory tests termed as Laboratory Blood Glucose (LBG). SMBG involves collecting a very small sample of blood using a finger stick, and then measuring the glucose concentration (either as whole blood or plasma) in a small, handheld glucose meter or through Continuous Glucose Monitoring (CGM) sensors. All the glucose measurements calculated are calibrated to plasma equivalent glucose values. LBG are used to measure Fasting Plasma Glucose (FPG), Post-Prandial Plasma Glucose (PPG) and/or Oral Glucose Tolerance Test (OGTT) or Meal Tolerance Test (MTT). For LBG, blood is drawn from the vein, and the glucose level is analyzed in a laboratory. Jennifer Mayfield [20] has concluded in her research work that measurement of FPG level is more acceptable and accurate than OGTT. The National Diabetes Data Group emphasizes on maintaining a FPG level ≥ 120 mg per dL and A1C level ≥ 7.0 %.

2.2 Blood Glucose Data Preparation

Next step is the data preparation. This is considered as the most crucial step. Model evaluation will entirely depend on the quality of the data. The factors to be considered in the data preparation process are as follows:

- Presence of duplicate or irrelevant observations.
- Presence of missing or null data points.

The data preparation stage is a pipelined procedure normally involving six essential processes. This is as illustrated in Figure 2.

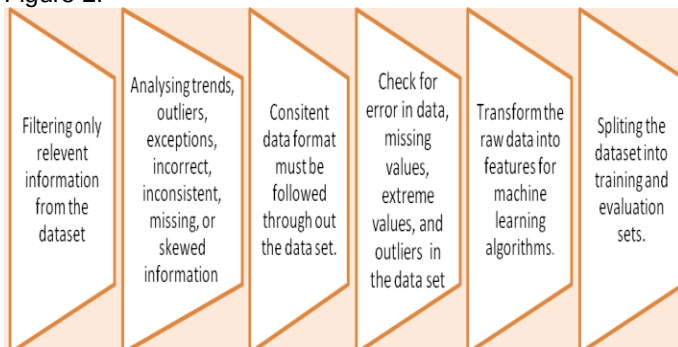


Fig 2: Pipeline Process of Data Preparation Stage

Jinyu Xie et.al. [21] has split the data preparation step into two stages: resample stage and imputation stage. A time period with 5 minute interval was derived, then all the samples were aligned to this time period in a “forward filling” manner, i.e. if the data is missing at the designated sample time, then the closest value before that time point was used. At the imputation stage, the missing data is calculated by using Kalman Smoothing Technique. Harleen Kaur [22] has used Pima Indian Diabetes dataset of female patients with minimum twenty one year age from UCI machine learning repository. This dataset consists of 768 samples classified into diabetic and non-diabetic classes. It has eight factors namely: number of times pregnant, plasma glucose concentration of two hours in an OGTT, diastolic blood pressure, triceps skin folds thickness, two-hour serum insulin, body mass index, diabetes pedigree function and age. Using R based feature selection Boruta algorithm the dataset was filtered and only four important attributes were selected to be processed by ML algorithms. Sanjaya De Silva [23] also considered the Pima

Indian Diabetes dataset. Data preparation was done using WEKA tool. In a research paper by J. Li et al.[24] diabetic data set is created by obtaining data from hospital which contains two hundred and forty nine instances with seven attributes. WEKA tool is used for data preparation.

2.3 ML Algorithms Based Detection Of Adverse Glycemic Events

The need of the hour is to analyze the huge amount of data available to ascertain some concrete facts that helps in improving the health outcomes of patients. In order to perform the right kind of analysis there is a need of a good prediction model. Hence the focus in this section is to review research on design and development of prediction model for blood sugar level by using ML algorithms. ML algorithms are categorized into supervised and unsupervised algorithms. A supervised learning algorithm uses the past data to predict the new data, whereas unsupervised algorithms learning identifies trends in the data and responds based on the presence or absence of such trends in each new dataset. The supervised learning is also called classification. Normally it is widely used to produce a more accurate predictive model and commonly applied for diabetes prediction problem. A time series is an ordered sequence of observations from the present and past. Time series datasets differ from regular datasets because there is a natural ordering to the observations. Another unique feature of these datasets is that adjacent observations are dependent [25]. Blood glucose prediction is a time series dataset that is noisy and non-stationary in nature. Real-world time series that exhibit these properties require advanced algorithms to model predictions. This motivates the use of techniques such as SVMs and neural networks. SVMs outperform neural networks as shown by many publications listed in [26]. A literature survey of ML algorithms employed for time series blood glucose level prediction is as presented. In a paper by Quan Zou [27-28] decision tree, random forest and neural network approach is used to predict diabetes mellitus. The dataset is the hospital physical examination data in Luzhou, China. It contains 14 attributes and principal component analysis (PCA) and minimum redundancy maximum relevance (mRMR) is employed to reduce the dimensionality. In this study, five-fold cross validation is used to examine the models. The results showed that prediction with random forest could reach

the highest accuracy (ACC = 0.8084) when all the attributes were used. Maniruzzaman M et.al [29] has developed an optimized and robust machine learning (ML) system. Here the features are extracted and optimized from the six feature selection techniques (random forest, logistic regression, mutual information, principal component analysis, analysis of variance, and Fisher discriminant ratio) and combined with ten different types of classifiers (linear discriminant analysis, quadratic discriminant analysis, naïve Bayes, Gaussian process classification, support vector machine, artificial neural network, Adaboost, logistic regression, decision tree, and random forest) under the hypothesis that both missing values and outliers when replaced by computed medians will improve the risk stratification accuracy. Pima Indian diabetic dataset (768 patients: 268 diabetic and 500 controls) was used. using

2.4 Performance Parameters for Evaluation of ML Algorithms

The metrics used to evaluate the ML algorithm is as follows:

1. Accuracy: It is the ratio of number of correct predictions to the total number of input samples.
2. Confusion Matrix: A confusion matrix provides a more detailed breakdown of correct and incorrect classifications for each class.
3. Logarithmic Loss: Logarithmic loss (logloss) measures the performance of a classification model where the prediction input is a probability value between 0 and 1. Log loss increases as the predicted probability diverges from the actual label. The goal of machine learning models is to minimize this value.
4. Regression Metrics "Root Mean Squared Error and Mean Absolute Error": The Mean Absolute Error (or MAE) is the sum of the absolute differences between predictions and actual values. On the other hand, Root Mean Squared Error (RMSE) measures the average magnitude of the error by taking the square root of the average of squared differences between prediction and actual observation.
5. Variance: It's the difference between the forecasted value and the actual value.
6. Mean percentage error (MPE). Average percent of error, a measure of variation.
7. Mean Absolute percentage error (MAPE). To account for both positive and negative errors, we compute the average of percentage errors with signs ignored, that is, average of absolute percentage error.
8. Sensitivity: Sensitivity is a measure of the proportion of actual positive cases that got predicted as positive. It is a measure of truly predicted values by sum of true positive and false negative.
9. Specificity: Specificity is defined as the proportion of actual negatives, which got predicted as the negative (or true negative). It is a measure of false positive values by sum of true negative and false positive.

2.5 Risk Factor, and Insulin Calculator prediction by ML algorithms

the combination of random forest feature selection and random forest classification technique yields an accuracy, sensitivity, specificity, positive predictive value, negative predictive value and area under the curve as: 92.26%, 95.96%, 79.72%, 91.14%, 91.20%, and 0.93, respectively. [30] implemented a simple Support Vector Regression (SVR) model. Two separate SVR models were trained, one for a 30 minute prediction, the other for a 60 minute prediction. This model outperformed the SVM technique used.

As per American Diabetes Association (ADA) Standards of Medical Care in Diabetes-2019 [31] hypoglycemia and hyperglycemia risk factor is defined as follows:

- Level 1 hypoglycemia is defined as a measurable glucose concentration < 70mg/dL.
- Level 2 hypoglycemia is defined as a measurable glucose concentration < 54mg/dL. It is the threshold beyond which neuroglycopenic symptoms like sweating, shakiness, tachycardia and anxiety occur. It requires immediate intervention.
- Hyperglycemia refers to high levels of blood glucose levels. Measurable fasting glucose concentration >130 70mg/dL and a postprandial value >180 mg/dl will be treated as hyperglycemia condition.

Support Vector Machine (SVM), Decision Tree, Random Forest, and Naive Bayes are [32-33] prominently used classifiers for diabetes diagnosis. These classifiers can identify the main attributes causing uncontrolled diabetes. It can identify hyperglycemia and hypoglycemia conditions with ease. Bharath Sudharsan et. al [34] trained a probabilistic model using various machine learning algorithms with a dataset containing SMBG values. The threshold for hypoglycemia was set to an SMBG value < 70 mg/dL. The model is said to have achieved a sensitivity of 92 % for 24 hour prediction horizon. Kevin Plis et. Al. [35] designed a Support Vector Regression physiological model for hypoglycemia detection. It achieved a precision of 42% with 30 minutes prediction horizon. SVR system is able to predict 23% of the hypoglycemic events with a false positive rate under 1%. Nahla et.al. [36] used SVM classifier. Evaluation results on a real-life diabetes dataset show that SVMs achieve a prediction accuracy of 94%. Polat et al. [37] built LS-SVM to classify diabetes dataset. The proposed system 82.05% classification accuracy using 10-fold cross validation. Li and Zhou [38] used a semi-supervised learning algorithm named Co-Forest. Though blood glucose level forecast and hyper or hypo risk analysis can be achieved using predictive models, patient's lifestyle which is the greatest influencer of uncontrolled blood glucose level is not considered by predictive models. The problem faced in implementing

AI is twofold. Firstly, it requires good amount of right quality data. The data must be structured and digitized; missing data if any must be accommodated. Data privacy and the probable security risks must be taken care. Secondly, patients encouraged to use AI based diabetes care need to be technology savvy. They must have access to the cloud for data storage, retrieval and receive treatment updates. This eventually is the bottleneck given the socio-economic and age-related inequalities. Hence the mission of AI revolutionizing the healthcare sector remains impasse. However the solution to the access to right dataset problem can be optimized. Care must be taken by the predictive system to consider both physiological data (directly available data) and psychological data (indirectly available data).

3 Insight of Physiological Data on Diabetes Mellitus

In this paper the author has identified various physiological signals, which can be easily monitored, to provide a robust and reliable estimate of blood glucose levels in diabetes patients. The types of physiological signals examined includes: Electromyographic (EMG), Electroencephalogram (EEG), Electrocardiogram (ECG), Accelerometry, pulse, skin temperature and galvanic skin response (GSR) data [38]. The correlation between physiological data and the blood glucose levels were studied. The effect on blood glucose levels due to variation of physiological signals is presented in this section. The American Diabetes Association has recommended Glycated Hemoglobin (HbA1c) as an important parameter for diagnosis of diabetes. HbA1c is an important indicator of long-term glycemic control with the ability to reflect the cumulative glycemic history of the preceding two to three months. HbA1c not only provides a reliable measure of chronic hyperglycemia but also correlates well with the risk of long-term diabetes complications. Elevated HbA1c has also been regarded as an independent risk factor for coronary heart disease and stroke in subjects with or without diabetes. The valuable information provided by a single HbA1c test has rendered it as a reliable biomarker for the diagnosis and prognosis of diabetes.

The electrical activity in the brain represents the metabolic state of the brain cells and can be measured by electroencephalography (EEG). Baskaran A [39] conducted a study on EEG power spectral analysis to investigate whether alterations in EEG are associated with changes in blood glucose levels. This study included 24 healthy volunteers who underwent resting-state EEG and completed two attention examinations following a fasting period of at least 8 hours. The same tests were repeated after the participants ingested a glucose-rich drink. The study demonstrated that due to hypoglycemia there was decreased power in the theta and low alpha bands on a resting-state EEG. A similar analysis was drawn by Pan A [40]. An association between hypoglycemia and changes in the EEG has been demonstrated, although blood glucose levels alone do not seem to predict neuroglycopenia. This review provides an overview of the current literature regarding changes in the EEG during episodes of low blood glucose.

Electromyography (EMG) is an electro-diagnostic medicine technique for evaluating and recording the electrical activity produced by skeletal muscles. Decreased blood flow and increased blood sugar level are the causes of diabetic neuropathy. When the blood sugar level is higher than normal for an extended period of time, the blood vessels and nerves

start to degenerate. Symptoms usually develop 10-20 years after the initial diabetes diagnosis. Patients can experience numbness or abnormal tingling sensations and pain in the hands and especially in the feet. Other symptoms are lightheadedness, heartburn, swallowing problems, diarrhea or constipation, bladder problems and failure to achieve sexual arousal. In the article by Christian Nordqvist [41] he has investigated acute changes in nerve conduction associated with glycemic control. It was shown that Glycemic control quickly alters the speed of nerve conduction. In diabetes, nerve dysfunction can result from reversible metabolic factors associated with hyperglycemia, as well as structural changes.

An ECG (electrocardiogram) records the electrical activity of your heart at rest. It provides information about your heart rate and rhythm, and shows if there is enlargement of the heart due to high blood pressure (hypertension) or evidence of a previous heart attack (myocardial infarction). Hypoglycemia leads to reduction in its amplitude with flattening and lengthening of the T wave in the ECG signal, which is quantified by measuring the length of the QT interval. The most common cause of transient ECG changes in diabetics is due to hypoglycemia. In the adult human, acute hypoglycemia results in end-organ stimulation and a profuse release of epinephrine (adrenaline). This promotes the hepatic production of glucose. The hemodynamic changes associated with hypoglycemia include an increase in heart rate and peripheral systolic blood pressure, a fall in central blood pressure, reduced peripheral arterial resistance (causing a widening of pulse pressure), and increased myocardial contractility, stroke volume, and cardiac output [42-45]. This transient cardiac stress may have dangerous consequences in many older people with diabetes, especially individuals with type 2 diabetes, many of whom have coronary heart disease. To be able to effectively manage diabetes with the aid of dietary control, patient's education, understanding, and participation is vital. The patient needs to exercise control in:

- Diabetes treatment option and awareness of the prescribed medication.
- Food plan and physical activity plan.
- Monitoring of blood sugar levels on a regular basis.

To achieve this control the psychological condition of the patient plays a very important role. The next section provides an insight into the psychological data to be considered for predicting blood glucose levels.

4. Sagaciousness of Psychological Data on Diabetes Mellitus

AI based diabetes care requires diabetic patients to bring in a self-care conduct for better diabetic management. This includes having discipline in diet control, life style change, regular workout and medication; cater to insulin dosage adjustment and performing regular SMBG. But this disciplined behavioral change is often not accomplished, even though patient is well educated about its significance. Mazza SA [46] in his article has proved that, the parameter HbA1c gives a good insight for monitoring this controlled behavior. In a review paper by Mark Peyrot [47], the key behavioral/psychosocial interventions available to diabetes care providers has been identified. A conceptual framework for application of these interventions by a typical health care provider is provided. In an article published by Dr J.K. Wales [48], has shown that there is a strong evidence of psychological stress deteriorating the glycemic control in diabetic patients. Holt RI [49] in his work has presented strong

evidence that psychological distress is linked to high morbidity and mortality risk in type 2 diabetes. A study by [50-55] evaluates the psychological health of diabetic patients in a hospital in Korea. Their result revealed that treatment outcome was pointedly linked with patient's age, satisfactory treatment times, consultancy with the same medical expert every visit, feel at ease with the diet and exercise suggested.

However, the author is of the opinion that psychological factors not being considered by the AI based diabetes prediction model, can result in erroneous predictions and wrong diagnosis which can be life threatening. Till date the difficulty lies in quantifying these psychological factors like depression, stress, sleep quality, socioeconomic circumstances to name a few. Since these parameters can't be measured, it is termed as unimportant and neglected till date. But if a relationship can be recognized between these psychological parameters and measurable physiological parameters, then the AI model designed will be more humane and prediction can be more accurate.

In the next section, author provides a detailed review of psychological and physiological parameters to be considered in synergy for providing optimal diabetes care.

5 Synergy of Physiological and Psychological Data in Diabetes Care

Bullard et.al [56] identified 14 parameters inclusive of psychological and physiological data that are significant to render right diagnosis by the AI system in diabetes care. This includes access to care, air quality, blood pressure, blood glucose levels, depression, diet, education, heart rate, medication, physical activity, respiration, stress, and substance abuse such as addiction to smoking and alcohol respectively. As per American Diabetes Association [57] due to stress body prepares a fight-or-flight response. During this operation levels of many hormones tend to rise. This results in dissipation of stored glucose to the cells. In diabetic patients, during this operation insulin is not able to regulate this increase of blood glucose level. Ryan, C. M et.al. [58] proposed a model to relate chronic stress with Glucocorticoid Receptor Resistance (GCR). It was proved that exposure to a stressful life event can result in increased GCR. [59] Ducat et.al. [59] proves that stress increases cortisol level leading to Cushing's Disease (CD). Cortisol is a steroid hormone, that regulates a wide range of body processes, but it displays its main effect after food intake. It contributes to glucose intolerance and to reduced insulin sensitivity. About 50% of patients with CD will have varying degrees of altered glucose metabolism. Hence the cortisol level can be a good indicator for managing diabetes mellitus. Brahm Kumar Tiwari et.al. [60] has discussed the biomarkers of oxidative stress during type 2 diabetes mellitus. Glutathione (GSH) is an efficient antioxidant; reduced level of GSH indicates uncontrolled diabetes. Catalase is an anti-oxidative enzyme that protects pancreatic β -cells from unregulated hydrogen peroxide induced due to oxidative stress. Reduced Catalase indicates hyperglycemia serving as a biomarker. Antioxidant capacity of plasma is a biomarker to evaluate oxidative stress. Reduction in antioxidant capacity increases glucose level. U. Snehalatha et.al. [61] has devised a non-invasive glucose measurement technique, correlation between Galvanic Skin Response (GSR) and blood glucose level for diabetic and non-diabetic individuals is obtained. In diabetic patients, there is a negative correlation between blood glucose and GSR. The next section,

parameters exhibiting synergy of psychological and physiological data to be considered for AI system in diabetes care is detailed out.

6 Data Attributes

The data attributes to be considered for effective blood glucose prediction by the AI system are as listed below:

- **Blood Glucose Level:** Blood glucose level is being the readily available data is typically collected via finger prick for SMBG or via venous blood for LBT. The normal range for blood glucose level in a diabetic patient should be between 80-180mg/dL. Any deviation below or above this range is an alarm for hypoglycemia or hyperglycemia state.
- **A1C Test:** Glycemic management is primarily assessed by A1C tests. A1C of less than 7% is recommended for non-pregnant adults. And for patients with history of hypoglycemia A1C must be less than 8%.
- **Insulin Therapy:** Insulin dosage is prescribed based on age, weight, pregnancy and illness. Based on the amount of carbohydrates intake, pre-meal glucose levels the insulin dosage is varied. This demands the need to educate the patient and exercising good self-management. CGM sensors aid in alleviating the problem of hypoglycemic incidents due to insulin therapy.
- **BMI:** Individuals with a BMI greater than 25kg/m² are at a risk of diabetes. Obesity results in higher BMI and needs to be under check to control diabetes. Metabolic surgery should be recommended as an option to treat type 2 diabetes in appropriate surgical candidates with BMI > 40kg/m², as this reduces the risk of cardiovascular disease and aids in obtaining good glycemic control.
- **Blood Pressure:** Hypertension and diabetes can normally co-occur due to similar factors, such as overweight, unhealthy diet, and inactive lifestyle. About 25% of people with Type 1 diabetes and 80% of people with Type 2 diabetes have high blood pressure [62]. Combination of diabetes and high blood pressure increases risk of heart disease, stroke, kidney disease and other health problems.
- **Weight:** Weight is normally related to BMI measurement. A balanced diet and an active lifestyle can help maintain a healthy weight. Insulin resistance gets better with a combination of weight loss and exercise. Weight control helps in reversing diabetes. The impact of medications on weight and being overweight must be considered during prescription of medications.
- **GSR:** The Galvanic Skin Response is a measure Electro Dermal Activity (EDA). EDA is a measure of change in the sweat gland activities proportional to the emotional health like stress etc. Stress reduces GSR. And it is known that GSR reduces significantly with diabetes and can be used as a diagnostic tool in the detection of Diabetic Autonomic Neuropathy (DAN). Hence, GSR indirectly gives insight into diabetes induced by stress.
- **Heart Rate:** Low blood sugar levels diabetic patients known as hypoglycemia is common. Hypoglycemia

causes bradycardia accompanied by abnormal heart beats

- No of pregnancies: Due to the new demands that a pregnancy will put on the body, it will affect blood sugar levels. About seven out of every 100 pregnant women in the United States get gestational diabetes. Gestational diabetes is diabetes that happens for the first time when a woman is pregnant [63]. It increases the risk of developing Type 2 diabetes later. During pregnancy, the placenta supplies a growing fetus with nutrients and water. The placenta also makes a variety of hormones to maintain the pregnancy. In early pregnancy, hormones can cause increased insulin secretion and decreased glucose produced by the liver, which can lead to hypoglycemia (low blood glucose levels). In later pregnancy, some of these hormones (estrogen, cortisol, and human placental lactogen) can have a blocking effect on insulin, a condition called insulin resistance. As the placenta grows, more of these hormones are produced, and insulin resistance becomes greater. Normally, the pancreas is able to make additional insulin to overcome insulin resistance, but when the production of insulin is not enough to overcome the effect of the placental hormones, gestational diabetes results.
- History of Depression: Depression tends to increase the risk of diabetes. Psychological care should be suggested for diabetic patients with depression, anxiety, disordered eating and behavioral abnormalities. This ensures better treatment care and self-management.
- Diabetes Distress: Diabetes Distress (DD) is a common negative psychological reaction related to emotional distress due to suffering from chronic diabetes disease [64]. High levels of DD impacts the self-management; regular medication behavior and causes increased A1C, poor lifestyle and lower self-efficacy. Psychological care needs to be suggested.
- Diet: Food intake affects the blood glucose level. This makes the parameter highly geological. The culture, race and locality of the individual will alter the glucose levels and treatment plan. Having good amount of protein based diet with reduced carbohydrates can exercise control over the changing glucose levels. An individualized eating plan needs to be devised.
- Physical Activity: Physical activity is typically measured via step counts tracking and heart rate. Exercise will increase the insulin sensitivity of cells. The step count provides information on physical

activity and calories consumed and needs to be considered for improved accuracy[65].

- Accessibility: Access to healthcare facility indicates the capacity with which the individual can interconnect with the healthcare providers with ease and obtain the right treatment in emergency conditions. Accessibility depends highly on the socio-economic background. And this parameter varies between the developed and developing countries.
- Education: Education is important for diabetes patients since self-management involves many complex factors and most diabetic patients lack such knowledge.
- Substance abuse. Substance abuse normally refers to tobacco and alcohol. Smoking tobacco roughly doubles the risk of diabetes among a healthy population of men [66]. Cigarette smoking and alcohol consumption either indirectly through their effects on obesity or directly through physiological factors related to insulin secretion or insulin resistance increases the risk of diabetes.

7 Conclusion and Future Directions

Artificial Intelligence (AI) is revolutionizing the healthcare industry. It has got the eloquence to provide globally accessible, improved diagnosis at affordable price. AI is seen as the most germane technology remodeling the diabetes care sector. AI models till date do consider only the measurable psychological parameters for diabetes monitoring and providing timely care. The human dimension, i.e. the psychological data of the patient is nowhere considered by the AI models. Psychological research has an important role to play in improving the prevention and care of diabetes. Disregardance of this aspect will lead to fallacious treatment being administered to a patient. Putting AI based diabetic care on the wrong track. Hence in this paper, author stresses upon the need to consider both physiological and psychological data of a patient, this review paper indicated the type of data to be considered for investigation while modeling the AI algorithms. This paper aids in building AI models that can guarantee to administer personalized precise clinical diagnosis and quality diabetes care, paving way for futuristic AI models with human touch.

REFERENCES

- [1] Forbes Insight "AI And Healthcare: A Giant Opportunity" Feb 11, 2019, AI Issue 4,
- [2] <https://www.forbes.com/sites/insights-intelai/2019/02/11/ai-and-healthcare-a-giant-opportunity/#51e00dad4c68>
- [3] Infoholic Research "The global artificial intelligence in diabetes management market is expected to reach \$626.3 million by 2022", January 2018, <https://www.infoholicresearch.com/report/global-artificial-intelligence-in-diabetes-management-market-drivers-restraints-opportunities-trends-and-forecasts-to-2023/>
- [4] Kavakiotis I, Tsavali O, Salifoglou A, Maglaveras N, Vlahavas I, Chouvarda I. Machine Learning and Data Mining Methods in Diabetes Research. Comput Struct Biotechnol J. 2017; 15:104–116. Published 2017 Jan 8. doi:10.1016/j.csbj.2016.12.005
- [5] Barakat NH, Bradley AP, Barakat MN. "Intelligible support vector machines for diagnosis of diabetes mellitus". IEEE Trans Information Technology Biomed. 2010 Jul; 14(4):1114-20. Epub 2010 Jan 12.

- [6] Little JW, "Recent advances in diabetes mellitus of interest to dentistry" *Spec Care Dentist*. 2000 Mar-Apr; 20(2):46-52
- [7] Mayfield J, "Diagnosis and classification of diabetes mellitus: new criteria" *Am Fam Physician*. 1998 Oct 15; 58(6):1355-62, 1369-70.
- [8] Kuzuya T, "Early diagnosis, early treatment and the new diagnostic criteria of diabetes mellitus" *Br J Nutr*. 2000 Dec; 84 Suppl 2:S177-81.
- [9] Tillil H, Nick O, Köbberling J "Modern diagnosis and classification of diabetes mellitus" *Z Arztl Fortbild Qualitatssich*. 1998 Sep; 92(7):456-66.
- [10] Kuzuya T, Nakagawa S, Satoh J, Kanazawa Y, Iwamoto Y, Kobayashi M, Nanjo K, Sasaki A, Seino Y, Ito C, et al. "Report of the Committee on the classification and diagnostic criteria of diabetes mellitus" *Diabetes Res Clin Pract*. 2002 Jan; 55(1):65-85.
- [11] Woldaregay AZ, Årsand E, Botsis T, Albers D, Mamykina L, Hartvigsen G, "Data-Driven Blood Glucose Pattern Classification and Anomalies Detection: Machine-Learning Applications in Type 1 Diabetes" *J Med Internet Res* 2019;21(5):e11030, DOI: 10.2196/11030
- [12] American Psychological Association, "Psychology Plays Vital Role in Tackling Diabetes", October 3, 2016, <https://www.apa.org/news/press/releases/2016/10/psychology-diabetes>
- [13] Christine M. Hunter, "Understanding Diabetes and the Role of Psychology in Its Prevention and Treatment", *American Psychologist*, 2016, Vol. 71, No. 7, 515–525.
- [14] Mary de Groot, Sherita Hill Golden, Julie Wagner, "Psychological Conditions in Adults With Diabetes", *American Psychologist*, 2016, Vol. 71, No. 7, 552–562
- [15] Deborah J. Wiebe, Vicki Helgeson, Cynthia A. Berg, "The Social Context of Managing Diabetes Across the Life Span", *American Psychologist*, 2016, Vol. 71, No. 7, 526–538
- [16] Linda A. Gonder-Frederick, Jaclyn A. Shepard, Jesse H. Grabman, and Lee M. Ritterband, "Psychology, Technology, and Diabetes Management", *American Psychologist*, 2016, Vol. 71, No. 7, 577–589
- [17] American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2009;32 Suppl 1(Suppl 1):S62–S67. doi:10.2337/dc09-S062
- [18] Sarah Wild "Global Prevalence Of Diabetes", *Diabetes Care*, Volume 27, Number 5, May 2004
- [19] Bellazzi R, Abu-Hanna A. Data mining technologies for blood glucose and diabetes management. *J Diabetes Sci Technol*. 2009;3(3):603–612. Published 2009 May. doi:10.1177/193229680900300326
- [20] CDISC Therapeutic Area Data Standards User Guide for Diabetes (Version 1.0), September 1, 2014, Clinical Data Interchange Standards Consortium, Inc.
- [21] JENNIFER MAYFIELD, "Diagnosis and Classification of Diabetes Mellitus: New Criteria", *Am Fam Physician*. 1998 Oct 15;58(6):1355-1362.
- [22] Jinyu Xie, Qian Wang, "Benchmark Machine Learning Approaches with Classical Time Series Approaches on the Blood Glucose Level Prediction Challenge", *CEUR-WS.org/vol-2148*
- [23] Harleen Kaur, Vinita Kumari, Predictive modelling and analytics for diabetes using a machine learning approach, *Applied Computing and Informatics*, 2018
- [24] Sanjaya De Silva, "Predicting Diabetes Using a Machine Learning Approach", Dec. 30, 2016 · AI Zone, <https://dzone.com/articles/predicting-diabetes-using-machine-learning-approach>
- [25] J. Li, O. Arandjelovic, Glycaemic index prediction: a pilot study of data linkage challenges and the application of machine learning, in: *IEEE EMBS Int. Conf. on Biomed. & Health Informat. (BHI)*, Orlando, FL, (2017) 357–360.
- [26] Paolo Magni, and Giuseppe De Nicolao Riccardo Bellazzi, "Bayesian Analysis of Blood Glucose Time Series from Diabetes Home Monitoring," *IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING*, vol. 7, p. 47, july 2000.
- [27] Devang Odedra, Subir Samanta, and Ambarish S. Vidyarthi Shankaracharya, "Computational Intelligence in Early Diabetes Diagnosis: A Review," *The review of Diabetic Studies*, vol. 7, no. 4, December 2010.
- [28] Quan Zou, Kaiyang Qu, Yamei Luo, Dehui Yin, Ying Ju, Hua Tang "Predicting Diabetes Mellitus With Machine Learning Techniques" *Front Genet*. 2018; 9: 515. Published online 2018 Nov 6. doi: 10.3389/fgene.2018.00515 PMID: PMC6232260
- [29] Quan Zou, Gang Liu "Sequence clustering in bioinformatics: an empirical study", September 2018 Briefings in Bioinformatics DOI: 10.1093/bib/bby090
- [30] Maniruzzaman M, Rahman MJ, Al-Mehedi Hasan M, Suri HS, Abedin MM, El-Baz A, Suri JS. *J Med Syst*. 2018 Apr 10; 42(5):92. Epub 2018 Apr 10.
- [31] PLIS, K.; BUNESCU, R.; MARLING, C.; SHUBROOK, J.; SCHWARTZ, F.. A Machine Learning Approach to Predicting Blood Glucose Levels for Diabetes Management. *AAAI Workshops, North America*, jun.2014. Date accessed: 10 Jul. 2019.
- [32] Deborah J. Wexler, MD1, James B. Meigs, MD, MPH12, Enrico Cagliero, MD1, David M. Nathan, MD1 and Richard W. Grant, "Prevalence of Hyper- and Hypoglycemia Among Inpatients With Diabetes", *Diabetes Care* 2007 Feb; 30(2): 367-369.
- [33] Maniruzzaman M, Kumar N, Menhazul Abedin M, Shaykhul Islam M, Suri HS, El-Baz AS, Suri JS. "Comparative approaches for classification of diabetes mellitus data: Machine learning paradigm" *Comput Methods Programs Biomed*. 2017 Dec; 152:23-34. Epub 2017 Sep 8
- [34] Nilashi M, Bin Ibrahim O, Mardani A, Ahani A, Jusoh A. "A soft computing approach for diabetes

- disease classification."Health Informatics J. 2018 Dec; 24(4):379-393. Epub 2016 Nov 14.
- [36] Sudharsan B, Peebles M, Shomali M. Hypoglycemia prediction using machine learning models for patients with type 2 diabetes. J Diabetes Sci Technol. 2014;9(1):86–90. Published 2014 Oct 14. doi:10.1177/1932296814554260
- [37] Kevin Plis, Razvan C Bunesco, Cindy Marling, Jay Shubrook, and Frank Schwartz. A machine learning approach to predicting blood glucose levels for diabetes management. In AAAI Workshop: Modern Artificial Intelligence for Health Analytics, number 31, pages 35–39, 2014.
- [38] Polat, Kemal and Salih Gunes, "An expert system approach based on principal component analysis and adaptive neurofuzzy inference system to diagnosis of diabetes disease," Expert system with Applications, pp. 702-710, Elsevier, 2007
- [39] Zhou, ZH. & Li, "Semi-supervised learning by disagreement " M. Knowl Inf Syst (2010) 24: 415. <https://doi.org/10.1007/s10115-009-0209-z>
- [40] Balcan M-F, Blum A, Yang K (2005) Co-training and expansion: towards bridging theory and practice. In: Saul LK, Weiss Y, Bottou L (eds) Advances in neural information processing systems 17. MIT Press, Cambridge, pp 89–96
- [41] Baskaran A, Milev R, McIntyre RS. A review of electroencephalographic changes in diabetes mellitus in relation to major depressive disorder. Neuropsychiatr Dis Treat. 2013;9:143–150. doi:10.2147/NDT.S38720
- [42] Pan A, Lucas M, Sun Q, et al. Bidirectional association between depression and type 2 diabetes mellitus in women. Arch Intern Med. 2010;170(21):1884–1891.
- [43] Christian Nordqvist, "What to know about diabetic neuropathy", Last updated Tue 19 March 2019, <https://www.medicalnewstoday.com/articles/245310.php>
- [44] Kittnar O, "Electrocardiographic changes in diabetes mellitus.", Physiol Res. 2015;64 Suppl 5:S559-66. Epub 2015 Dec 15
- [45] Valensi PE, Johnson NB, Maison-Blanche P, Extramania F, Motte G, Coumel P. Influence of cardiac autonomic neuropathy on heart rate dependence of ventricular repolarization in diabetic patients. Diabetes Care. 2002; 25: 918–923.
- [46] iunti S, Bruno G, Veglio M, Gruden G, Webb DJ, Livingstone S, Chaturvedi N, Fuller JH, Perin PC. Electrocardiographic left ventricular hypertrophy in type 1 diabetes. Diabetes Care. 2005; 28: 2255–2257.
- [47] Ziegler D, Zentai CP, Perz S, Rathmann W, Haastert B, Meisinger C. Prediction of mortality using measures of cardiac autonomic dysfunction in the diabetic and nondiabetic population. The MONICA/KORA Augsburg Cohort Study. Diabetes Care. 2008; 31: 556–561
- [48] Steven A Mazza, Ph.D., Nicky H Moorman, R.N., M.S.N., Madelyn L Wheeler, R.N., M.S., James A Norton, Ph.D., Naomi S Fineberg, Ph.D., Frank Vinicor, M.D., Stuart J Cohen, Ed.D. and Charles M Clark Jr, M.D. "The Diabetes Education Study: A Controlled Trial of the Effects of Diabetes Patient Education", Diabetes Care 1986 Jan; 9(1): 1-10.
- [49] Richard R Rubin, PHD and Mark Peyrot, PHD, "Psychosocial Problems and Interventions in Diabetes: A review of the literature", Diabetes Care 1992 Nov; 15(11): 1640-1657.
- [50] Dr J.K. Wales, "Does Psychological Stress Cause Diabetes?", Wiley Online Library, February 1995, <https://doi.org/10.1111/j.1464-5491.1995.tb00439.x>
- [51] Holt RI, de Groot M, Golden SH. Diabetes and depression. Curr Diab Rep. 2014;14(6):491. doi:10.1007/s11892-014-0491-3
- [52] Weyerer S. Physical inactivity and depression in the community. Evidence from the Upper Bavarian Field Study. Int J Sports Med. 1992;13:492–6.
- [53] Barnard K, Peveler RC, Holt RI. Antidepressant medication as a risk factor for type 2 diabetes and impaired glucose regulation: systematic review. Diabetes Care. 2013;36:3337–45. This systematic review examines the evidence for a causal relationship between antidepressants and diabetes
- [54] Gonzalez JS, Safren SA, Cagliero E, Wexler DJ, Delahanty L, Wittenberg E, et al. Depression, self-care, and medication adherence in type 2 diabetes: relationships across the full range of symptom severity. Diabetes Care. 2007;30:2222–7
- [55] Lyoo IK, Yoon SJ, Musen G, Simonson DC, Weinger K, Bolo N, et al. Altered prefrontal glutamate-glutamine-gamma-aminobutyric acid levels and relation to low cognitive performance and depressive symptoms in type 1 diabetes mellitus. Arch Gen Psychiatry. 2009;66:878–87.
- [56] Courtet P, Olie E. Circadian dimension and severity of depression. Eur Neuropsychopharmacol. 2012;22 (Suppl 3):S476–81.
- [57] Kan C, Silva N, Golden SH, Rajala U, Timonen M, Stahl D, et al. A systematic review and meta-analysis of the association between depression and insulin resistance. Diabetes Care. 2013;36:480–9.
- [58] Ali, M. K., Bullard, K. M., Saaddine, J. B., Cowie, C. C., Imperatore, G., & Gregg, E. W. (2013). Achievement of goals in U.S. Diabetes Care, 1999–2010. The New England Journal of Medicine, 368, 1613–1624. <http://dx.doi.org/10.1056/NEJMsa1213829>
- [59] American Diabetes Association (ADA). (2015). Foundations of care: Education, nutrition, physical activity, smoking cessation, psychosocial care, and immunization. Diabetes Care, 38, S20–S30. <http://dx.doi.org/10.2337/dc15-S007>
- [60] Ryan, C. M., van Duinkerken, E., & Rosano, C. (2016). Neurocognitive consequences of diabetes. American Psychologist, 71, 563–576. <http://dx.doi.org/10.1037/a0040455>

- [61] Ducat, L., Philipson, L. H., & Anderson, B. J. (2014). The mental health comorbidities of diabetes. *Journal of the American Medical Association*, 312, 691–692. <http://dx.doi.org/10.1001/jama.2014.8040>
- [62] Brahm Kumar Tiwari, Kanti Bhooshan Pandey, A. B. Abidi, and Syed Ibrahim Rizvi, "Markers of Oxidative Stress during Diabetes Mellitus," *Journal of Biomarkers*, vol. 2013, Article ID 378790, 8 pages, 2013. <https://doi.org/10.1155/2013/378790>.
- [63] U. Snehalatha, T. Rajalakshmi, C. H. Vinitha Sri, G. Balachander and K. S. Shankar, "NON-INVASIVE BLOOD GLUCOSE ANALYSIS BASED ON GALVANIC SKIN RESPONSE FOR DIABETIC PATIENTS", *Biomedical Engineering: Applications, Basis and Communications* Vol. 30, No. 02, 1850009 (2018), <https://doi.org/10.4015/S1016237218500096>
- [64] "Diabetes and high blood pressure", *Blood Pressure Association* 2008, <http://www.bloodpressureuk.org/BloodPressureandyou/Yourbody/Diabetes>
- [65] "Gestational Diabetes", <https://www.webmd.com/diabetes/gestational-diabetes-guide/gestational-diabetes#1>
- [66] van der Feltz-Cornelis, C. M., Nuyen, J., Stoop, C., Chan, J., Jacobson, A. M., Katon, W., Sartorius, N. (2010). Effect of interventions for major depressive disorder and significant depressive symptoms in patients with diabetes mellitus: A systematic review and meta-analysis. *General Hospital Psychiatry*, 32, 380–395. <http://dx.doi.org/10.1016/j.genhosppsych.2010.03.011>
- [67] Steeves, J. A., Liu, B., Willis, G., Lee, R., & Smith, A. W. (2014). Physicians' personal beliefs about weight-related care and their associations with care delivery: The U.S. National Survey of Energy Balance Related Care among Primary Care Physicians. *Obesity Research and Clinical Practice*, 9, 243–255. <http://dx.doi.org/10.1016/j.orcp.2014.08.002>
- [68] Young-Hyman, D., & Peyrot, M. (2012). Introduction. In D. YoungHyman & M. Peyrot (Eds.), *Psychosocial care for people with diabetes* (pp. vii–x). Alexandria, VA: American Diabetes Association.