



ADVANCED CONSIDERATIONS FOR ENHANCING PRECISION CONTROL FOR INSULIN DOSAGE IN TYPE 2 DIABETES PATIENTS USING A FUZZY LOGIC-BASED SYSTEM

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ABSTRACT

Diabetes is one of the oldest diseases in history and insulin therapy the most effective means of diabetes management. The purpose of this research is to develop a new method using fuzzy logic based computational system that increases precision control in insulin delivery to type 2 diabetes patients, thereby enabling better glycemic control. Previously, predicted insulin dosage, using the fuzzy system, was noted to provide better glucose regulation compared with non-fuzzy based insulin dosing system. A previous study by our research group was conducted in order to calculate a predictable total daily insulin dosage by using patient specific factors such as weight, BMI (body mass index) and average carbohydrate intake [10]. The same patient population was monitored for an extended period of time and used in this study to increase the accuracy of insulin dosage. The insulin dose was further refined based on additional patient reported data i.e. average fasting blood glucose level and the level of physical activity. The corresponding insulin output, using the same fuzzy system developed in MATLAB, was analyzed and the improvement in patient quality of life was compared with the previous findings. The system used the previously calculated insulin dosage, and two new factors i.e. fasting blood glucose level and physical activity as inputs and generated an output of personalized insulin dosage. The inclusion of these two additional factors provided a more precise and accurate outcome across the patient population. Therefore, using this method may lead to further decline in instances of hyper or hypoglycemic events among type 2 diabetes patients and reduce safety considerations.

KEY WORDS

Insulin, Fuzzy Logic, MATLAB, Type 2 Diabetes, Dose Adjustment, Drug Dosing, Blood Glucose, Diabetic Lifestyle

INTRODUCTION

The International Diabetes Federation (IDF) Diabetes Atlas predicts that there will be approximately 642 million people suffering from diabetes in the near future which is currently prevalent among 422 million patients and is considered as one of the leading causes of mortality and morbidity around the world [1]. According

to WHO 90% diabetic patients are suffering from type 2 diabetes with a prevalence of 8.1% among adults; this posits it at the sixth position in leading causes of death [2]. Eight core defects including decreased insulin secretion, improved glucose reabsorption, enhanced lipolysis, lessened glucose uptake, reduced incretin effect, neurotransmitter dysfunction, amplified hepatic

glucose production, and increased glucagon secretion collectively known as “the ominous octet” plays a vital role for the development of type 2 diabetes [3]. Different type of microvascular and macrovascular complications including diabetic retinopathy, diabetic nephropathy, diabetic neuropathy, cerebrovascular diseases, cardiovascular diseases and major organ damage including eyes, kidney, nerve, blood vessels and heart evolve due to the presence of type 2 diabetes [4]. Diabetes patients are at four-time greater risk to suffer from cardiovascular diseases which are the reason of death of 70% patients [5]. The number of diabetic patients is intensifying around the globe and 80% of them resides in lower and middle-income countries where Bangladesh alone contribute 11% of them [6]. According to IDF Diabetes Atlas, by the year 2011 Bangladesh had 8.4 million diabetics which is projected to be 16.8 million in 2030 [7]. However, type 2 diabetes could be controlled with the help of oral hypoglycemic agents as well as with insulin therapy prescribed by physician for improved blood glucose level regulation. Insulin dose for individual patients is calculated based on critical patient related factors (PRFs) such as body weight, height, BMI (body mass index), daily carbohydrate intake, fat intake, exercise, alcoholism and smoking habit. Succession rate of insulin therapy depends on these PRFs, but mismanagement of blood glucose level called hyperglycemia (increased blood glucose level) or hypoglycemia (decreased blood glucose level) often originates because of erroneous dosing of insulin [8].

One of the primary reasons behind this erroneous insulin dosing is due to considering one or two patient related factors in general. In order to subjugate all the complexities regarding insulin therapy, a precise and accurate dosing system is obligatory which will take into account all the patients related factors for prescribing insulin dose to individual patients for better glycemic control. A newer approach to prescribe an accurate insulin dose to individual patients is using a computer based artificially intelligent (A.I.) system known as fuzzy logic which can generate an output insulin dose based on several PRFs [9]. Fuzzy logic is a relatively basic concept in the world of artificial intelligence which can be very similar to how humans think and go about decision making. Nowadays it is gaining steam in the medical world since it can be used to incorporate

several factors to address a number of complexities that are involved with studying the human body [25].

In the first phase of this study Khan et al. (phase 1 of dose refinement) focused on three PRFs which resulted in lower instances of hypo or hyperglycemia for some of the patients [9, 10]. In this study however (phase 2 of dose refinement), inclusion of two additional PRFs, namely patient’s average fasting blood glucose level and reported physical activity, were used to increase precision control of insulin dosing for the same patient population.

Usually, patient’s weight, BMI, carbohydrate intake are considered as the main factors for determining insulin dose, however, average fasting blood glucose and physical activities also may play vital role in this case [11, 12]. According to the analytical data of The UK Prospective Diabetes Study (UKPDS), targeting fasting glucose to treat diabetes reduces the chance of mortality up to 20% [12]. Average fasting glucose and insulin ratio is also a good measurement of insulin sensitivity which is safe and easy to determine as well as highly sensitive [13]. Additionally, physical activity is another key factor for determining insulin dosing since it reverse the chances of insulin resistance and reduces risk of type 2 diabetes by ~9% [14, 15]. Moreover, physical activities increase the insulin sensitivity and considered as one of the major components of type 2 diabetes prevention [16]. As a result, an A.I. system that takes into account all of these patients’ factors to develop rules and membership functions among the factors and generate an accurate and precise insulin dose to individualize patient’s insulin dosing may be very beneficial [17, 18]. This system in turn may help to prevent the hypo and hyperglycemic events in patients by providing relatively more precise doing of units of insulin to individuals to better manage blood glucose level [9, 19, 20].

MATERIALS AND METHODS

2.1. Patients population

39 type 2 diabetes patients undergoing insulin treatment were randomly selected from the population of the city of Dhaka, Bangladesh; a patient pool comprising of 20 males and 19 females. Initially the patients provided the following individual information: weight, height, and average carbohydrate intake per day over a period of a month. For the purposes of this study, the same patients reported the number of

minutes of physical activity per day and average fasting blood glucose levels every day for one month and the respective prescribed insulin dose by the physician. In each of the cases, first, the physician(s) calculated a nominal insulin dose based on the patient's body weight and then secondly proceeded to adjust the daily amount of insulin given in accordance to subsequent consultation sessions with the patients. The additionally reported data was used to calculate average fasting blood glucose level and physical activity score for each patient. Full disclosure was provided to each patient

about the specific method by which this data was to be used and consent was obtained regarding the usage and publication of the results obtained.

2.2. Insulin dosage from previous study

One of the inputs used for this study was the predicted insulin dosage from our previous study [10] with the goal of refinement. The original dosage output from the fuzzy based system is listed in Table 1 and was calculated based on the patient's weight, BMI and average carbohydrate intake.

Table 1. Predicted dose vs. prescribed dose of daily insulin units for each of the 39 patients [10]

Patient number	Predicted insulin dose by the fuzzy system	Physician prescribed insulin dose
1	40.0	35.0
2	33.0	32.0
3	46.5	40.0
4	40.0	35.0
5	46.5	40.0
6	52.6	30.0
7	39.5	25.0
8	40.0	30.0
9	40.0	30.0
10	40.0	40.0
11	40.0	35.0
12	33.0	30.0
13	39.5	25.0
14	33.0	32.0
15	40.0	30.0
16	46.5	35.0
17	40.0	34.0
18	33.0	35.0
19	39.5	28.0
20	46.5	40.0
21	46.5	35.0
22	40.0	32.0
23	39.5	28.0
24	46.5	38.0
25	39.5	40.0
26	46.5	42.0
27	39.5	40.0
28	33.0	35.0
29	52.5	50.0
30	40.0	35.0
31	33.0	40.0
32	33.0	35.0
33	40.0	30.0
34	46.5	28.0
35	46.5	45.0
36	46.5	40.0
37	39.5	35.0
38	40.0	30.0
39	39.5	32.0

2.3 Physical Activity Score

Regular physical activity (jogging, running, cycling, climbing, sports, etc.) of diabetic patients can be instrumental in reducing the total daily insulin dose requirement [16, 22]. For the purposes of this study, this inverse relationship was carefully considered while constructing the decision matrices for the fuzzy system. The patients were surveyed regarding their daily

physical activity. The patients reported their total minutes of physical activity over the course of a week and were assigned a physical activity score on a scale of 0 to 3 (to one decimal place). For example, a patient who reported total physical activity of 48 minutes is given a score of 2.4 out of 3 according to our physical activity scoring scale. The standard of references is shown in the Table 2.

Table 2. Physical Activity Reference Scores based on duration of physical activity

Patient Reported Physical Activity (minutes)	Physical Activity Reference Score
0	0
20	1
40	2
60	3

2.4. Average fasting blood glucose level

Each patient reported their fasting blood glucose level (FBGL) over the course of one month. The respondents measured their FBGL each day and reported their weekly average, continuing for four weeks. This data was then used to calculate the cumulative average FBGL for each patient throughout the course of the month. The units for this measurement were kept standard at mmol/L. Since a higher FBGL usually is indicative of beta cell dysfunction in the pancreas, the membership functions in the fuzzy based system was adjusted in accordance [18, 23, 24].

2.5. Fuzzification of the membership functions

To define the fuzzy membership functions of input variables Predicted Insulin Dose (PID), Average Fasting

Blood Glucose (AFBGL) in mmol/L, Average Physical Activity (PA) score, and the output variable Insulin Dose (insulinDose) the MATLAB Fuzzy Logic Designer Toolbox was used. All variables, having different ranges, are fuzzified with the triangular membership functions. All three input variables (PID, AFBGL, and PA) have membership functions with three fuzzy value of different ranges- namely Low (L), Optimum (O), and High (H); the output variable (insulinDose), on the other hand, has membership function with five fuzzy value- A,B,C,D, and E. The ranges of the input and output variables are illustrated on Table 3; and Table 4 shows the whole breakdown of the input variables.

Table 3. Ranges of the input and output variables

Input		Output	
PID	AFBGL	PA	Insulin Dose
25 - 55	3 - 12	0 - 3	25 - 55

Table 4. Fuzzy value breakdown of input variables

	PID			AFBGL		PA	
	Range	Unity membership point		Range	Unity membership point	Range	Unity membership point
Fuzzy values	L 25 - 40	25		3 - 7.5	3	0 - 1.5	0
	O 30 - 50	40		5 - 10	7.5	0.5 - 1.5	2.5
	H 40 - 55	55		7.5 - 12	12	1.5 - 3	3

The unity membership point represents the point where the membership function has a membership value of 1. To elaborate, an AFBGL of 7.5 implies a perfectly optimum Average Fasting Blood Glucose level; any other value within the range of 5 to 10 is also optimum

but with a lower degree, thus having a membership value less than 1.

The output variable insulin Dose is fuzzified as per the breakdown delineated on Table 5.

Table 5. Fuzzy value breakdown of output variable

		Insulin Dose	
		Range	Unity membership point
Fuzzy values	A	25 – 35	25
	B	30 - 40	35
	C	35 - 45	40
	D	40 - 50	45
	E	45 - 55	55

All the triangular membership functions (i.e. L, O, H) of the input variable PID, constructed in the MATLAB Fuzzy Logic Toolbox, are shown on Figure 1. The membership functions for PID are constructed as per the Ranges and Unity membership points outlined on Table 4.

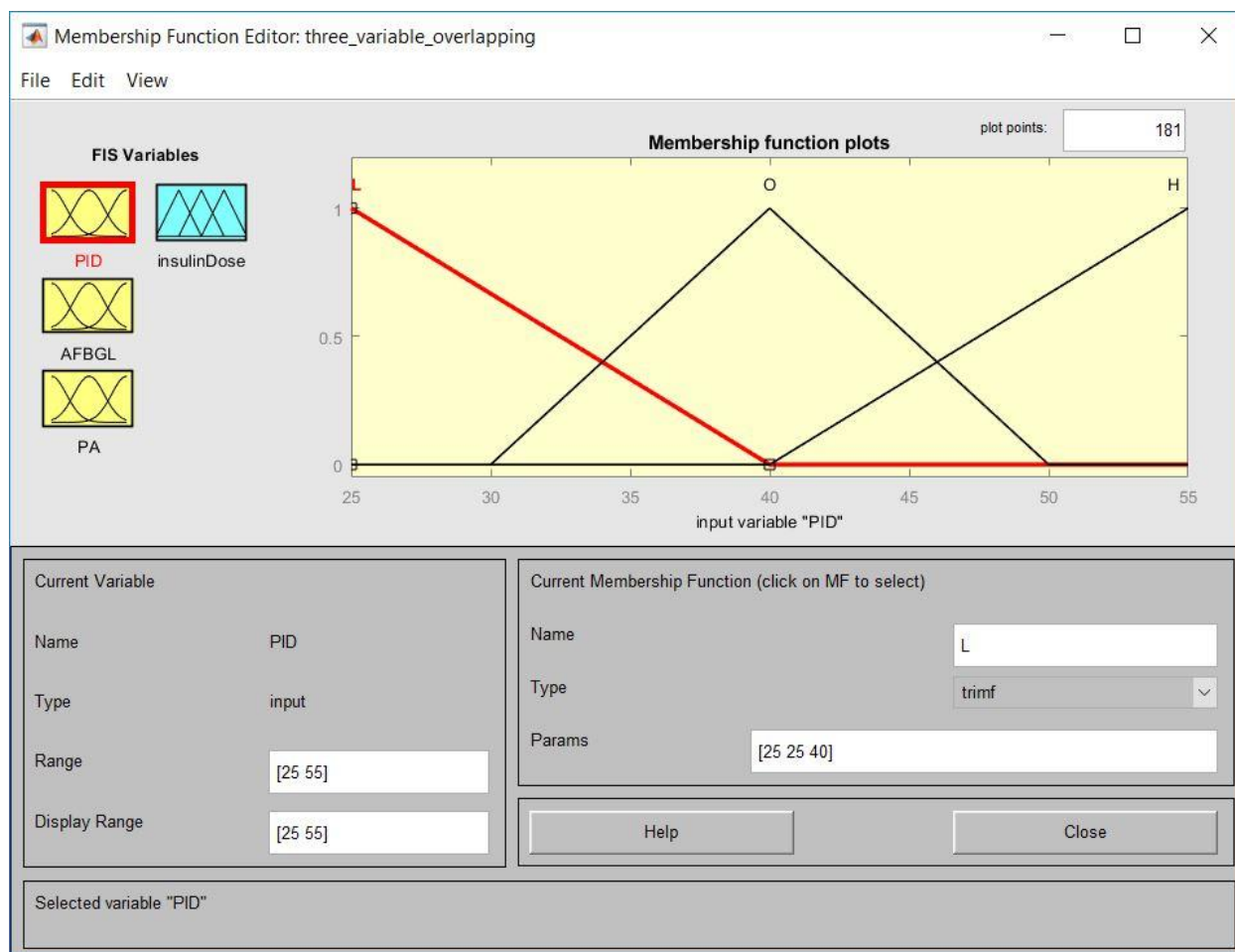


Figure 1. Membership functions for PID

Figure 2 illustrates the three membership functions for the input variable AFBGL, as outlined on Table 4.

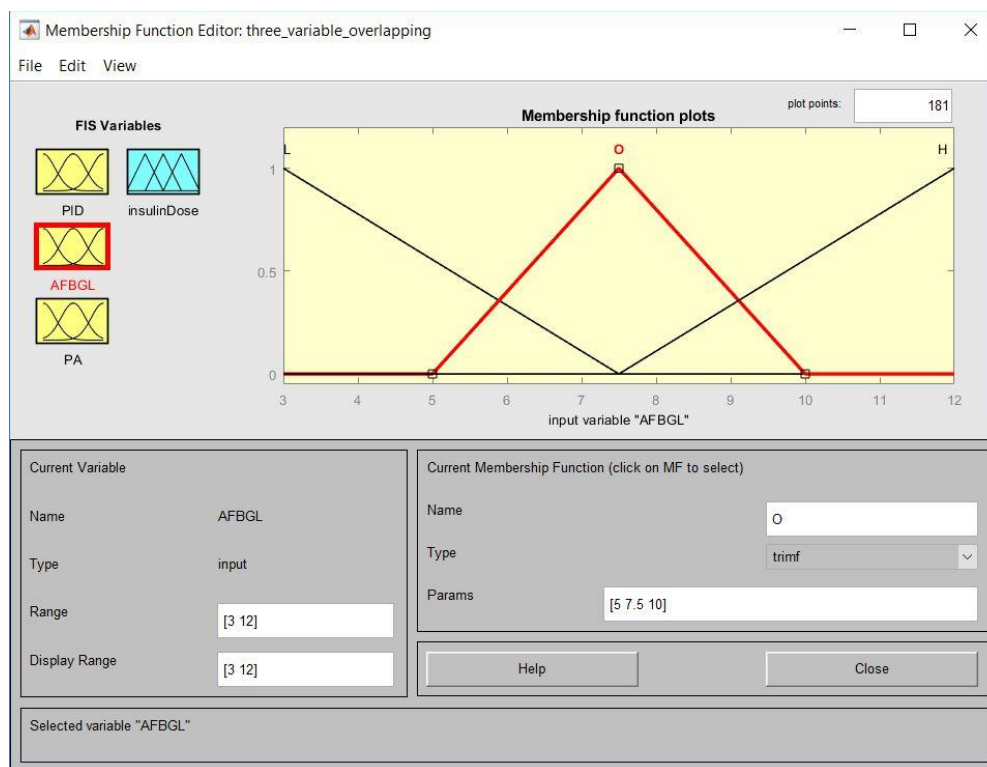


Figure 2. Membership functions for AFBGL

The third input variable PA also has three membership functions as show on Figure 3. The Ranges and Unity membership points for PA are also given on the Table 4.

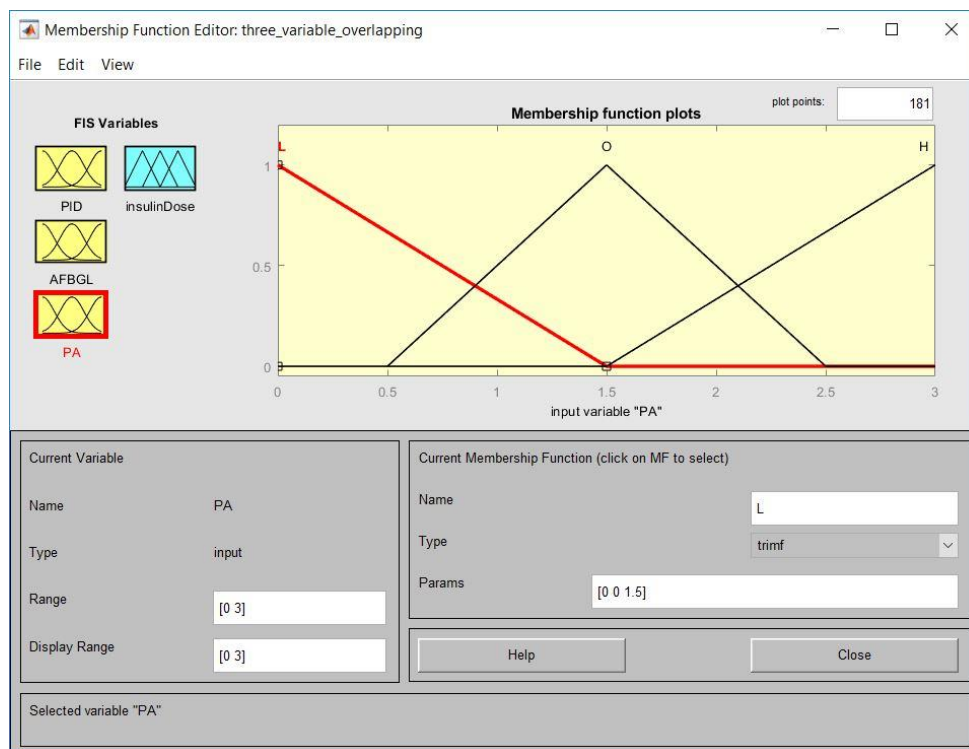


Figure 3. Membership functions for PA

Lastly, the construction of the output variable insulin Dose, having five triangular membership functions, is illustrated on Figure 4. The breakdown for insulin Dose is as given on Table 5.

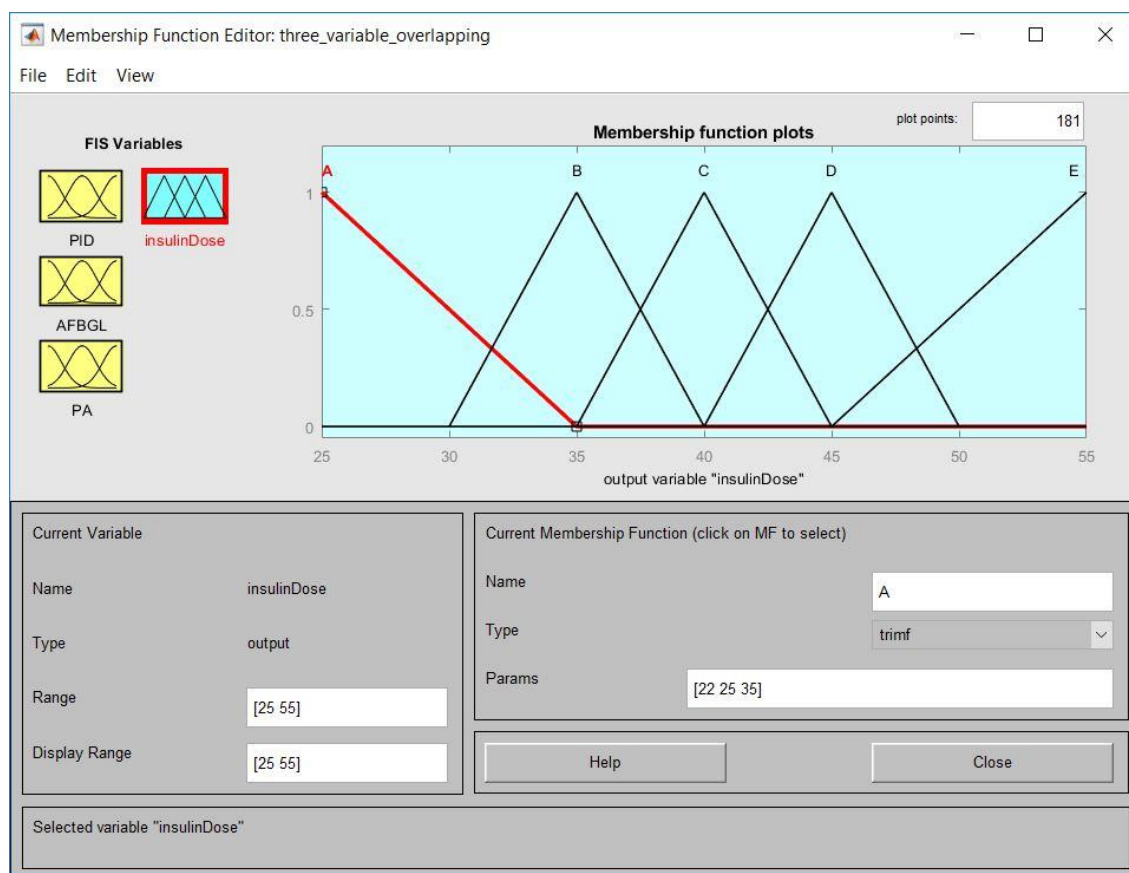


Figure 4. Membership functions for insulin Dose

The facts and figures provided till now depicts that it is a three input-one output system, with membership functions having different Ranges and Unity membership functions. Every membership function is triangular, and they have different overlapping regions. The points in the overlapping regions indicate that they are members, with varying degree, of both the membership functions that take part in creating the overlap.

2.5. Rules for fuzzy inference

Once the membership functions are defined, integrating rules for the input/output relations follow. Without setting the rules the system will not function, for it will have no idea which output point to map against a set of inputs. Setting the rules essentially provides the system with a decision-making capability. To set the rules, the if/then relationships are used. Aided with the decision matrices given on Table 6 through Table 8 the if/then relationships are mapped.

Table 6. The decision matrix, considering PID= L

		PA		
		L	O	H
AFBGL	L	A	B	B
	O	C	C	B
	H	C	C	C

Table 7. The decision matrix, considering PID= O

		PA		
		L	O	H
AFBGL	L	B	C	C
	O	C	C	B
	H	C	B	B

Table 8. The decision matrix, considering PID= H

		PA		
		L	O	H
AFBGL	L	C	D	D
	O	D	E	D
	H	D	D	C

In the case where insulin dosage is to be determined for PID= H 40 - 55), the Table 8 is referred. Thus, from the decision table provided on Table 8 it can be deducted that, when AFBGL= O (5 - 10), and PA= H (1.5 - 3), the insulin dosage will be insulin Dose= D (40 - 50). This

condition can be linguistically stated as “If (PID is H) and (AFBGL is O) and (PA is H) then (insulin Dose is D)” and this is what was previously referred as the if/then relationship. All the fuzzy if/then rules are set in the similar fashion and are given below:

1. If (PID is L) and (AFBGL is L) and (PA is L) then (insulin Dose is A)
2. If (PID is L) and (AFBGL is L) and (PA is O) then (insulin Dose is B)
3. If (PID is L) and (AFBGL is L) and (PA is H) then (insulin Dose is B)
4. If (PID is L) and (AFBGL is O) and (PA is L) then (insulin Dose is C)
5. If (PID is L) and (AFBGL is O) and (PA is O) then (insulin Dose is C)
6. If (PID is L) and (AFBGL is O) and (PA is H) then (insulin Dose is B)
7. If (PID is L) and (AFBGL is H) and (PA is L) then (insulin Dose is C)
8. If (PID is L) and (AFBGL is H) and (PA is O) then (insulin Dose is C)
9. If (PID is L) and (AFBGL is H) and (PA is H) then (insulin Dose is C)
10. If (PID is O) and (AFBGL is L) and (PA is L) then (insulin Dose is B)
11. If (PID is O) and (AFBGL is L) and (PA is O) then (insulin Dose is C)
12. If (PID is O) and (AFBGL is L) and (PA is H) then (insulin Dose is C)
13. If (PID is O) and (AFBGL is O) and (PA is L) then (insulin Dose is C)
14. If (PID is O) and (AFBGL is O) and (PA is O) then (insulin Dose is C)
15. If (PID is O) and (AFBGL is O) and (PA is H) then (insulin Dose is B)
16. If (PID is O) and (AFBGL is H) and (PA is L) then (insulin Dose is C)
17. If (PID is O) and (AFBGL is H) and (PA is O) then (insulin Dose is B)
18. If (PID is O) and (AFBGL is H) and (PA is H) then (insulin Dose is B)
19. If (PID is H) and (AFBGL is L) and (PA is L) then (insulin Dose is C)
20. If (PID is H) and (AFBGL is L) and (PA is O) then (insulin Dose is D)
21. If (PID is H) and (AFBGL is L) and (PA is H) then (insulin Dose is D)
22. If (PID is H) and (AFBGL is O) and (PA is L) then (insulin Dose is D)
23. If (PID is H) and (AFBGL is O) and (PA is O) then (insulin Dose is E)
24. If (PID is H) and (AFBGL is O) and (PA is H) then (insulin Dose is D)
25. If (PID is H) and (AFBGL is H) and (PA is L) then (insulin Dose is D)
26. If (PID is H) and (AFBGL is H) and (PA is O) then (insulin Dose is D)
27. If (PID is H) and (AFBGL is H) and (PA is H) then (insulin Dose is C)

2.6. Defuzzification and surface diagrams for insulin dosage

The final step of fuzzy inferencing is “defuzzification”. Till now we have dealt with ranges for different variables but having a range for insulin dose is not practical. To retrieve a crisp number as a recommendation, the defuzzification step is essential.

MATLAB offers a range of methods for defuzzification and for this paper the “centroid” method is used, as this is the default method and provides the best-fit approximation. Figure 5 illustrates the defuzzification method for a set of inputs and recommends a crisp number for insulin dosage.

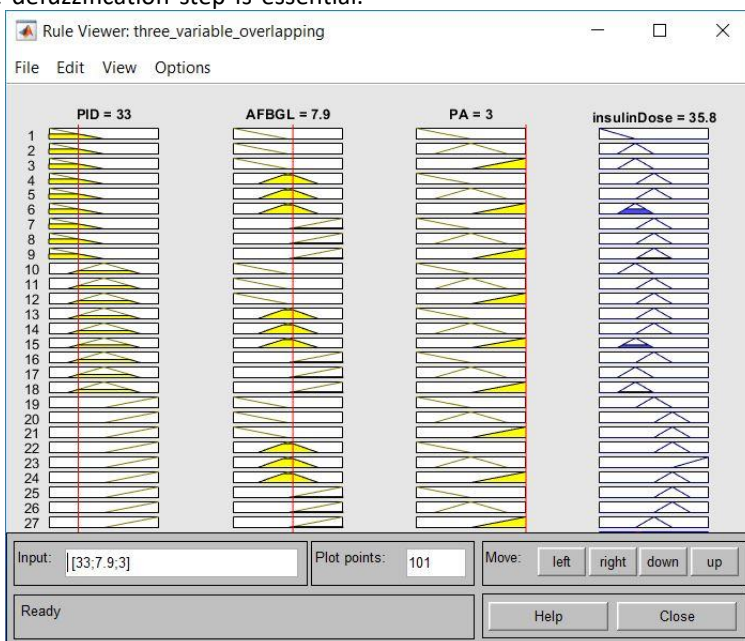


Figure 5. Defuzzification process for a set of inputs

In Figure 5, it is seen that a subject with PID= 33, AFBGL= 7.9, and PA= 3, the system returns a defuzzified insulin dose recommendation of insulin Dose= 35.8 units.

To perceive the whole system graphically, the surface diagram feature of the MATLAB Fuzzy Logic Toolbox provides an excellent solution. The surface diagram

provides an insight about the relationships among the input and output variables; in this case, the relationships among PID, AFBGL, PA, and insulin Dose. Figure 6 through Figure 7 shows the surface diagrams for different input/output combinations.

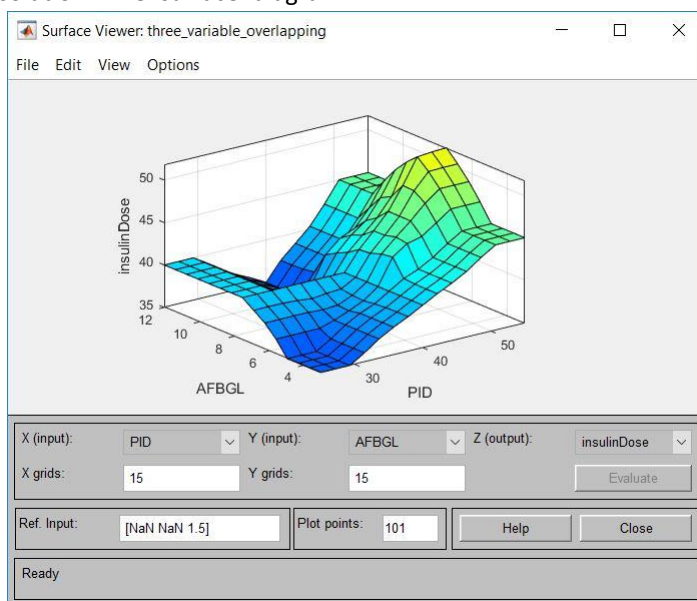


Figure 6. Surface diagram for the relationships among PID, AFBGL, and insulin Dose

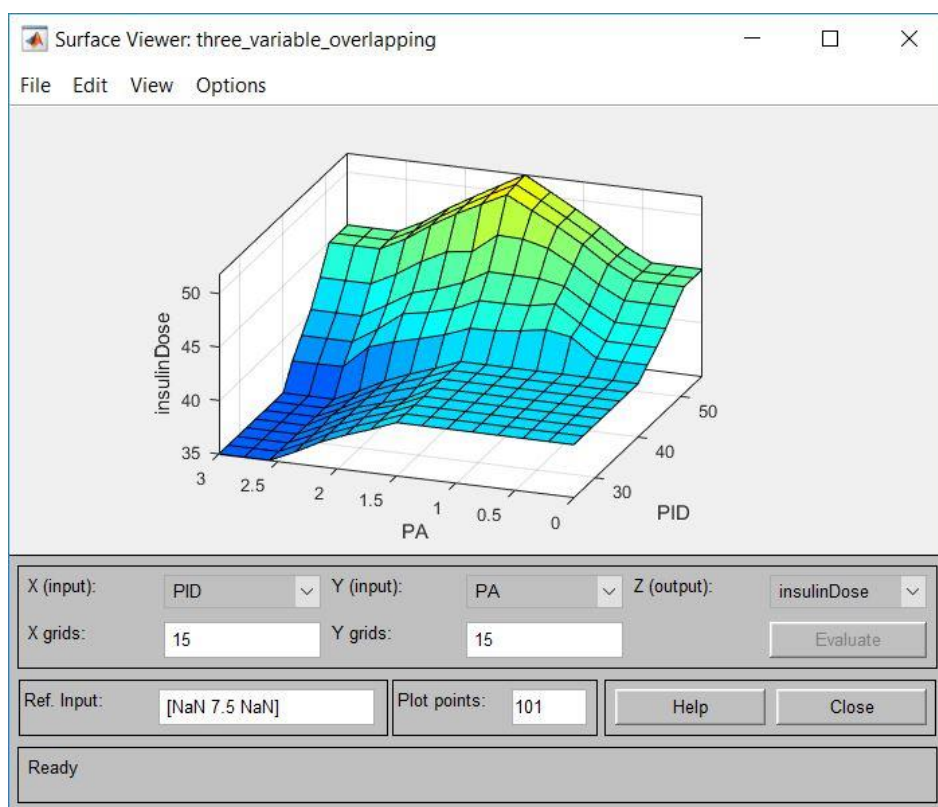


Figure 7. Surface diagram for the relationships among PID, PA, and insulin Dose

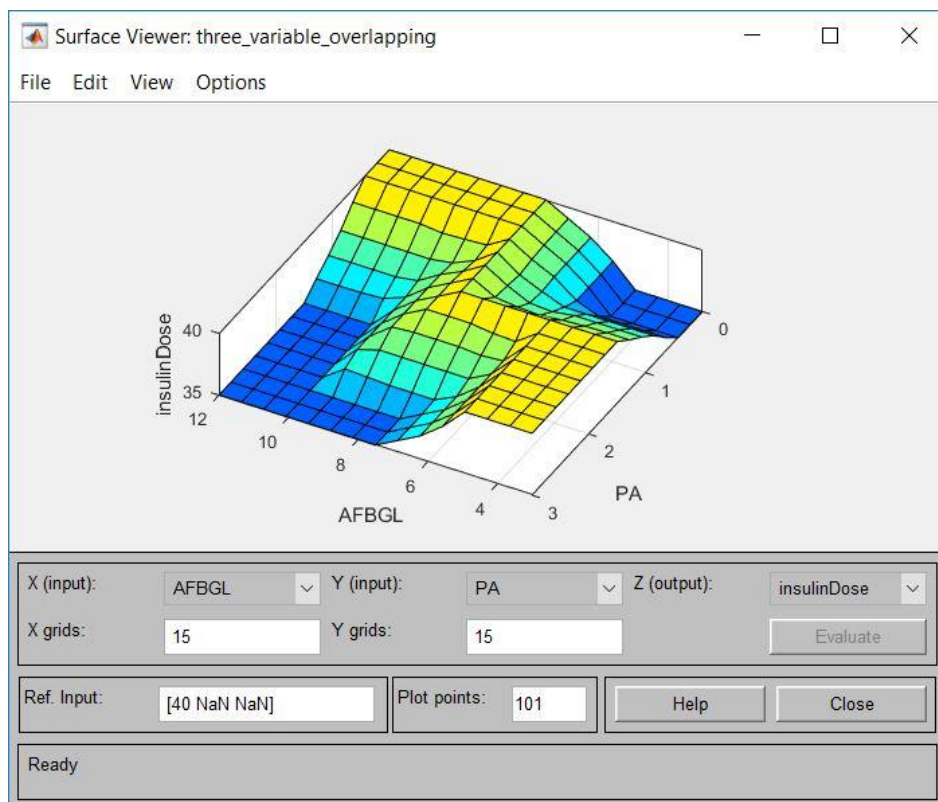


Figure 8. Surface diagram for the relationships among AFBGL, PA, and insulin Dose

RESULTS AND DISCUSSION

All the patients in this research were randomly selected from different parts of Dhaka city that are by this time suffering from type 2 diabetes and being treated with insulin prescribed by physicians on regular basis. Initially, these patients were selected as they were experiencing difficulty maintaining insulin homeostasis hence their insulin dosage was adjusted using a fuzzy logic based computational system. This adjustment was done in two phases. In the first phase, their daily dose was adjusted based on their weight, BMI and average carbohydrate intake [10]. The adjustment in phase 1

improved the quality of life of some of the patients but further refinement was warranted to serve a wider patient population. In this study, the focus was directed at the second phase of dose adjustment; wherein the predicted dose from the first phase (PID) was used along with patient's fasting blood glucose level and physical activity to further refine the daily insulin dose. Table 5 shows the PIDs for the 39 patients with prescribed insulin doses by physicians (PPD) and the adjusted insulin doses (APID) as well as the numerical difference between PPD and PID along with PPD and APID i.e. ND1 and ND2, respectively.

Table 9. Prescribed dose predicted dose and Adjusted Predicted dose of Insulin for individual 39 patients.

Patient number	Predicted Insulin dose (PID) by Fuzzy System (Phase 1)	Physician's Prescribed Dose (PPD)	Numerical Difference between PID and PPD (ND1)	Adjusted Predicted Insulin Dose (APID) by Fuzzy System (Phase 2)	Numerical Difference between APID and PPD (ND2)
1	40.0	35.0	5.0	40.0	5.0
2	33.0	32.0	1.0	37.8	5.8
3	46.5	40.0	6.5	43.6	3.6
4	40.0	35.0	5.0	37.1	2.1
5	46.5	40.0	6.5	44.2	4.2
6	52.6	30.0	22.6	45.0	15.0
7	39.5	25.0	14.5	36.0	11.0
8	40.0	30.0	10.0	40.0	10.0
9	40.0	30.0	10.0	37.2	7.2
10	40.0	40.0	0.0	37.3	-2.7
11	40.0	35.0	5.0	35.0	0.0
12	33.0	30.0	3.0	38.5	8.5
13	39.5	25.0	14.5	37.9	12.9
14	33.0	32.0	1.0	35.8	3.8
15	40.0	30.0	10.0	37.1	7.1
16	46.5	35.0	11.5	42.7	7.7
17	40.0	34.0	6.0	35.7	1.7
18	33.0	35.0	-2.0	34.4	-0.6
19	39.5	28.0	11.5	37.4	9.4
20	46.5	40.0	6.5	43.6	3.6
21	46.5	35.0	11.5	40.0	5.0
22	40.0	32.0	8.0	36.3	4.3
23	39.5	28.0	11.5	37.1	9.1
24	46.5	38.0	8.5	41.4	3.4
25	39.5	40.0	-0.5	38.4	-1.6
26	46.5	42.0	4.5	43.6	1.6
27	39.5	40.0	-0.5	39.7	-0.3
28	33.0	35.0	-2.0	34.4	-0.6
29	52.5	50.0	2.5	45.9	-4.1
30	40.0	35.0	5.0	38.9	3.9
31	33.0	40.0	-7.0	37.9	-2.1
32	33.0	35.0	-2.0	38	3.0
33	40.0	30.0	10.0	37.1	7.1
34	46.5	28.0	18.5	40.4	12.4

35	46.5	45.0	1.5	43	-2.0
36	46.5	40.0	6.5	43.6	3.6
37	39.5	35.0	4.5	37.9	2.9
38	40.0	30.0	10.0	37.9	7.9
39	39.5	32.0	7.5	36	4.0

The aim of the study was to ensure better consistency in terms of total daily insulin dosage so that a wider variety of type 2 diabetes patients could be catered to. Table 5 shows that there were difference among PPD, PID and APID in both phases 1 and 2. In order to compare the effectiveness of PPD, PID and APID, ND1 and ND2 were the defining parameters. In phase 1, patient no. 6 was experiencing hyperglycemic events by taking physician's prescribed dose whereas hyperglycemic events were significantly decreased after administering PID [10]. This initially accounted for a numerical difference, ND1, (between PPD and PID) of 22.6. However, in phase 2, the APID reduced the dose to 45 units per day, which accounted for a numerical difference, ND2, of 15 (between PPD and APID). After a follow up with the patient, the patient was still not experiencing hyperglycemic symptoms but had to use less insulin. The inference that can be made from this follow up is that the APID was a superior dose considering it was more balanced with fewer units of insulin but was still effective for the patient in terms of controlling the symptoms. In addition, there was a general trend observed in most cases where ND2 was lower than ND1 and still no reports of hypoglycemia or hyperglycemia were reported. In case of Patient 17, output from our fuzzy logic system suggested a decrease of 4.3 units of insulin as compared to phase 1 study and overall it contributed to the numerical difference of just 1.7. This strongly implies that refinement of their previous insulin intake resulted in a more accurate dose. Upon a 30-day follow-up, the

patient reported zero instances of hyperglycemic or hypoglycemic events. Similar findings were procured in case of Patient 22 where the newly refined insulin dose was 3.7 units lower (ND2) than the previous dose and this patient also reported a better quality of life free from any hyperglycemic or hypoglycemic events when followed up after 30 days. Therefore, the dosage precision for individual patients is further supported by the lack of hyperglycemic or hypoglycemic event occurrences among them, enabling improved quality of life. However, in case of Patient 13, it was observed that the numerical difference, ND2, was 12.9 units upon dose refinement as compared to the previous numerical difference, ND1, of 14.5 units. Therefore, not much precision was obtained for this patient, suggesting other factors (e.g. dietary habits, lifestyle, etc.) might have impaired the usefulness of the refined those. Post follow-up, this patient reported two instances of hyperglycemia that she accounted was serious.

As seen in Figure 10, with the majority of the patients, the ND2 values and their overall standard deviations were lower indicating the merits of a more precise dosing strategy. The original PPD was a good frame of reference to compare the numerical differences, since the physicians usually follow a particular protocol when prescribing insulin dosage. Even though it is probable that the final number will likely tend to a different value other than that of PPD, a lower numerical difference, in this case ND2 in particular, indicates that some degree of precision control was achieved.

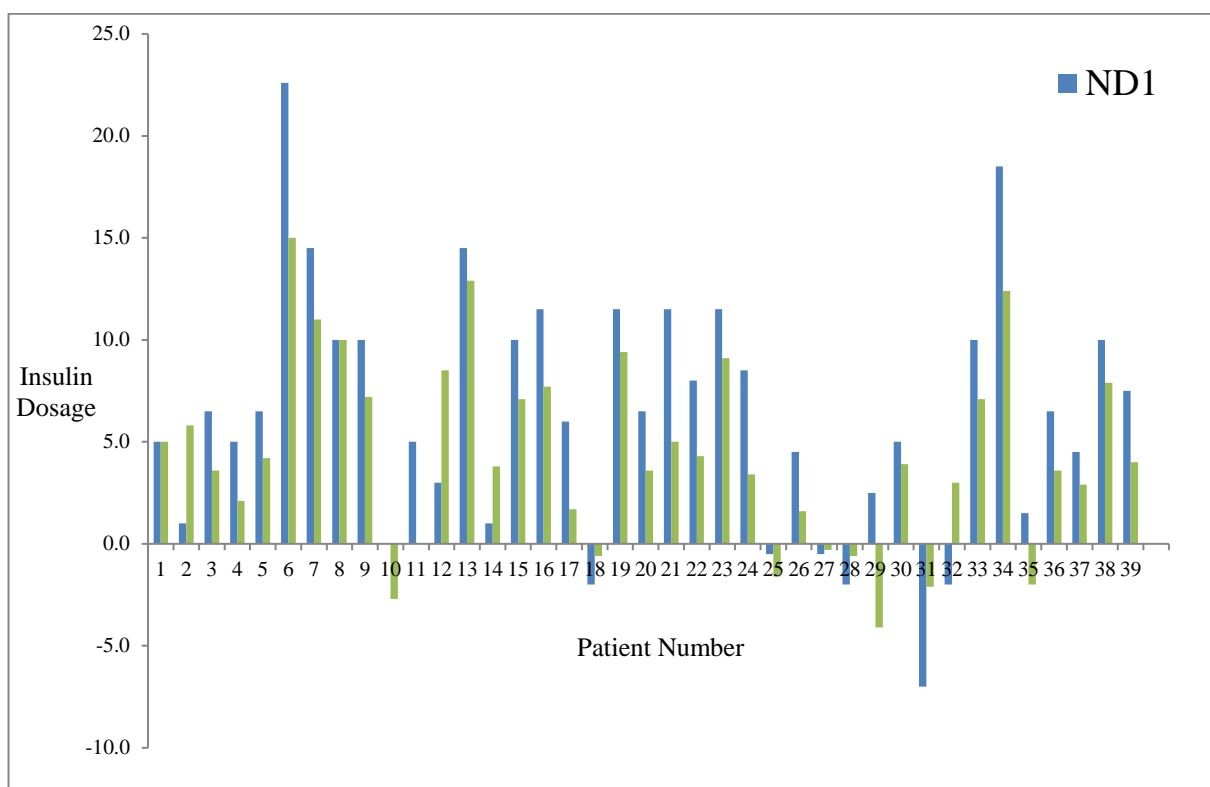


Figure 9: Numerical difference between ND1 and ND2

In addition to the improved numerical differences, the APID was consistent with the hypoglycemic safety standards set forth by Rubin et al 2011. According to this retrospective case control study conducted in 1990 on hospitalized patients suffering from insulin related hypoglycemia, an insulin unit threshold value of lower

than that of 0.6 units/kg drastically lessens the possibilities of hypoglycemic events [21]. Table 6 demonstrates the insulin doses in unit/kg after phase 2 for individual patients. All of the values were below 0.6 unit/kg and so the doses were declared to be safe by those standards.

Table 10. Insulin dosage in units/kg for each patient in order to assess the hypoglycemic safety standards

Patient number	Patient weight	Adjusted Predicted Insulin Dose (APID)	Units/kg
1	85	40	0.47
2	73	37.8	0.52
3	81	43.6	0.54
4	95	37.1	0.39
5	87	44.2	0.51
6	91	45	0.49
7	78	36	0.46
8	75	40	0.53
9	75	37.2	0.50
10	89	37.3	0.42
11	80	35	0.44
12	72	38.5	0.53
13	79	37.9	0.48
14	83	35.8	0.43
15	78	37.1	0.48
16	87	42.7	0.49
17	90	35.7	0.40

18	82	34.4	0.42
19	79	37.4	0.47
20	86	43.6	0.51
21	81	40	0.49
22	80	36.3	0.45
23	78	37.1	0.48
24	93	41.4	0.45
25	78	38.4	0.49
26	76	43.6	0.57
27	87	39.7	0.46
28	82	34.4	0.42
29	96	45.9	0.48
30	85	38.9	0.46
31	79	37.9	0.48
32	84	38	0.45
33	75	37.1	0.49
34	86	40.4	0.47
35	91	43	0.47
36	88	43.6	0.50
37	76	37.9	0.50
38	80	37.9	0.47
39	77	36	0.47

CONCLUSION

The management of type 2 diabetes is becoming increasingly difficult as diabetes pervades the world day by day. Artificial intelligence seems to provide a promising tool which can be used to ameliorate diabetes management. Since one of the main culprits in this case may be insulin dosing, our experimental approach may be very beneficial to future patients. In this study, a precise and personalized insulin dosing system was developed using a fuzzy logic based computational system that incorporated several patient related factors that may play a key role in diabetes management. It was seen that for a large number of patients, the insulin dosage predicted was superior in comparison to the original PPD. Of course, further studies are warranted, and more patient related factors may need to be included along with a more sophisticated artificially intelligent system for any future refinement. For now, it can be reasonably concluded that our system is able to provide a relatively safe and effective method to identify individualized insulin dosage.

CONFLICT OF INTEREST

The authors report no declaration of interest.

REFERENCES

1. Cho NH. Q&A: Five questions on the 2015 IDF Diabetes Atlas. *Diabetes Res Clin Pract.* 2016;115(March):157-159. doi: 10.1016/j.diabres.2016.04.048
2. WHO. The top 10 causes of death. World Health Organization. URL:/entity/mediacentre/factsheets/fs310/en/index.html
3. DeFronzo RA, Eldor R, Abdul-Ghani M. Pathophysiologic approach to therapy in patients with newly diagnosed type 2 diabetes. *Diabetes Care.* 2013;36 Suppl 2(Supplement_2): S127-38. doi:10.2337/dcS13-2011
4. Papatheodorou K, Papanas N, Banach M, Papazoglou D, Edmonds M. Complications of Diabetes 2016. *J Diabetes Res.* 2016;2016. doi:10.1155/2016/6989453
5. Sharma MD, Farmer JA, Garber A. Type 2 diabetes and cardiovascular risk factors. *Curr Med Res Opin.* 2011;27(sup3):1-5. doi:10.1185/03007995.2011.620083
6. Mendenhall E, Norris SA, Shidhaye R, Prabhakaran D. Depression and type 2 diabetes in low- and middle-income countries: A systematic review. *Diabetes Res Clin Pract.* 2014;103(2):276-285. doi: 10.1016/j.diabres.2014.01.001
7. Whiting DR, Guariguata L, Weil C, Shaw J. IDF Diabetes Atlas: Global estimates of the prevalence of diabetes for

- 2011 and 2030. *Diabetes Res Clin Pract.* 2011;94(3):311-321. doi: 10.1016/j.diabres.2011.10.029
8. Swinnen SG, Hoekstra JB, DeVries JH. Insulin therapy for type 2 diabetes. *Diabetes Care.* 2009;32 Suppl 2. doi:10.2337/dc09-S318
9. Khan RI, Nirzhor SSR, Chowdhury AM, Shishir TA, Khan AI. A fuzzy logic-based approach for the adjustment of insulin dosage for type 1 diabetes patients. *Journal of Innovations in Pharmaceutical and Biological Sciences.* 2017; 4(4): 145-152
10. Chowdhury AM, Khan RI, Nirzhor SSR, Jabin J, Khan AI. A novel approach in adjustment of total daily insulin dosage for type 2 diabetes patients using a fuzzy logic-based system. *Journal of Innovations in Pharmaceutical and Biological Sciences.* 2017; 4(4): 65-72
11. Bird SR, Hawley JA. Update on the effects of physical activity on insulin sensitivity in humans. *BMJ Open Sport Exerc Med.* 2017;2(1):e000143. doi:10.1136/bmjsem-2016-000143
12. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HAW. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med.* 2008;359(15):1577-1589. doi:10.1056/NEJMoa0806470
13. Legro RS, Finegood D, Dunaif A. A fasting glucose to insulin ratio is a useful measure of insulin sensitivity in women with polycystic ovary syndrome. *J Clin Endocrinol Metab.* 1998;83(8):2694-2698. doi:10.1210/jcem.83.8.5054
14. Conn VS, Koopman RJ, Ruppar TM, Phillips LJ, Mehr DR, Hafdahl AR. Insulin Sensitivity Following Exercise Interventions: Systematic Review and Meta-Analysis of Outcomes Among Healthy Adults. *J Prim Care Community Health.* 2014;5(3):211-222. doi:10.1177/2150131913520328
15. Helmrigh SP, Ragland DR, Leung RW, Paffenbarger RS. Physical activity and reduced occurrence of non-insulin-dependent diabetes mellitus. *N Engl J Med.* 1991;325(3):147-152. doi:10.1056/NEJM199107183250302
16. Jeon CY, Lokken RP, Hu FB, Van Dam RM. Physical activity of moderate intensity and risk of type 2 diabetes: A systematic review. *Diabetes Care.* 2007;30(3):744-752. doi:10.2337/dc06-1842
17. Albisser AM, Schiffrin A, Schulz M, Tiran J, Leibel BS. Insulin dosage adjustment using manual methods and computer algorithms: A comparative study. *Med Biol Eng Comput.* 1986;24(6):577-584. doi:10.1007/BF02446259
18. Fabietti PG, Canonico V, Federici MO, Benedetti MM, Sarti E. Control oriented model of insulin and glucose dynamics in type 1 diabetics. *Med Biol Eng Comput.* 2006;44(1-2):69-78. doi:10.1007/s11517-005-0012-2
19. Mfhanović S, Mijčić M. The automatic regulation of the basal dose on the insulin pump for the treatment of patients that have Diabetes type 1. *Bosn J Basic Med Sci.* 2010;10(2):100-106.
20. Piwernetz K, Renner R, Hepp KD. Glucose control in mobile type 1 (insulin-dependent) diabetic patients by means of a semi-automatic feedback-controlled insulin infusion system. *Diabetologia.* 1982;23(3):229-234. doi:10.1007/BF00252846
21. Rubin DJ, Rybin D, Doros G, McDonnell ME. Weight-based, insulin dose-related hypoglycemia in hospitalized patients with diabetes. *Diabetes Care.* 2011;34(8):1723-1728. doi:10.2337/dc10-2434
22. Mikines KJ, Sonne B, Farrell P a, Tronier B, Galbo H. Effect of physical exercise on sensitivity and responsiveness to insulin in humans. *Am J Physiol.* 1988;254(3 Pt 1): E248-E259. doi:10.1152/ajpendo.1988.254.3. E248
23. Abbasi F, Silvers A, Viren J, Reaven GM. Relationship between several surrogate estimates of insulin resistance and a direct measure of insulin-mediated glucose disposal: Comparison of fasting versus post-glucose load measurements. *Diabetes Res Clin Pract.* 2018; 136:108-115. doi: 10.1016/j.diabres.2017.11.021
24. Hanefeld M, Koehler C, Hoffmann C, Wilhelm K, Kamke W, Gerstein H. Effect of targeting normal fasting glucose levels with basal insulin glargine on glycaemic variability and risk of hypoglycaemia: A randomized, controlled study in patients with early Type 2 diabetes. *Diabet Med.* 2010;27(2):175-180. doi:10.1111/j.1464-5491.2009.02915.
25. Shamim M, Enam S, Qidwai U, Godil S. Fuzzy logic: A "simple" solution for complexities in neurosciences? *Surg Neurol Int.* 2011;2(1):24. doi:10.4103/2152-7806.

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