Ubiquitous Healthcare Systems: Improving the Management of Diabetes Mellitus through the Ubiquitous Technologies

ユビキタス在宅医療：ユビキタス技術を用いた糖尿病治療法の改善

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Waseda University
Graduate School of Fundamental Science and Engineering
Department of Computer Science and Engineering,
Research on Distributed Systems

Mohammed KALKATTAWI
カルカタウィ モハメド
ABSTRACT

The Ubiquitous Healthcare System (UHS) field aims to expand the healthcare services beyond the standard clinical environment. The main goal is to enhance the quality of health services and reduce the costs through prevention and post-operative care. The mentioned systems could be useful for patients, who are suffering from chronic diseases such as diabetes and heart diseases. As the diabetes mellitus demands an extensive type of management, we believe that the filed of UHS can help to enhance and simplify the management of the diabetes mellitus. The diabetes mellitus is widely known as the inability to regulate plasma glucose due to some certain circumstances within the body. In such a case, the patient needs regulate the plasma glucose manually through medication, dieting and exercising. Diabetic patients, who are relying on external insulin delivery as part of their treatment, are called insulin dependent patients. Treatment of insulin dependent patients is considered challenging, because it requires much dedication from the patient's side. Some of these challenges are managing the insulin doses in daily bases and avoiding low plasma glucose values known as Hypoglycemia episodes. Diabetic patients are always directed to keep following up with their primary care doctors in regular bases. The reason is that diabetes mellitus can be associated with some other serious complication such as kidney failure, depression or eye glaucoma. For this reason, diabetic management requires dealing with a lot of daily information. Relying on human brain alone for this management can be extremely stressful and liable to human errors. Smart gadgets today have powerful processing power and high connectivity capability. As a result, they are capable to handle complex operation such as the diabetic management; for example, automating the data collection through smart devices applications, detecting hypoglycemia episodes through
wearable systems, or facilitating the communication between patients and practitioners outside the clinical environment. Within this research we placed our focus on two different studies: First, we conducted a study on the importance of intelligent insulin pen technology among diabetic patients for enhancing and modernizing the Multiple Daily Injections therapy. Second, we conducted another study that focused on detecting Hypoglycemia episodes through Wearable and Ubiquitous Computing.

The first study dealt with patients, who were under multiple daily injections for external insulin delivery. The first objective was to highlight the most common issues existed within the current multiple daily injections practices, and then investigates the usage of smart gadgets in managing the diabetes mellitus, such as the use of intelligent insulin pens as an alternative instrument for multiple daily injections therapy. The second objective was to testify the use of a smart ubiquitous multiple daily injections system among the diabetic patients. We testified that by proposing a smart system composed from smartphones and intelligent insulin pens. The main purpose was to give some example in how to expand the functionality of intelligent insulin pens through the data communication with smart devices. The study first conducted a series of surveys and interviews, which managed to collect some information about the management of medication, using smart devices or collection of daily diabetic data, and the use of intelligent insulin pens as an alternative instrument within multiple daily injections. The final part of this study included a series of pilot experiments. The experiments focused on applying a proposed system, which was mainly an automated cloud-based reminder system. Within this study, we wanted to measure the influence on the daily adherence to the insulin medication; we also wanted to observe the interaction between the system and its users. The results from the survey showed that there were still many challenges still existed among the insulin dependent patients.
The majority of patients mainly approved the use of intelligent insulin pens as an alternative; however, by comparing current existed issues and the functionality of these pens, the current type of intelligent pens can solve some of these issues but not all of them. As per the pilot experiments, the initial results from the pilot experiments showed some positive influence toward the adherence level. The received feedback from participants was mainly positive; they believed that the system could act as a good backup for the usual routines.

The second study were concerning Hypoglycemia episode, which is still considered one of the major concerns among diabetic patients. As there is still no definitive method that would help in detecting the episode at its early stages, there is still a need to find another reliable method that can minimize the Hypoglycemia risks, and also it can be implemented easily without hindering daily activities. Within this research, we proposed to enhance one of the former suggested method, which was focusing on detecting hypoglycemia through its symptoms. The literature review showed that most of the methods are still suffering from inaccuracy with detected cases. We thought the enhancement could be achieved by utilizing ubiquitous technologies such as context awareness and machine learning.

In general, utilizing the ubiquitous technologies within diabetic management is still limited right now. Future development should focus on how to provide features that can overcome the unresolved challenges. We hope that through these studies, we would able to provide a contribution toward simplifying the complexity of diabetic management.
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1. INTRODUCTION

1.1 Ubiquitous Healthcare Systems

Ubiquitous Healthcare System (UHS) is a novel branch from the ubiquitous computing field. The UHS field focuses on using ubiquitous technologies, such as smart phones, wearable sensors, cloud-servers, etc, in order to provide extensive caring services outside of the usual clinical environments [30]. These kinds of systems can be critical for patients, who dependently rely on others to stabilize their health conditions. For example, patients, who are in the risk of heart issues, can wear wearable heart sensors that can continuously monitor cardiac values. In the case of triggering any abnormal cardiac values, the system would immediately send an alarm to the caregiver to check on the patient’s condition. The previous example is one of the main objectives of expanding the healthcare field through the ubiquitous technologies. Some of these objectives are:

1. **Providing better diagnosis and treatment:** Through the continuous collection of patients’ vital signs, practitioners can keep up to date with the patient’s condition progress. Moreover, they will be able oversee the patients lifestyle and daily routines. For example, they can monitor the patients’ compliance to the medication or recommended regular exercises.

2. **Higher connectivity:** The goal to provide a wide communication network between the different medical facilities and also between patients and practitioners. Practitioners can have a full picture of the patients’ medical history. This step will save time and minimize risks of conflict diagnoses. Also, patients can seek support anytime through this kind of communication and save a trip to the emergency room.
3. **Continuous support for patients:** By monitoring the patient’s lifestyle, personalized recommendations can be sent to the patients. The aim is to keep the patients healthy and maintaining high living qualities.

Although the utilization of ubiquitous technologies has good potential in changing the shape of healthcare field, there are many technical and logistic challenges that slow the transition to complete ubiquitous healthcare solutions. Some of the technical challenges are as the following [27]; there is a need to develop biosensors that can measure vital signs with accurate readings. Also, developers need to create solution that can solve issues within power management. For example, using kinetic energy to recharge the sensor batter. There is also a need to provide infrastructure and software that can receive the transmitted data and analyze them in order to interpret them as body condition. Logistic challenges are mainly concerning the produced data and their storage. Since there are different types of regulations between different countries, ownership and privacy of data are both big issues. Also, security and protecting the data from unauthorized access and use is still catching big attention among researchers. Although ubiquitous healthcare systems are still far from being fully deployed, they have good potential to ease the control of chronic disease, such as hypertension, diabetes or heart diseases. Most of these diseases rely on managing the daily routines and continuous follow-ups. In this research, we are putting our focus on the diabetes mellitus. The diabetes mellitus raises many challenges within its daily management. We believe ubiquitous technologies can help easing the control of diabetes mellitus and open the door for more improved management.
1.2 The Challenges within Diabetes

1.2.1 The Complexity in the Diabetic Management

Diabetes is known as losing the control over blood glucose due to certain circumstances. Diabetes in general is categorized into several types. The most known ones are Type 1 and Type 2. Type 1 patients lose the ability to produce insulin hormone within the body; for this reason, they are called insulin dependents and require having external resources for insulin. On the other hand, Type 2 is totally a different case; patients might neither produce enough insulin nor utilize the insulin inside their body. For this reason, Type 2 patients are required to take oral medications and sometimes insulin too to assist the digestion process for carbohydrates intake. Both types still require a strict control of daily routines. Diabetic patients are required to balance between three main activities in their daily routines; meals, medications and body exercise in order to maintain a good average of blood glucose (Figure 1).

![Figure 1: Balancing between Daily Activities](image-url)
The goal is to keep the blood glucose level stable and close to the normal readings (between 150-120 mg/dL). Diabetic patients are required to follow up with their primary care in monthly bases (from 1-month to 6-month bases). Usually, within these follow ups, diabetic patients keep measuring their Glycated hemoglobin (A1C) level. A1C is a measurement data that can tell the average of glucose level within blood within 1 month to 3 months. Diabetic patients always aim to have this measurement between 7% and 6.5% of the overall glucose level [4]. If the patient managed to reach this value, it would mean the daily routines were well controlled and the patient was keeping a stable glucose level most of the times. Nevertheless, with all the efforts done to control the glucose level, there are still some challenges that might keep diabetic patients anxious all the times.

1.2.2 The Risk of Hypoglycemia

Figure 2: Hypoglycemia Stages

Hypoglycemia is considered one of the most critical risks that diabetic patient might encounter. If by any chance the patient would not react quickly to the Hypoglycemia condition,

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1 Illustrations of Hypoglycemia symptoms and other conditions have permission for reproduction for non-profit education purposes from their own creators, © Novo Nordisk Inc, and Purdue University.
the patient might encounter a coma or, possibly, passing away. For this reason, to avoid such incidents, diabetic patients keep monitoring the glucose level most of the time during the day. The possible reason for encountering Hypoglycemia episodes are large doze of medication, heavy activities or insufficient carbohydrates intake. Hypoglycemia has three levels of gradual stages; each stage has certain symptoms that start to appear gradually as we advance through stages (Figure 2).

Detecting Hypoglycemia during the early of its “mild” stage (between 99 mg/dL and 70 mg/dL) is safer and more manageable, as the patient is still in full conscious. The challenge is that the stage symptoms are usually mild and hard to be noticed. Patients might start feeling the symptoms either the late of the stage or after it would enter the intermediate stage. At this point, patients would remain conscious but encountering severe weakness. The patient needs to react quickly before the stage would advance toward the severe stage, which might cause the patient to lose conscious. There are still no ways to detect Hypoglycemia at early stages other than doing frequent blood tests between meals or before bedtime.

1.2.3 Associated Daibetic Complication Symptoms:

Daibetic complication symptoms are one of the major risks associated with the diabetes mellitus. Some of these cases are deep depression, high hypertension and cholesterol level, eyes glaucoma, kidney failure, damaged nerves and some other cases. For this reason, diabetic patients need to keep flowing up about their conditioners, educate themselves and consulting their primary care frequently. Failing to follow such practices might lead into encountering these cases out of the patient’s awareness. If they were discovered at late stages, it would be difficult to reverse them to the normal conditions.
1.3 The Role of Technology in Assisting Diabetic Patients

If we want to define the human body inner behavior, we will find that they are sharing the same concept of ubiquitous computing. The body processes the different inner activities out of the individual's awareness. In the case of the diabetes mellitus, before the body would encounter the disease, the body can automatically deliver the exact amount of insulin hormone that match with carbohydrates intake. The process will be accomplished without any required action from the individual side. Once the body encounters diabetes and loses the sense to control blood glucose level, the patient will start taking the role pancreas and manage the process manually. The patient will start putting much attention to a lot of input and output in order to regulate the blood glucose level. Ubiquitous technology, under its concept, might able to retain some of original body behavior and help to process these input and outputs in a more convenient matter. In this way it might help to decrease the amount of required focus toward the process itself. In the case of insulin dependent patients, patients are required to know some information before adjusting their meal doses. The required data are carbohydrates intake, current glucose level and type of exercise or activity done before the dose (i.e., heavy activities vs. normal activities), then the patients can adjust dose manually in the delivery instrument. If we can gather these data into one place and make them available continuously as references for the patients, it will greatly ease the adjustment of insulin dose and increase its accuracy. Another point is the time management of insulin medication. There a lot of cases reported that many patients fail to comply with the insulin dosing direction, which states that the insulin dose should be taken within specified period to avoid cases of Hypoglycemia or Hyperglycemia episodes; some other cases reported
that patients are in the risk of missing or double dosing. Until this moment, there is no a common reliable method that can solve these issues. Current ubiquitous technologies are capable to ease or solve these previous challenges at least partially. For example, most smart devices now have many sensors that keep tracks of the users’ movements and activities. Moreover, it became easier to keep collecting data continuously with the availability of cloud services. With the previous technologies, we can keep track of the patient’s daily activities and use them as references for the insulin therapy treatment. Also, if we can send doses data through cloud services, we can keep tracks of the patients’ compliance and direct them automatically in case there are some incompliant cases. In the case of the detecting hypoglycemia, currently, the only effective way to avoid or detect hypoglycemia is conducting self-glucose blood tests frequently. The method is known for being costly and, not to mention, painful for the diabetic patients. A suggested method is detecting the Hypoglycemia episode through its symptoms [39]. Using wearable sensors we can predict that patient is in the near risk of encountering Hypoglycemia episode. This method is good for being non-invasive and also it could be extremely useful for those who have impaired senses of detecting Hypoglycemia episodes. The problem is that the method is far from being complete and accurate as many of the symptoms overlap with other symptoms such as weather or any similar causes [8]. Nevertheless, we can utilize some of the ubiquitous knowledge such as context-awareness and machine learning to raise the accuracy of detected results. For example, if the system could know that the patient was practicing heavy exercises before detecting the symptoms, then the system can conclude that the detection is mostly probably caused by a Hypoglycemia episode. For the challenge in assisting patients with diabetic complications, social media and Internet blogs are currently being used to seek support outside of the clinical environments. Yet, there is still a big challenge in relying on these methods for support. Most of
these resources can be full of misleading information or advertisement materials, which put the patient in the risk of false practices or unapproved medication [17]. Nevertheless with the availability of smart devices, such as smart phones and tablets, accessing web contents and social media became more effective and faster. Monitoring and cleaning the false materials from the web became much easier. Moreover, communication between practitioners and their patient can become smoother and less formal than before. This will help to patients to seek support outside of the follow-up meetings and decrease the number of trips to emergency rooms.

There are still many benefits can be gain from utilizing ubiquitous technologies within the diabetes mellitus. There is a need to create some interdisciplinary studies that focus on understanding diabetic treatment therapies and their challenges, and then find some practices within ubiquitous technologies that can help to overcome these challenges and provide an improved solution for the diabetic routines.

1.4 Study Objectives

The main objective from this research is to overcome some of the challenges existed within current diabetic practices through the utilization of ubiquitous technologies. We would like to simplify the role of diabetic management by enhancing or automating some parts within the whole process. In this research we would like to direct the focus toward the following two cases:

1. Modernizing multiple daily injections (MDI) therapy through the utilization of ubiquitous technologies.

2. Detecting hypoglycemia episodes through wearable and ubiquitous computing.
1.4.1 Study 1: Modernizing MDI Therapy through the Utilization of Ubiquitous Technologies.

MDI therapy is one of long practiced routines for managing the diabetes mellitus (Figure 3). Though it has been a popular practice for long time, an effective management, which leads to have close to normal A1C value, requires extra work and dedication from the patient’s side. Basically, there are two types of required doses. The first type is known as Basal, i.e., long acting dose; the basal dose lowers the glucose level outside the meal time period, e.g., between meals or sleeping time. The dosage amount is usually determined by the practitioners and must be taken within a fixed period of time, i.e., every 24 hours; for example, the Glargine type in Figure 3. The other dose type is known as bolus, i.e., short (fast)-acting dose, which is usually associated with mealtime. The patient needs to calculate the value of the carbohydrates intake and carbohydrate ratio in order to adjust this dose properly; for example, the Glulisin type in Figure 3. The patient needs also to check the glucose level before administering any dose, in order to check if the dose adjustment is needed or not. Also, if the glucose level goes higher than the usual (above 180 mg/dL), the patient needs to correct the glucose level by taking a small dose of short (fast)-acting dose. This load of work might negatively effect the compliance toward the management itself, which it will directly lead into poor glycemic control. The mission requires a lot of time management and calculation. We believe by applying the ubiquitous computing concepts on parts of this mission, we can enhance and simplify the mission for the patients. For example, we can apply an automated system that can do the time management for daily doses without the patient’s involvement.
1.4.2 Study 2: Detecting Hypoglycemia Episodes through Wearable and Ubiquitous Computing.

There were many approaches that were aiming to detect Hypoglycemia episodes through their symptoms and wearable sensors, however, most of these approaches could not be reliable and lack some accuracy within their outcomes. Nevertheless, these approaches had some potential for being non-invasive compared to usual practices. We believe if we could apply some knowledge from the context-awareness and machine learning, we might able to raise accuracy of the Hypoglycemia detection. The main goal is to make these systems more reliable in the future.
The final systems should be implemented in a way that it can weave into the daily life of diabetic patients normally out of their awareness.

1.5 Study Approaches

1.5.1 Study Approaches within Modernizing MDI Therapy through the Utilization of Ubiquitous Technologies.

1.5.1.1 Qualitative analysis

The study involved studying the latest technology in insulin delivery within MDI therapy through survey and interviews. It focused on collecting information about the patients’ behavior. Also, it focused on the use of technology for the diabetic purposes. The study included a couple of usability studies to observe the interaction between the patients and the used instrument. The final outcomes were used as bases for the conceptual design and experimental studies.

1.5.1.2 Conceptual design

This step focused in designing a system constructed from current diabetic instrument with new ubiquitous concept. Based on the qualitative analysis, the proposed design targeted some of the observed challenges existed within the MDI routines.

1.5.1.3 Prototyping and experiments

A series of pilot studies were conducted using a prototype from the proposed system. The main purpose was to testify the potential of applying ubiquitous technology concept on the
current instrument. Also, the experiments aimed to observe the influence using the system on the users themselves and observe the interaction with the system itself.

1.5.2 Study Approaches within Detecting Hypoglycemia Episodes through Wearable and Ubiquitous Computing.

1.5.1.1 Conceptual design

The study used previous solutions that used wearable sensors to detect hypoglycemia symptoms. The study added new concepts from the ubiquitous computing discipline, such as context awareness and machine learning.

1.5.1.2 Prototyping and experiments

The study aimed to construct the prototype based on the conceptual design. After that a series of experiments were conducted with different scenarios. The main purpose is set the initial values for the detection system for each module.

1.6 Organization of this Thesis

1.6.1 Assessment Study of the Intelligent Insulin Pens

The chapter presents a couple of assessment studies to evaluate the necessity of the technology among diabetic patients. First, it gives a brief background about the history of insulin delivery and the evolution of insulin pens. Then, it gives details about the research methodology.
The section is followed by the list of obtained results. The chapter is concluded with a brief discussion about the obtained results.

### 1.6.2 Automated Cloud-based Reminder System for Insulin Doses

This chapter focuses on diabetic patients who undergo multiple daily injections therapy (MDI) for their diabetic management (MDI). As a step to improve the adherence level among diabetics, the chapter introduces a proposed cloud-based reminder system that can promote a change in the patients’ behavior. This chapter is divided into two scopes: the first scope concerns the evaluation of current technologies within diabetic management, while the second scope focuses on testing the proposed system among a number of patients. The chapter gives details about the all attempted experiments. It then lists all the obtained results from the experiments. Finally, the chapter concludes with discussion about the obtained results.

### 1.6.3 Detection Hypoglycemia through Wearable and Ubiquitous Computing

The chapter focuses on a proposed system for Hypoglycemia detection. The proposed system utilizes knowledge from the wearable systems and ubiquitous computing fields. The chapter gives some background about the hypoglycemia episode and associated risks; then, it highlights some of the proposed attempted solutions that aimed to minimize the risks from Hypoglycemia. The chapter gives details about the conceptual design and suggested algorithm for the study. It then gives some details about the some plans about the suggested experiments. The chapter concludes with some discussion regarding the study itself.
2. INTELLIGENT INSULIN PENS: ASSESSMENT STUDY

2.1 Related Work

2.1.1 Insulin Delivery and Evolution of Insulin Pens

Insulin medication was first discovered by the Nobel Prize winner, Frederick Banting, MD. The first human insulin administration started in 1922, while the initial commercial production started in 1923. The medication source initially used to be extracted from pancreases taken from animals, such as cows, pigs or fish. As early medication used to have some issues such as medication allergy, Eli Lilly introduced the first genetic produced insulin using human DNA in 1982 [26]. The new production became much closer the normal body insulin; it has been known as human insulin. Ever since, several kinds of insulin have been produced within the market:

- Fast-acting: acts immediately within 5 to 15 minutes and lasts for 3 to 4 hours, some examples are aspart, lispro, and glulisine.
- Short-acting (also known as regular insulin): it acts within 30 minutes and can last from 5 to 8 hours.
- Intermediate-acting (also known as NPH insulin): it acts within 1 to 3 hours and stays active for 16 to 24 hours.
- Long acting: it starts acting after 1 to 2 hours and lasts up to 24 hours. This type is known for the absence of peak points, i.e., the point where the insulin has maximum performance. Some examples are glargine and detemir.
- Ultra-long acting: it has been recently produced; it basically starts within 30 to 90 minutes and its onset exceeds 24 hours. This type is also known for its absence of peaks as well.
- Mixed types: Basically, it is a pre-mixture between long and short acting types.

Figure 4 shows the differences in onset behavior between some several types.

![Figure 4: Different Types of Insulin Onset Behavior](image)

The insulin medication cannot be taken orally. For this reason, the medication needs to be taken through subcutaneous injections. At first, the only available instrument was syringes with needles; however, in 1976 the first insulin pump was invented. The invented solution was an attempt to ease the administration and minimize the pain associated with regular syringes. Nevertheless, due to the difficult and expensive nature of insulin pumps, many patients remained using regular syringes for insulin administration [7]. Until today there are still some attempts to
replace the subcutaneous injections method with painless methods, such as insulin inhalation, but these methods are still suffering inaccuracy and some other major issues [16]. The syringes and insulin pumping have remained as the most popular methods for external insulin administration. Nevertheless, as an attempt to ease the insulin administration using syringes, the Danish company Novo Nordisk introduced the first insulin pen in 1985 [49]. The main focus was to find a more practical solution, which can eliminate the need for regular syringes and insulin vials. The introduced solution proved its easy administration, especially among elderly and young patients. It has been greatly appreciated for its accuracy and simplicity [65]. The insulin pens have already become more popular more than traditional syringes, to the extent that they have become the standard instrument for the Multiple Daily Injections therapy (MDI) [44]. Both types of instrument have the same concept for dosing. They are both relying on human force, i.e., mechanical based motor, for those administration. Nevertheless, there are several different features and nature between them.

For regular syringes, patients need to insert the needle inside the insulin vial, and then pull the end of the syringe to fill the syringe tube with the required dose. On the other hand, the vial for insulin pen, which is called cartridge here, is inserted inside the pen itself. Patients just need to adjust the required amount using the knob at the end of the pen, and then by pushing the knob, the dose will be administered.

There are a couple of advantages over using syringes in this case.

1. The pushing action instead of pulling will prevent the air bubbles from coming inside the tube and mix with dose. The problem with air bubbles they can affect the accuracy of the dose itself.

2. The knob at the end of the pen is easier, faster and more visible for dose.
3. The integration of the cartridge inside the pen itself makes it more portable and convenient for carrying.

Nevertheless, there are still some disadvantages in using insulin pens compared to regular syringes.

1. The cost of using insulin pens is considered a little bit higher than the cost of using regular syringes [50].

2. The dosing with insulin pens is considered slower than regular syringes. During the dosing, because the patient needs to push through the whole insulin cartridge, the patient has to keep the instrument inside the skin few extra seconds [24]. This will make sure that the dose has been fully administered.

3. For those who are mixing two different types of insulin, e.g., Regular and NPH insulin, they cannot mix insulin in the same pen; however, the issue might consider a minor disadvantage for some others because some new types of insulin are actually not mixable with each others, e.g., Insulin Glargine and Insulin Glulisine.

For the evolution cycle of insulin pens, since their introduction, they have had only minor upgrades; the evolution has been very slow most of the time. Most of the upgrades were focusing on outer designs. Some of them had some enhancements with the dosing, but there were not any new functions or concepts; they remained intact to the old mechanism for quite some time [55]. The first significant upgrade was in 2007. At that year, Eli Lilly and company introduced the new model of HumaPen® MemoirTM [25]; this was the first model that introduced the ability to keep records of date, time and dose amount for a couple number of doses. The main objective is to avoid the risks from double or missing doses; however, the dosing mechanism was still
mechanical-driven as its predecessors. The model has been discontinued due to some certain issues [46].

In 2012, Novo Nordisk introduced a similar memory feature in two of their own models NovoPen® 5 [66] and NovoPen Echo®; it shows the total dosage taken within the last 12 hours. Novo Nordisk implemented also a smaller scale dosing, i.e., scale of 0.5 unit, within the NovoPen Echo® model for diabetic children, who usually have higher insulin sensitivity [42]. Again, the dosing mechanism was also mechanical-driven.

A new intelligent insulin pen model has recently been introduced in limited markets within Europe and South Korea [3]. The model was originally manufactured by the South Korean company Diamesco Co., Ltd. The manufacturer itself is specializing in insulin pumps. The new developed model inherited a couple of features originally available within pump devices. The most notable change from previous models is replacing the dosing concept from mechanical-driven motor into digital-driven motor. This change eliminates the need of human-force. It also provides more precise dosing scale, i.e., 0.1-unit scale. Another remarkable add-on is the ability to keep a large number of dosing data, i.e., more than 100 records. This data can also be synched to personal computers through specialized software. There are some other additional features such as alarming for battery and empty cartridge, pre-saving doses and countdown for dose administration. This model has been marketed in Europe as Pendiq Intelligent Insulin Pen and as SmartPlus in South Korea.

2.1.2 Technology within Insulin Delivery

Between the two common methods, manual injecting and insulin pumping, insulin pumping relies heavily on technologies. This technological nature in insulin pumps has provided
multiple features for diabetic management [53]. For example, pumps now can provide continuous readings for insulin and glucose levels running within the body; they provide a built-in list for food data associated with carbohydrates values in order to adjust the doses in an automated way; finally, they keep track of data related to daily doses. These data can also be synced to the patients’ personal devices like PC for example. In addition to the previous advantages, the technological nature of insulin pumps has eased the development of new models with new-implemented features. One notable example is the insulin pump pad—known as Omnipod in the market [1]. The pump pad comes tubeless packed in one unit. This is different from the regular insulin pumps, which require several parts like infusion set and cannula. Each unit of these pump pads is packed with all the needed parts, i.e., the insulin reservoir, cannula and infusion set. The unit comes with wireless connectivity module. The patient can adjust the doses and start pumping through a dedicated wireless remote controller. With this setup, it allows more free movements for the patients, and eliminates the exposure of skin to the outer environment. The last two issues have always been major hindrances within regular pumping models, especially among patients, who are frequently active with their movements like athletics [34]. The wireless modules within pumps have also opened the door to invent more new models like the semi closed-loop pumps [45]. The solution is integration between the pump devices and one of the popular technologies within pumping known as continuous glucose monitoring devices (CGM). Basically, the patient can now monitor the CGM readings directly on pumping device, and then the patient can adjust the infusion rate manually based on those readings; the CGM module can also interrupt the infusion action in case there is an alarm for Hypoglycemia risks. The method is still under enhancements because the CGM readings are still far accurate from the regular blood tests. Overcoming such an issue will open the door to create what is
known as the closed-loop pumping solution [23]. This is a full-automated solution, which aims to imitate the same work as the body pancreas. Nevertheless, it is good to mention here that although the inclusion of wireless module opened the door to create more creative solutions, it also invited some other challenges never existed before. For example, the controlling through remote devices makes the pumps liable to the risk hacking and malicious attacks. A couple of previous experiments showed how these pumps can be hacked and controlled out of the patient’s awareness [58]. Although there are a couple of solutions that have been suggested to overcome such risks, but the issue itself is still matter of interest among developers [35]. The main point here we need to give careful consideration to the challenges associated within any new proposed technical solutions.

For insulin injecting, we mentioned before that insulin pens were considered the most common instrument for insulin injecting nowadays. Insulin pens in general have mainly stayed simple without any advanced technologies for a while. In the usual cases, they rely heavily on the patient’s self-management and some other simple technologies like glucometers. For MDI routines in particular, the patient needs to measure the value of the carbohydrates intake in order to adjust the right amount of dose. The patient needs also to conduct a blood test the glucose level using glucometer before taking any dose in order to check if the dose needs any adjustment or not. For example, if the glucose level is lower than the usual, the patient needs to decrease the attempted dose, and if the glucose level is higher, then the dose amount has to be increased. Therefore, glucometer devices are considered vital within MDI routines. Nevertheless, the technology within glucometer is considerably simple and not equipped with sophisticated modules. In the recent days, models have started to include simple smart features such as smart indicators and directions [59], but there are some other models—still limited within market—that
have also started to implement sophisticated features such as wireless modules for cloud computing data synching [48]. For CGM in particular, they were mainly developed for pump users only, but there were some researches that showed benefits of using CGM within MDI routines [64]. After this summerization, we can notice that both ways, insulin pumps and insulin pens, have their own pros and cons within their uses. For example, insulin pumps have been remarkable for their tight glycemic control [22], but at the same time, they are extremely difficult and require some training to master their operations. They require also being worn on-body all the time, which might be considered as a hindrance for some patients. On the other hand, insulin pens are straightforward and they are extremely flexible for use, but at the same time, they require strict self-management routines. Table I gives a brief summary for the differences between insulin pens and insulin pumps therapies.

Table 1: Comparison between Insulin Pumps and Insulin Pens

<table>
<thead>
<tr>
<th>Features</th>
<th>Insulin Pens</th>
<th>Pumps</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of accuracy and precision</td>
<td>Lower</td>
<td>Higher</td>
</tr>
<tr>
<td>Flexibility and convenience</td>
<td>Higher</td>
<td>Lower</td>
</tr>
<tr>
<td>Costs</td>
<td>Lower</td>
<td>Higher</td>
</tr>
<tr>
<td>Performance and glycemic control</td>
<td>Lower</td>
<td>Higher</td>
</tr>
<tr>
<td>Level of risks</td>
<td>Lower</td>
<td>Higher</td>
</tr>
<tr>
<td>Ease of mastering</td>
<td>Higher</td>
<td>Lower</td>
</tr>
<tr>
<td>Level of complexity</td>
<td>Lower</td>
<td>Higher</td>
</tr>
<tr>
<td>Hight-tech and upgradability</td>
<td>Lower</td>
<td>Higher</td>
</tr>
</tbody>
</table>

Nevertheless, as it was implied within the previous explanation, there is a wide technological gap between them. Insulin pumps have evolved greatly into advance technological tools, while insulin pens have almost stayed simply the same. Technology has great potential to
simplify the daily diabetic management. MDI routines using insulin pumps need to follow the same manners as insulin pumps. They need to start utilizing some of the current technologies, such as cloud computing, wireless communication or smart devices.

2.2 Research Survey and Interviews

We conducted a series of surveys and interviews among individuals from the diabetic community. Our focus was on patients who were mainly under insulin medication therapy as part of their diabetic treatment. All patients, who indicated the use of oral medication only, were excluded from the study. The total number of participants was 101 participants. All the questions were given either to the patients themselves or to their caregivers. All the questions were designed based on the literature reviews and our experience with the diabetes mellitus. The total number of questions 35 questions (Appendix A). The questions were divided into the following categories:

- **Patients’ general information:** The questions were generally related the patient’s personal information such as age, country and gender. The questions also inquired about the use of smart devices and its uses within diabetic management.

- **Patients’ diabetic information:** The questions focused mainly on information related to the diabetes mellitus, such as the period of diagnoses and diabetes types. They also focused on the patient’s diabetic management, such as types of insulin, insulin delivery method or data records.
• **Patients’ Hypo/Hyperglycemia encounter:** The questions within this category sought detailed information about the encounter of Hypoglycemia and Hyperglycemia episodes, which were mainly about their frequency and possible reasons.

• **Intelligent insulin pens:** The last two sections within the survey focused on the technology on intelligent insulin pens. The main purpose was to investigate about their interest among the insulin dependent patients. The technology of intelligent insulin pens is still considered new within the diabetic routines. For this reason, the technology was presented to the participants through explanatory material within the survey itself. After that, the participants were presented with a series of questions to collect some information related to their impression about the technology, such as their overall rate about the technology. The last part focused on the interest of the communication between this technology and smart devices, such as smartphones and smart tablets. Since there are still no technologies with the previous capabilities, participants were presented with some possible scenarios that can be implemented in the future, and then a series of questions were given to the participants regarding these scenarios. The main purpose is to set a right path toward within this research and to help creating ideas for prototyping for later stages.

In the first part of the study, the recruitment was initially through online communities. This was either by sending direct emails or contacting online groups and forums. The total number of participants was 76 during this stage. In the second part, the recruitment was held through specialized clinics. 25 participants were recruited through the Ministry of Health Training, Postgraduate Studies and Research Center in Jeddah, Saudi Arabia. During this stage, some practical experiments have been conducted. One experiment was observing the compliance
to the dose administration among the patients while using of regular insulin pens. Other experiments were focusing on the usability of intelligent insulin pens. Basically, patients were observed while using the technology to note down the patients actual impressions. We also conducted some interviews with diabetic practitioners, who were working within the research center. The questions were similarly focusing on information under the following categories:

- **The use of smart devices under diabetes mellitus:** The main purpose is to investigate about the involvement of smart devices within the treatment plans. Practitioners were inquired about their opinions and whether if they have any recommended applications for diabetic management.

- **The preferred format for patients’ records:** The practitioners were inquired about the preferred method for receiving self-reported records from the patient’s side and the main reasons for picking such a method.

- **The intelligent insulin pens technology impression:** The technology was presented to the practitioners with some details about their capabilities. Our main objective is to observe the interest from the practitioners’ sides. The interviews included some discussion regarding the future of these technologies within the diabetic treatment plans like the communication with smart devices.

### 2.3 Results from the Conducted Surveys

**1) Patients’ General Information:** For the age groups, 32% of the participants were from the young and teenage groups. Participants, who were between the age of 20s and 40s, were about 39%. The remaining participants 29% were in the age of 50s or above (Figure 5). Female
group was about 56%, while male group was 44%. We inquired about the usage of smart devices in daily bases, 81% of the participants indicated that they were using smart devices regularly, the remaining 19% indicated either non-use of smart devices or use of non-smart devices only, i.e., landlines or regular cell phones.

![Pie chart showing age groups](image)

**Figure 5: Number of Participants & Age groups**

2) **Patients’ Diabetic Information:** Participants, who indicated independency for self-management, were about 79% of the whole groups, and participants, who pointed being caregivers for others, were 21% of the whole groups. The majority of participants were diagnosed with diabetes type 1 66%, while the remaining 34% were diagnosed with diabetes type 2. Participants, who were diagnosed recently with diabetes, within the last 5 years, were about 25% of the whole group. Participants, who had more than 15 years of diabetic experience, were about 43%. The remaining 32% were having a diabetic experience between 5 to 15 years.
For insulin therapy, participants who indicated using two different types of insulin medication were about 66% of the whole group. The remaining 34% indicated using one type of insulin medication. 72% of the participants reported that they were using insulin pens (and occasionally syringes as well) as the main instrument, while syringe users were about 17%. Participants, who were using insulin pumps, were about 11%. We inquired the participants, who were using smart devices in regular bases only, about the utilization of smart devices for diabetic management purposes. A few number of participants 30% indicated using their smart devices for their diabetic management (Figure 6).

![Smart Devices Usage for Diabetes](image)

**Figure 6: Smart Devices Usage for Diabetes**

We inquired the participants about the mistakes and level of adherence related to the insulin medication, i.e., missing doses, double doses or inaccurate dosage. 24% of participants reported that they were regularly running into some mistakes with their insulin medication, while
39% were occasionally running into some mistakes or follow poor adherence. The remaining 37% reported that they were barely running into any mistakes with their medication.

As per keeping the daily diabetic records, 57% of participants were noting down their daily blood tests; 21% of participants were noting down their carbohydrates intake; 44% of participants were noting down their daily insulin doses. As per the preference for format, 41% of participants reported physical format preferences, i.e., diabetic note dairies, while 37% indicated digital preferences. Only 20% of participants reported that they preferred both ways—digital and physical—at the same time. The remaining 2% of participants indicated other preferences beside the two methods, such as the usage of voice memo or self-memory.

3) Patients’ Hypo/Hyperglycemia Encounter: 35% of participants reported that they were regularly running into Hypoglycemia episodes every month, while 31% were occasionally running into Hypoglycemia episodes every month. The remaining 34% reported that they were barely running into any Hypoglycemia episodes every month. 45% of participants reported that they were regularly running into Hyperglycemia episodes every month, while 35% were occasionally running into Hyperglycemia episodes every month. The remaining 20% reported that they were barely running into Hyperglycemia episodes every month. The possible main reasons for encountering Hypoglycemia were due to: 51% insufficient amount of carbohydrates intake, 27% heavy exercise, 21% over medication or mistakes and only 1% for some other reasons, such as illness, high insulin sensitivity or oversleeping. On the other hand, the possible main reasons for Hyperglycemia episodes were due to: 62% high carbohydrates intake, 16% lack of exercise, 12% insufficient medication or mistakes and 10% indicated other possible reasons, such as stress, illness or poor control.
4) Patients’ Views about Intelligent Insulin Pen Technology: The technology of intelligent insulin pens was presented to the participants. In the first stage, the presentation was done through demonstration and visual aids included within the survey materials. In the second stage, the presentation was done through usability studies. We found out that the majority of the participants 80% never had the chance to use or hear about intelligent insulin pens before this study. The current available features within current technologies were put in a list, and then the participants were asked to choose the most preferable features among the list, i.e., the ones that could be essential or convenient for the diabetic management. The presented features were (ranked by the scores from high to low rated by the patients):

1. Memory feature: The feature allows keeping records of amount, date and time for daily doses.

2. Alarming system: The feature gives alarming sounds in the case of empty cartridge, battery outage or blocked flow of medication. The alarming issues a countdown with a completion sound while administering the dose in order to make sure that the dose has been fully administered.

3. Synching data to PC: The current technology allows transferring the recorded data into personal devices using dedicated management software.

4. Precise scale: the feature enables to dose very small scale of doses different than the normal scales; i.e., 0.5 U or 0.1 U

5. Pre-saving time period and dosage amount: In order to avoid re-adjusting the same dose every time in every day, the technology allows saving the frequent dose, and then in the time of dose administration, the pen will adjust the dose automatically according to the saved data.
6. Switching between manual and digital modes: In case of battery outage for example, the dosing mechanism can be switched to the old mechanism of mechanical-driven motor.

Following that, the participants were asked about the expected improvements after using this type of technology. Most of the participants were expecting to encounter fewer Hypoglycemia and Hyperglycemia episodes. Easier management and data collection were in the second place. Precise dosing capability for each meal and then encountering fewer mistakes came as the last two expectations in the rank.

The participants were inquired about hindrances that would make it hard for them to obtain this type of technology. The top hindrance was the availability within the local market. High cost was in the second one. Difficulty of use and compatibility with insulin brands came as the least two reasons.

Finally, the participants were asked to rate the technology as being important for diabetic management. In the scale of 5 = essential to 1 = useless, 37% of participants thought that intelligent insulin pens would be essential for diabetic management, while 26% though it could be useful. 4% of the participants thought it could be unnecessary, and 5% thought it could be totally useless for diabetic management. The remaining groups 28% were neutral about the technology (Figure 7).
5) Patients’ Views about the Connectivity between Intelligent Pens and Smart Devices: In the last section, if we could communicate the intelligent insulin pens and other diabetic devices with smart devices (Figure 8), and they could be able to provide the following functions:

1) Automated reminder and confirmation for doses

2) Automated data collection and synch

3) Warning and error detectors while dosing

4) Remote controlling through smart devices
Figure 8: Smart MDI System

Figure 9: Impression about Connecting Intelligent Insulin Pens with Smart Devices
The participants were inquired once again how they would evaluate the importance of using smart devices under these scenarios. Similar to the previous rating system, in the scale of 5 = essential to 1 = useless, 49% of the participants rated this type of communication as essential, while 26% rated it as useful. One the other hand, 4% the participants rated this as unnecessary and 7% as useless. The remaining 14% were neutral to the suggested idea (Figure 9).

The participants were asked which scenario among the above list that could be helpful for their diabetic management. The automated reminder and data collection features were rated as the first and second as the most preferred scenarios, respectively, while the warning and remote controlling features were rated as the third and fourth, respectively.

6) Results from the Usability Study: In the second stage of this study, we added a two extra experimental sessions. The first session was focusing on the compliance while administering the doses. Basically, we observed the patients while administering the doses using regular insulin pens, the purpose was rate their compliance toward the recommended instruction from diabetic practices. For the second session, the main purpose was to evaluate the intelligent insulin pens usability among the selected groups. Among the 25 participants 22 of them reported using insulin pens to take their doses. The recommended instructions state that the patient should wait few seconds before removing the pen from the body. Among the 22 cases, only 4 cases did not follow the appointed instructions. As for the other patients, they were following the recommended instructions but the waiting time to take out the pen was varying from case to case.

After that, we gave instructions to all the 25 participants that were detailing the use of intelligent insulin pens. The model used within this experiment was the intelligent insulin pen manufactured by Diamesco Co., Ltd. The majority of the participants managed to use the
intelligent pen on their own after stating the instruction at least once. Some of the positive comments that we got from the participants were: the digital screen makes the dosing more visible and easier for adjustment; the elimination of finger-force to administer the dose; the pen gives countdown and reminder about the recommended instruction for dose administration.

For the other functions, such as viewing memory data or replacing cartridges, there were some difficulties in handling them from the participants’ sides. The participants needed to hear the instructions multiple times in order to manage these functions on their own. Some of the negative comments that we got regarding the intelligent pens were: the intelligent pen was considered heavier and bulky compared to regular pens. This makes carrying them around more difficult in most of the time. Also, some patients considered the intelligent pen slower in dosing compared to regular ones. This is because of to priming steps, which is considered mandatory for dose administration. Some patients believed that the priming step should be optional here rather than being mandatory.

7) Results of the Oral Interview with Diabetic Practitioners: Table II provides the list of participants along with some other information provided by the participants. Regarding the recommendation of using smart devices under diabetes mellitus, the 1st P.C., 2nd P.C. and 4th P.C. mentioned that they were using smart devices regularly, but they were lacking the deep experience about diabetic application under the local language for their recommendation. The 3rd P.C. mentioned that she was using smart devices regularly and at the same time she was recommending using them for diabetic management; i.e., mainly for medication reminders and monitoring calories. The 5th P.C. mentioned that he also was using smart devices regularly and was recommending his patients to use smart devices as well. Most of the recommendations were
for communication purposes with the primary care, blood test applications and diabetic education as well. Both, the 3rd and 5th P.C., did not point to any specific applications.

As per the preferred format for patients’ records, the 1st P.C. and 2nd P.C. mentioned that they preferred both types of format, i.e., Digital and Paper, because there are many patients, who have limited technical knowledge. They desired to keep it easy and straightforward for all patients. The 3rd P.C. preferred paper format; she thought that generating digital record was still very complicated for the majority of patients. The 4th P.C. preferred using digital format to avoid any misreading of patient’s data due to difficult handwriting or any similar issues. The 5th P.C. preferred digital format in order to keep them as references for the patients’ records.

As per the intelligent insulin pen technology, after conducting a couple of experiments, the 1st P.C. chose the memory system and the alarming functions as her best features within current models. She mentioned that the memory system would give more background about the patient’s daily routines and behavior, while the alarming system will keep the patient alerted and assure a compliant dose administration. The 2nd P.C. thought that the intelligent pen with the current features had limited capabilities, which would not be useful for all groups of patients. The 3rd and 4th P.C. appraised the memory system and PC data synch functions. They thought that both features would help them to understand the patient’s behavior better and keep collect more references about them. Additionally, they believed that both features would help the patients effectively as they would be act as references for them when they would be associated with other data from their daily routines. In this way, it would reduce the number of encountered Hypo/Hyperglycemia episodes. Moreover, it would avoid the risks from missing or duplicating doses. The 5th P.C. thought that the memory system and digital-motor were good features, but he still believed that not all patients would able to use the intelligent pens smoothly without any
hindrances. The rate of the intelligent insulin pen technology for each P.C. was summarized in Table II.

For the hindrances that would make it more difficult to obtain this technology, the 1st P.C. and 2nd P.C. thought that the availability within the local market would be a major hindrance here; in addition to that, the 1st P.C. thought that the memory system itself might actually be a possible obstacle rather than helping for using such a technology. This is because some patients have the habit of concealing part of their daily information while reporting to their primary care. So using such a device will stop them from keeping up with these habits. The 3rd P.C. and 5th P.C. listed high prices and difficulty of use—especially among elderly—as the main hindrances for using this technology. The 4th P.C. thought that both high cost and local availability would be the main hindrances here.

For the connectivity with the smart devices, Each P.C. rated this type of communication and the results were summarized in Table II.

Table 2: Interview with Practitioners

<table>
<thead>
<tr>
<th>Primary Care (P.C.)</th>
<th>Age</th>
<th>Gender</th>
<th>Intelligent pen technology rate</th>
<th>Connectivity with smart devices rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st P.C.</td>
<td>30-49</td>
<td>Female</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2nd P.C.</td>
<td>30-49</td>
<td>Female</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3rd P.C.</td>
<td>30-49</td>
<td>Female</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>4th P.C.</td>
<td>30-49</td>
<td>Female</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>5th P.C.</td>
<td>30-49</td>
<td>Male</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

Rating scale of 5 = essential to 1 = useless

The 1st P.C. thought that the automated reminder function would be the best scenario for future implementation. The 2nd and 5th P.C. thought that the automated data collection feature
would be an extremely important feature, as it would ease the mission of collecting patients’ data. The 3rd and 4th P.C. thought that providing an interactive interface through smart devices would allow different types of features, such as easy control, flexible dose adjustment or automated carbohydrates ratio calculation.

2.4 Analysis and Discussion of the Surveyed Data

In general, the observed data showed that most of the participants had no previous experience with the intelligent insulin pens technology before this study, but the idea of including them as part of the diabetic routines was mostly rated with positive opinions. There were still some negative opinions toward the technology itself. Most of these cases were patients, who have been using insulin pumps therapy as part of the treatment, or patients, who were having some difficulties in dealing with technologies. There was still a group of participants, who have neutral opinions about this technology, but at the same time they cannot see any additional values in using it. It is still difficult to have an absolute conclusion from this study only about the importance of inclusion of intelligent pens within current routines.

As per the rating of the intelligent pens features and capabilities, there were about 63% of participants who reported liability of dosing errors, either regularly or occasionally. So apparently, the memory feature would get the major attention among these participants, which led to be placed in the first place among the rated rank. The alarming feature was positioned as the second place in the rank. The feature was probably appreciated more than the others because it helps alert about battery and insulin cartridge level, which would be useful for not forgetting about replacing the cartridge or refilling the current stock of medication. It also helps to assure a
compliant dose administration, i.e., because of the automated alarm countdown while administering the dose. The patients might see an advantage in it because it would save the effort of doing the counting manually.

The precise scale and data transfer both features got a lower rank than the previous two. It could be because only limited groups of patients would benefit from these features. Precise scale is certainly critical for those who usually have high insulin sensitivity. The case is usually common among young patients and athletics. In our data, young participants were about 32% of the group, while people, who picked the excessive exercises as the main reason for Hypoglycemia, were about 27%. Both groups were still not dominant in the sample, so certainly precise scale would not get a higher rank than the previous two features.

Similarly, for synching data to PC, it did not get a higher rank because the group who reported noting down their daily doses was less than half, about 44%. The majority did not want to follow the routines of keeping records for their own personal reasons. On the other hand, the feature was greatly appreciated by primary cares because it would help to ease the diagnoses and follow-ups process.

Pre-saving of daily doses got a lower rank within the list. Although the majority of the participants 62% were using two types of insulin medication, the feature was assumed to get more appreciation from the patients. Nevertheless, it is probably because some patients make frequent adjustment in daily bases for each meal to match the carbohydrates intake, or some patients do frequent correcting to their high blood glucose level. The feature in these cases became unnecessary for them. Most likely, the pre-saved function will be a hindrance to the adjustment process. Basically, patients will keep re-adjusting all the pre-save doses, which is basically is not different from the regular routines. The feature could be more useful if they were
for example associated with some smart features; for example, like including an alarm or warning for not taking the dose during the usual time. Such a feature could be useful for those who would frequently forget to take their meal doses either before or after their meal.

Finally, as per the ability to switch between manual and digital dosing mechanism, this feature would be useful in the emergency cases, such the battery outage; however, with the availability of the alarm feature, battery outage can be easily avoided, which makes the manual mode less appreciated. Moreover, in such a case, the patient can go back and use regular pens without the need to switch to the manual mode.

We still need to know how important this technology would be for diabetic management. Most patients observed some potential within the technology itself, but we need to look deeper into the actual characteristics of the technology and compare it with the patients’ behavior and actual needs. The two remarkable features within the current technologies are the memory system and precise scale capability. If the patient is among the patients, who frequently encounter mistakes, like one of the 24% of our participants, then this kind of solution will be essential in order to avoid any serious risks of Hypoglycemia or Hyperglycemia episodes. In a similar manner, if the patient is one of the individuals, who have are usually suffering from high sensitivity to insulin medication, this kind of solution will be handier for dose administration. Other than this, both features will be more like and extra features for general groups; the patient might not need to use them in regular bases, they would be useful in certain occasions. For example, when the patient would be under busy schedule, which would increase the liability to missing doses. Additionally, when the patients practice exercises in irregular bases, which would be useful to have more control on the amount of dosing. Moreover, Having a large data memory can be useful as reference for individuals like primary cares, but for the patients, it would be
handier if they can be associated with other diabetic data. Associating the data with each other can help to understand the diabetic behavior more comprehensively, which will contribute into the enhancement of diabetic self-management.

In general, the majority of patients were hoping for a fewer encounters with Hypoglycemia or hyperglycemia episodes after using the of intelligent insulin pens, but at the same time, after observing the data, participants indicated that the most likable reason for these episodes was due to inaccurate carbohydrates intake measurements. Encountering these episodes because of mistakes came as the least reason among the other ones. Unfortunately, there is no capability available within current technologies, which can help easing the measurement of carbohydrate intake values, i.e., similar to the automated dose adjustment capability within pumps.

As per the hindrance participants and primary cares indicated that the availability within local market and high prices would be the two likely reasons for passing on this technology. Unfortunately, the current models are still suffering from one of these two issues or even both of them. For high cost in particular, high cost can truly be a hindrance; however, if the solution could justify its effectiveness, patient might pass on costs for the sake of achieving high glycemic control. This case has actually been noted among the patients, who are under insulin pumping therapy. Insulin pumping devices and its supplements are well known for their high prices, regardless of that, they are still popular among Type1 patients, especially in United States. This is because pumps have been known for their remarkable performance and outcomes. During our usability study, lack of user-friendliness got some attention also among some participants and primary cares. Intelligent pens were noted for being a little complicated than regular pens, but they are still not hard as the use of insulin pumps. There is a possibility that
User-friendliness in our data did not get major concerns because most of the participants were from the middle age groups. If the majority would more from the elderly groups, we might see a higher value for difficulty if use as a hindrance.

The suggested conclusion here is that current solutions of intelligent pens can be essential only for limited groups of patients, but for the general patients, it could be a good alternative if the patient could justify their needs when compared to current methods and overcoming any possible hindrances.

On the other hand, from our side, we still can sense see some potential from for the intelligent insulin pen technology by looking through a different angle. We believe the features of intelligent insulin pens can still be expanded through the utilization of current ubiquitous technologies, such as smart devices and cloud computing.

In our last section of our study, which was related to the connectivity with smart devices, we saw some changes within the evaluation of intelligent insulin pens under the proposed vision. The next section gives details about the conducted pilot studies and experiments, which will help us to understand the previous claim.
3. CLOUD-BASED SMART REMINDER SYSTEM FOR INSULIN DOSES

3.1 Related Work

3.1.1 Ubiquitous Technology and Healthcare

Smart devices are now having critical roles in our daily life: shopping, entrainment, education and certainly healthcare as well. For diabetes, there are multiple applications developed specifically for the diabetic purposes. The majority of these developed applications circulate around four types of categories: patient’s records, decision support, education and social communication [6]. Patient’s records functions are mostly related to the patient’s diabetic data, like the daily blood tests, daily doses, carbohydrate intake and burned calories. The majority of these applications require manual entry for the patients’ data; only few applications right now can be synchronized with other diabetic devices to download the patients’ data [11].

As per the decision support functions, they are mostly focus on the management of daily activities, such as medication, carbohydrate intake and burned calories. There is one example that can explain this point; Diabetic data can be collected and used to create graphical charts known as trends. The patients can analyze these trends charts to detect any fluctuation within the daily glucose values. For example, having frequent high blood glucose after dinner everyday, or encountering Hypoglycemia episodes between lunch and dinner occasionally. The patients can try to track the possible reason for encountering such cases. Another groups of applications are functions like medication reminders and carbohydrates ratio calculators. These functions have the potential to improve the medication routines and assure batter adherence level. All the previous functions can assist the patient to take the right decisions regarding to approach certain
routines, such as doing more exercises, consuming the proper carbohydrates daily intake or give more attention to the taken medications.

As per the education functions, these functions usually provide different types of information related to the diabetes mellitus itself, such as guidelines, tips about medication and knowledge about associated diabetic complication symptoms. Currently, there are some attempts to make these type of applications more personalized for the patients; these applications can give information based on the patient’s profile and collected data [62].

For the communication functions, they are mainly related to the communication between patients and practitioners or communication through social media, such as FACEBOOK, Blogs or Internet groups. Communication with practitioners can help ease the exchange of data and consultation between the two parties or setting up regular follow-ups. As per the social media in particular, it is a new way to seek support and consultation outside the clinics. The goal is to share the experience among individual, who are suffering from the same disease. The advantage is to be out of the isolation, which can be caused by the diabetes mellitus itself.

Apparently there are really good potential in smart devices, which can help in assisting the diabetic management; however, until this point the use of smart devices for diabetes is still considered a non-standard practice and very limited [38]. Most of these applications are still not acknowledged by official sectors, for example, the U.S. Food and Drug Administration (FDA) [20]. The absence of these types of acknowledgment makes them less trusted and known among practitioners, which would result in their absence from usual consultations.

Moreover, some functions might have really good potentials, but they are difficult to handle them without enough experience. For example, providing trend charts for analysis can be useful, but not all the patients can interpret them easily without good knowledge and bases. For
communication functions in particular, security and reliability of shared information are still among major concerns within social media researches. For example, regarding the communication through social media, the major issues originated from the authenticity of shared information; some of this information can actually be advertisement disguised as users’ comments [18]. Advertising false medication to the patients without the practitioners’ consultation can lead to a major risk. Keeping Internet groups or forums free from false information and advertisement is still a big challenge among social media developers.

Cloud computing has also some potential in improving healthcare services. Healthcare can also benefit from the cloud technology either through the cost reduction, better health service at home or continues processing of medical data [31]. Although a lot of sectors (e.g. communication, gaming, e-commerce, etc) are already utilizing the cloud computing technology effectively today, the healthcare sector is still a little bit slow in adapting the cloud technology [10]. The reasons might go back to the difference in regulation in handling healthcare data globally [54], or because of the risk from the multiple threats surrounded the cloud technology [47]. Specialized sectors are aware of this potential and they are trying multiple ways to overcome the difficulties in within the healthcare data [67].

The main issue is that most of the standard diabetic gadgets are still closed-sources, which means that sharing data is still not possible among applications developed by third parties. As a result, most of the mentioned applications lack the capability to sync data with the diabetic devices or cloud servers. There are few diabetic devices within the market, which have started to utilize the powerful environment of smart devices and cloud servers, but this approach is still limited and needs more support from specialized organizations and practitioners [19]. In general, most of the developments focus on how to modernize traditional methods only by replacing them
with new digital methods. For example, rather than noting the daily blood test results in the patient’s diabetic physical diary, the patients can instead write them digitally on their smartphones. Nevertheless, in reality, both methods might require the amount of efforts from the patient’s side; furthermore, the data are only stored within the phone, but they are not being utilized smartly to enhance the patient’s daily management. What we suggest here is rather than focusing on approaches that would only digitize traditional practices, it would be more beneficial to develop solutions, which can ease the diabetic tasks and promote compliant behaviors. For example, an ideal scenario is to provide a way to upload all the data to the phone in a total automated way, and then utilize them to provide specific directions or recommendations to the patients, e.g., tagging them with some other diabetic data automatically. There are few diabetic gadgets applied the explained scenario. A U.S. based company Telcare Inc introduced a new type of cloud-based glucometer [12]. The glucometer utilizes the cellular communication to upload patient’s blood test data automatically to any personal devices through a cloud server. There are also some other created glucometer kits that can be attached to the smartphone. With these kits, the smartphones can have an extended capability to provide the blood testing function exactly the same as standard glucometer devices [2].

3.1.2 Reminder Systems for Medication

General recommendations suggest matching the time of medication taken in daily bases, such as insulin or hypertension medication, with daily routines and schedule, e.g., mealtime or bedtime; however, there are some other suggestions that insist in using reminder systems as well. The main purpose is that it can act as an alternative to the daily routine in case any changes would occur [57]. There are several suggested methods that can be used as reminder systems,
such as calendars, smartphone apps, alarms or text messaging. Nevertheless, studies found that the most popular method among the different types of method is using smart devices [32]. There are some evidences from different research showed that the use of short messages (SMS), calendars, apps and alarms managed to improve the adherence level among patients [29,43,61]; at the same time, there are some disadvantages in using smart devices. First, they encourage the users to rely on them rather than promoting complaint behavior. Second, most of the apps and alarms in current smart devices are not fully customizable and they might not fit with the users’ needs, for example adjusting the type of sounds or snoozing periods. Lastly, they lack a post-completion check or acknowledgment features. They can remind the patients but they cannot assure if the patients administered the medication or not. For this reason, it is very important to include a reliable post-completion check system that can keep track of taken medications. For example, some studies applied gamification concepts by utilizing the power of social media; patients are competing against each other in order maintain a higher rank of adherence level among other members [9]. There are some other researches suggest using wearable computing and wireless networks to send reminders for medication and refilling, and at the same time, they keep track of the patient’s action [36].

3.2 The Proposed Reminder System and Concept Design

In our survey studies, the idea of connecting the technology of intelligent insulin pens with smart devices was greeted with positive views from our participants. We observed some movements from the neutral scores to the positive scores. Among the questions, we asked the patients to pick one feature among the proposed list. The final results were used in our next
study, which aimed to test the effectiveness of using a system composed of intelligent insulin pens technology and smart devices. Since the most desirable feature was a system that would remind them automatically about their own doses, we decided to conduct a series of pilot experiments using this vision.

The concept of the system focused on how to remind the patients about the dose, and then how to confirm that the patient responded to the alarm correctly. Basically the patient can setup the alarm for certain appointed time one time only. Then, the alarm will issue automatically every day at the same appointed time. At this point, the patient has no control over stopping or reactivating the alarm. The system should automatically access the record data and check whether the dose has been administered or not. If the dose could be administered within the appointed time, it would stop the alarm immediately. If not, it would issue a snoozing alarm within certain period until it would make sure that the dose has been administered. Figure 10 illustrates the whole concept of the system.

![Figure 10: The Proposed Reminder System Concept](image_url)
Since we were proposing the system for experimenting only, we decided to create certain scenarios to accommodate the current capabilities and setups. First, since we needed to test the system capability to repeat the alarm in daily bases, we decided to choose the basal doses as our focus within these experiments. Basal doses suite the experiments very well as they are taken within fixed time every day, require same amount every time and finally they are usually taken once at a time every day. The nature of the basal doses medication would make it easier for the participants and administrator to use the system without any confusion. Second, because the current technology of intelligent insulin pens lack the capability to send the data wirelessly to the cloud, we had to rely on the Wizard of Oz [5] concept for creating our system. The exchange of data and confirmation were handled by the administrator sides out of the patient awareness. Finally, for the current setup, we decided to choose commercial reminder systems that were matching with experiments requirements. The main purpose was to assure a smooth operation for the system and avoid any bugs associated with home-developed apps. Moreover, this setup can help us to investigate all the negative and positive points, which we can use in the future if we need to build our own reminder systems.

3.3 Pilot Experiment for the Proposed Reminder System

We conducted three pilot experiments among a total of 13 individuals. Each experiment lasted 3 weeks. Table III lists the information regarding the participants within these experiments. All the patients during these experiments were using basal Insulin as part of their insulin therapy. Three participants withdrew in the middle of the study due to certain circumstances, i.e., busy schedule or technical difficulties, while the other ten participants
proceeded till the end of the experiments. Each experiment in the study was divided into two phases.

**Table 3: Participants of Pilot Experiments**

<table>
<thead>
<tr>
<th>ID</th>
<th>Gender</th>
<th>Usage of Smart Devices</th>
<th>Age</th>
<th>Study Completion</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>Male</td>
<td>High</td>
<td>21-39</td>
<td>YES</td>
</tr>
<tr>
<td>P2</td>
<td>Male</td>
<td>Low</td>
<td>60-75</td>
<td>YES</td>
</tr>
<tr>
<td>P3</td>
<td>Male</td>
<td>High</td>
<td>40-59</td>
<td>YES</td>
</tr>
<tr>
<td>P4</td>
<td>Female</td>
<td>Average</td>
<td>40-59</td>
<td>YES</td>
</tr>
<tr>
<td>P5</td>
<td>Female</td>
<td>High</td>
<td>40-59</td>
<td>YES</td>
</tr>
<tr>
<td>P6</td>
<td>Male</td>
<td>Low</td>
<td>60-75</td>
<td>YES</td>
</tr>
<tr>
<td>P7</td>
<td>Female</td>
<td>Average</td>
<td>40-59</td>
<td>YES</td>
</tr>
<tr>
<td>P8</td>
<td>Male</td>
<td>Low</td>
<td>60-75</td>
<td>YES</td>
</tr>
<tr>
<td>P9</td>
<td>Female</td>
<td>Low</td>
<td>60-75</td>
<td>YES</td>
</tr>
<tr>
<td>P10</td>
<td>Male</td>
<td>High</td>
<td>40-59</td>
<td>YES</td>
</tr>
<tr>
<td>P11</td>
<td>Female</td>
<td>Average</td>
<td>21-39</td>
<td>NO</td>
</tr>
<tr>
<td>P12</td>
<td>Female</td>
<td>Low</td>
<td>40-59</td>
<td>NO</td>
</tr>
<tr>
<td>P13</td>
<td>Male</td>
<td>Low</td>
<td>40-59</td>
<td>NO</td>
</tr>
</tbody>
</table>

The duration of the first phase of the experiment was 10 days in total. The main focus during this phase was observing the patients’ adherence levels and observing their interaction with the intelligent insulin pens technology. The duration of the second phase was also 10 days in total; however, the main difference this time was the inclusion of the proposed reminder system. The main focus during this phase was observing the interaction between the patients and reminder system, and then observing the influence on adherence level.

During the first phase, the patients were directed to keep the same daily routines for taking the basal doses while using the intelligent pens; on the other hand, during the second phase, the patients were asked to use the proposed reminder system, which was installed within
their personal smart device. The patient was directed to take the medication every day around the same appointed time; the patient was allowed to take the medication either 30 minutes earlier or 30 minutes later from the appointed time. The process of the system was as the following (Figure 11); the system will first check the data within the intelligent insulin pen. If the required dose was taken on the allowed period, the reminder alarm would automatically be deactivated, and then an acknowledgment would be sent to the patient. In case the administration of the dose could not be confirmed, a snoozing alarm would be activated for every 10 minutes.

Figure 11: Pilot Experiments Process
The snoozing alarm would be kept activated until either the confirmation of the dose or until a period of 30 minutes from the first alarm. In that case, a message would be sent to the patient stating that “the dose was not administered within the appointed time and it should be administered as soon as seeing this message”. The system was partially implemented with the Wizard of Oz prototyping concept because of lacking the proper technologies, but from the patients’ side the operations were fully automated. The main tools used within these experiments were:

1. Four intelligent insulin pens.
2. Four portable laptops with pre-installed diabetic management software.
3. Smart reminders with cloud feature installed in the patient’s personal devices.

The measurement of the adherence level was decided based on SANOFI’s directions for their insulin Glargine [41], i.e., “once a day” and “within 24-hour”. If the patient administered the dose within the allowed period, a full score would be given. If the patient administered the dose outside the allowed time, a half score would be given. If the patient did not administer the dose during that day, no score would be given.

Another measurement was evaluated to test the speed of response to the issued alarms. Table IV summarizes the scoring method for the response speed. After the completion of the experiments, we collected participants’ feedback for both phases.
Table 4: Response Speed Measuring Method

<table>
<thead>
<tr>
<th>Scores</th>
<th>Period of time</th>
<th>Patient's Awareness</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Before the time</td>
<td>Mostly responded before the 1st alarm</td>
</tr>
<tr>
<td>4</td>
<td>On time</td>
<td>Mostly responded to the 1st alarm</td>
</tr>
<tr>
<td>3</td>
<td>10 minutes passed</td>
<td>Mostly responded to the 2nd alarm</td>
</tr>
<tr>
<td>2</td>
<td>20 minutes passed</td>
<td>Mostly responded to the 3rd alarm</td>
</tr>
<tr>
<td>1</td>
<td>30 minutes passed Or more than 30 minutes earlier</td>
<td>Mostly responded to the last alarm or miscalculated the assigned time</td>
</tr>
<tr>
<td>0</td>
<td>Dose not taken</td>
<td></td>
</tr>
</tbody>
</table>

3.4 Results from the Pilot Experiments

1) **Scoring Data:** The obtained results for the adherence level before and after using the reminder system are summarized in Figure 12, while the results for the response speed among patients are summarized Figure 13. As per the level of adherence, the majority of participants had either the same level of adherence or slightly better after using the reminder system, while four cases showed major elevation in the adherence level after using the system, especially for the second and third patients. As per the response speed level, the results showed that majorly of the participants were likely respond by the second reminder alarm, which indicated that this group of patients might require at least two to three times of alarming action. Three cases had an immediate reaction to the reminder alarm. This indicated that this group of patients might require a less aggressive type of alarming system, i.e., maximum two times of alarming action. Two cases only had a slower response to the alarming function, which indicated they might need a more aggressive type of alarming action, i.e., more than three times, in order to administer their medication on the appointed time.
Figure 12: Level of Adherence

Figure 13: Response Speed Results
2) **Patients' Feedback**: The general views about the proposed reminder system were mostly positive. For the patients, who were using regular reminder systems, e.g., remainder apps or alarms, they thought that the proposed system could be a good alternative to the usual methods. The system could automate the snoozing action and post-acknowledgment for the doses, which regular methods originally cannot do. For patients, who were associating their doses time with a certain daily routine, they thought that the system was a good alternative as a back up to the daily routines; this was because daily routines were liable to changes or alteration at any point. For patients, who were relying on their memory and not following any of the previous mentioned methods; they felt that the system helped to enhance their routines for the administering the dose, especially under heavy schedule.

The ability to use the cloud communication and run the reminder system on multiple devices was greatly appreciated by patients; this is because when one device would be down for any circumstances, a second devices act can run the system without any major concerns.

There were some cases showed less appreciation to the system. The possible reason could be that the limitation in using smart devices in regular bases, i.e., using them only for calling or messaging only. Some other negative feedback was the inability to fully customize the system according the users’ needs. The sound level had some limitation, which caused missing a couple of alarms in a number of cases.

The other negative view was the requirement for continuous Internet communication. Since the system relied heavily on exchanging data through cloud services, the patient needed to
keep the devices connected to the Internet all the time. Sometimes it was hard to maintain this requirement due to weak signals or the absence of wireless coverage.

The patients were inquired about the reasons for not administering the dose on the appointed time while using the proposed system. Some cases reported that they could hear the alarms but they could not administer the dose on the appointed time because they were not carrying their medication and they had to take them in a later time. Some other cases missed the alarm while sleeping because the sound level was not loud enough to wake them up on the appointed time. Another reason was due to the engagement in some activities, which prevented them from being excused to administer their doses on the appointed time, e.g., being in a work meeting.

3.5 Analysis and Discussion for the Pilot Studies

The pilot studies were divided into two phases of experiments. The experiment was aiming on observing patients’ regular routines, while the second experiment was aiming to observe the influence of the applied reminder system on the patients’ compliance and interaction between the system and its users.

After observing the obtained results for adherence, we found that patients, who were using other reminder methods or daily routines, had a slight advantage from the proposed system. First, patients managed to keep the same adherence level in the second experiment but in more convenient way; there was no need to keep readjusting the reminder system manually for example. Second, the system was more reliable because it could do confirmation and snoozing
processes in automatic way without any required actions from the patient’s side. The system was a good alternative to the regular methods among this group of patients.

For the participants, who were not using any particular methods to remember their own doses, had a better advantage from using the proposed reminder system. Even under busy schedule, participants managed to achieve a better adherence level for the administered dose. Among this type of patients, these types of system can help to promote a better compliant behavior toward the medication directions.

As per the measurement of alarm response speed, the response speed results showed that this kind of system should offer a full customization that should meet with the patient’s situation and needs. For example, heavy sleeper might need a louder or more noticeable notification that would able to wake them up even during a deep sleep.

As per the feedback for the system, users could see a good potential in this type of systems. Most of the feedback were mainly positive and have more appreciation compared to the other methods. There were some still negatives views, which might relate to the complication in using advance technology. It could be hard to conclude whether the inclusion of these types function in future development would justify the need for this kind of smart solutions; nevertheless, longer studies might able to uncover more potential and help to overcome some of some the difficulties in using these types of advances solutions.

As a general opinion concerning future development within these types of researches, these kinds of systems rely heavily on using an advanced type of technologies, which should able record and exchange data among other devises. The exchange of data should be done in a way that minimize the user’s involvement, like the communication through cloud computing. Future
development of intelligent insulin pens might need to focus on how to include modules for automatic data exchange, which can be utilized through the cloud communication.

On the other hand, there were some concerns toward the use of intelligent pens technology itself, such as bulky size or difficult user interface. The existence of these hindrances would make these systems less justifiable for their needs. The main purpose from creating these types of systems is to ease the diabetic management itself. If these systems managed to solve certain issues but invited some other issues, then their justification will not be valid among the diabetic users. Future development should keep the balance between the enhancement and convenience existed within former solutions. It could be difficult to find such a balance, but the main objective is how to make a new introduced solution more justifiable and appealing among the users.
4. DETECTING HYPOGLYCEMIA WITH WEARABLE AND UBIQUITOUS COMPUTING

4.1 Literature Review for Hypoglycemia Detection through Hypoglycemia Symptoms

Miller et al [39] reintroduced a former wearable technology for Hypoglycemia detection originally introduced in 1982 [21]. It was the first attempt for Hypoglycemia detection through its symptoms. The devise was marketed as “Sleep Sentry”. It was mainly developed for those who frequently encounter Hypoglycemia during nighttime. The device was constructed from a temperature sensing system, conductance-sensing system and few other processing sensors. Once the device would sense a declining in the body temperature below a certain threshold value, it would issue an alarm to notify the patient about the possibility of encountering Hypoglycemia episode. As per the directions, the patient had to do a regular blood test in order to verify the actual occurring of the Hypoglycemia episode. Although the device had good potential when it was first introduced, it was suffering from two critical issues. First, the alarming system could not achieve a 100% of validity; the reason was that the devise had high sensitivity to the body temperature and perspiration, which could be not necessarily directly related to Hypoglycemia encounter. Second, the alarm sensitivity had serious critical issue. The devise was not able to detect the Hypoglycemia episode until it would reach a very late stage i.e., below 60 mg/dl, which is usually considered highly risky. There were also some additional technical issues like malfunctioning due to the frequent changes of body temperature or the inability to use the devise during warm days [63]. The devise was discontinued from the market after the clinical studies found that the failure rate exceeded 8%.
Elsborg et al introduced a new project for Hypoglycemia detection by observing the brain electroencephalogram (EEG); the project name was “Hyposafe” [13]. Before the implementation, Elsborg et al conducted multiple EEG tests to prove that the EEG waves have certain patterns and values during Hypoglycemia episodes. Elsborg et al noted that it was really hard to achieve these kinds of processing and validity levels before the ubiquitous technology would advance and reach current level of power. This was because in the past EEG measurements could not be done out of specialized clinics and hospitals. After observing several clinical trials, Elsborg et al reported that the “Hyposafe” sensor could manage to detect the Hypoglycemia episodes 20-30 minutes ahead of time. Moreover, although the clinical trails showed some numbers of false alarms, they managed to reach a 70% of validity. The prototype system was mainly composed of two components: a minimal invasive sensor under the skin and external chargeable device for processing and alarming functions. The invasive sensor required a 15-minute plastic surgery operation with local anesthesia in order to implant the sensor under the skin. There was no clarification whether the finalized system would follow the same concept as the prototype; however, it was highlighted that the device did not affect the patients’ daily routines at all during the clinical trials. GILI Medical LTD proposed a non-system devise with a potential of high validity rate [52]. GILI Medical LTD reported that they could increase the validity of the results by triggering three different psychological values simultaneously from a set of different types of values. These values were:

1) motorial activities
2) heart rate
3) respiring rate
4) vasoconstriction and skin temperature
5) Galvanic Resistance.

Once the devise detects three of the previous values that exceeded the assigned thresholds, it would issue an alarm alerting for Hypoglycemia. GILI Medical LTD already created a prototype from the device and ran several pilot clinical trails. According to the published results, the prototype could manage to achieve 100% of validity of rate without causing any nuisance to the patients; This means that all the issued alarms were directly related to the Hypoglycemia case; however, due to the high sensitivity of the devise, the devise could detect with specificity of 85% for all the detected cases; this means that some of the detection was not related to Hypoglycemia Episodes [51].

4.2 Hypoglycemia Detector System Key Concept

The previous literature review showed that the concept of detecting Hypoglycemia episodes from its symptoms had really good potential; the method is considered less invasive than the current situation, which requires conducting multiple glucose level tests per single day. Nevertheless, the method still far from being totally reliable and require more refining to obtain an optimal outcome results. The main objectives are to make these types of systems blended normally with the patient’s daily life, and help to provide ease of mind for the patients by minimizing the risks of encountering severe Hypoglycemia cases. The research within the literature review were mainly focusing on the following elements within their development for their systems:

1- Sensitivity: the system should able to detect all the possible symptoms associated with Hypoglycemia. The system should avoid letting the Hypoglycemia goes undetected or detected
at very late stage; during early stages of Hypoglycemia, the patient is still maintaining full conscious condition, which makes it easier for recovering from Hypoglycemia episodes.

2- Specificity: The system should able to tell the difference between actual Hypoglycemia symptoms from non-Hypoglycemia symptom. The matter is still challenging. The reason is that many of the Hypoglycemia symptoms are similar to other systems, such cold or anxiety.

3- Expediency: the main purpose from these systems is to raise the expediency within daily routines and minimize any elements that might lower these elements, for example, invasive systems are always avoided by the majority of patients especially among children; also, large sizes systems are considered bothersome as they interfere with regular daily activates. Developers need to keep a good balance between the competence of these systems and convenience of using them.

4.3 The Proposed System for Detecting Hypoglycemia

4.3.1 System Description and Details

The proposed system is mainly composed from four main components:

1- Smart device and software application

The main ubiquitous device and its application are responsible for the data processing and exchanging data with the wearable sensors. The list of the required functions is as the following:

- Issuing Hypoglycemia alarms for the patients and their caregivers
● Sending reminders for the user about required daily dosages and blood tests

● Collecting and analyzing the data from the wearable sensors.

● Collecting patients’ records and then sending them to cloud servers.

● Collecting patient’s diabetic data for processing and analyzing.

2- Heart rate sensor

The main purpose from the heart rate sensor is to sending the patients’ heart rate reading to the smart devices. The main purpose is to observe the following condition:

● Increase of heart rate data due to Hypoglycemia episodes

● Increase of heart rate data due to exercises

3- Skin galvanic response and motion sensors

The purpose is to collect three different types of readings: skin temperature, skin galvanic response (body sweat) and body motion. These readings can help to identify the following cases:

● A drop in the body temperature.

● An increase in the sensitivity of skin galvanic response.

● Activities leading to higher insulin sensitivity.

4- EEG (brain wave) sensor

Several researches pointed out that EEG brain waves have different values during the Hypoglycemia episode [28,33,56]. Glucose is one of the main components needed for brain activities. We believe that if we can keep track of the brain waves, we might able to detect Hypoglycemia episodes during its early stages. Usually tracking EEG brain waves requires special clinical equipments, but recently, several new wearable technologies for neural measurements have been available in the market [37]. These sensors allow us to track the brain wave outside of clinic practices within the regular daily routines. We hope that by suing these
types of wearables within our system, it will allow us to increase the validity and sensitivities elements for our Hypoglycemia detection.

4.3.2 System Details and Mechanism

In order to achieve the required balance between the earlier mentioned values, i.e., sensitivity, specificity and expediency, we need to implement the following three information systems within our application (Figure 14):

![Hypoglycemia Detector System Flowchart]

Figure 14: Hypoglycemia Detector System Flowchart
1. Patient’s diabetic data system

   This system is responsible about the patient’s personal data and daily activities. Initially, the system should collect data from the patient related to the diabetes mellitus. The system will keep sending reminders to collected information like carbohydrate intake, blood test and insulin dosage in regular bases. Also, using the motion and heart rate sensors, the system will keep records of the daily attempted exercises and their levels. The system should use these records to increase the validity of the detected results. For example, once a symptom would be detected, the system would check if there was any kind exercise or activity conducted before the encountered symptom. If, for example, the system found this to be true, it would approve the validity of the detection and issue an alarm to the patient; however in the case of absence of any preceding activities, the system can wait to collect more symptoms to validate the results.

2. The Hypoglycemia detector system

   This system is responsible about collecting body symptoms from sensors, detecting data below suggested thresholds and issuing alarms to notify the patient. Initially, the system will be set for average threshold values that usually associated with hypoglycemia episode. The system will keep collecting these values wirelessly until one of them becomes equal to or below the assigned threshold. At that point, the system will start doing a validation for that detection before issuing the Hypoglycemia alarm. Since the symptoms of Hypoglycemia differ from person to person, the threshold values should be adjustable to accommodate each patient case.

3. The tracking system

   This system should keep records of the following values: consecutive false alarms, late detections and successful detections. The purpose from this step is to make the sensitivity level
automatically adjustable. Initially, the system will require the patient to do one blood test each time an alarm would be issued. The system will keep asking that until the number of successful detection would be high enough; after that, once the system reaches that number, it will stop asking the patient for more blood test verification. With this, we can keep the blood test up to the minimum daily requirements, which will contribute to the overall expediency. As per the automatic adjusting for the sensitivity level, if the number of consecutive false alarms were high enough, it would lower the sensitivity of threshold values and then reset the number of false alarms again; on the other hand, if the number of late detections were high enough, the system would raise the sensitivity of the threshold values and reset the number of late alarm detection. With the previous process, we can implement an adjustable automated system, which should raise the accuracy in the detection action.

4.4 Discussion and Future Objectives for the Hypoglycemia Detection through Symptoms

The detection through Hypoglycemia symptoms remains one of the suggested ways, which have good potential of detecting Hypoglycemia episodes in a non-invasive way. There are several attempted researches [14] that aimed to provide several methods to minimize the invasive factor within the detection. One of these methods relies, for example, on measuring the distance between blood molecules by casting a near-infrared light through the skins. Narrow measurements indicate low-level values, while wide measurements indicate high-level values. However most of these researches are still under investigational process and still not ready for actual implantation. Judging from the previous researches within the literature reviews for the
detection through symptoms, we could sense some potential in the proposed method. The common issue we observed was the specificity of the detected cases. Although the issue might affect the user’s expediency, it might also increase the invasive factor as well. This is because the patient needs to conduct a blood test to confirm the occurrence of Hypoglycemia each time an alarm would be issued. The patients might do multiple number of unnecessary blood test if the alarms were not related to Hypoglycemia. For this reason, we need to find a way to raise the specificity within the detection process. The first way could be suggested through the same concept as the research done by GILI Medical LTD. GILI Medical LTD proposed using five different values for a couple of Hypoglycemia associated symptoms. If three of these values passed the assigned thresholds, an alarm would be issued. Our proposed system is following the same concept, however, in addition to the previous values, we would like to add some other types of values introduced in the other listed researches, the EEG and heart rates values. Both values had good indications for Hypoglycemia detections when they were tested in the mentioned researches. There are currently multiple types of wearable sensors, which can measure these values outside the clinical environment. We hope in the future that these types of wearable sensors can weave smoothly into the patients’ daily routines, and eliminate the need for users’ focus, such as implementing them within accessories, peripherals or smart devices. For the second suggestion to raise the specificity, we might achieve that by comparing the detected values with users’ action. We mentioned before that the Hypoglycemia would occur in the case excessive exercising or mismatching between the medication and carbohydrate intake. If we can check these two reasons once an alarm would be detected, then we can minimize the number of failure alarms. The level of exercise can be easily determined through the heart rate data. If the heart data indicated that the patient exceeded normal level of exercise, then it can conclude that
the patient would have higher insulin sensitivity than the usual case, which in turn it would raise the chance of encountering Hypoglycemia. Similarly, each type of insulin has certain known behavior. If by a chance we found that the detected case was during a peak point of insulin onset, then the chance of Hypoglycemia occurring is high. Unfortunately, the data for MDI doses in the current setup can only be entered manually into the system. Nevertheless, this can be done automatically if we use a similar approach to our previous proposed system, which propose a connectivity between smart instrument, like the previously mentioned intelligent insulin pens, and the smart devices. Once the patient would take the required dose, the information can be sent to the system, and then it can know the project the behavior of the current insulin onset in the personal smart devise. This approach has been actually implemented previously in a couple of researches [15,60], which aimed to use CGM and patients’ data to predicate the occurrence of Hypoglycemia episodes. Some of these researches had managed to raise the accuracy of predicting Hypoglycemia episodes at early stages. The last approach is to use a tracking method for all the successful, failure and late alarms. One of the main issues for diabetes is that each diabetic case differs from patient to patient. Each body has different insulin and carbohydrate ratio rate; this means that the appearance of Hypoglycemia symptoms and the advance through stages cannot be generalized among patients. For this reason, the suggested data can be used into two different ways; first, the system can give some indication to the system sensitivity through this tracking method. The user can then adjust the system sensitivity manually by analyzing the tracking data. It is a way to make the system more personal for each specific case. The other option is to use the collected data and apply them into one of the machine learning methods in order to automate the threshold adjustment process. This is a similar to one of the research, which used Extreme Learning Machine (ELM) algorithm to predict the occurrence of
Hypoglycemia episodes through tracking data within CGM devices [40]. The verification of the alarm status can be done through glucometer devices. Based on the obtained value, we can know whether the alarm was either accurate, late or failure. This step in the current setup can only be done manually; because current diabetic gadgets do not have the capability to exchange data with other systems. Nevertheless, we can automate this step if we can build and interface between the glucometer devise and the proposed system. Following this setup, the user will not need to enter the data manually each time an alarm would be issued.

This study was done in addition to our previous study, which focused on modernizing MDI practices. Both studies were utilizing ubiquitous technology to overcome a couple of unresolved challenges within the diabetes mellitus. Due to the limitation within our time and resources, we could not proceed with the validation process with the proposed system. Nevertheless, our suggestion proposes dividing the validation into different stages before implementing the whole system. The first stage should focus on testing the wearable sensors capability to detect hypoglycemia symptoms. This step should aim to find some common values, which can be used as starter thresholds during thy system implementation. The second stage should focus on testing the association of detected episode with the previous daily actions. These types of tests can be done through simulation testing at first and then though actual practices. The purpose is to verify the actual connection between the patient’s routines and encountered Hypoglycemia. The tracking system can be validated as a last stage after verifying the actual work of the system. The main purpose is to observe whether the system can successfully track every alarm. At later stage, we can decide on finding a proper machine-learning algorithm, which can use these data to re-adjust the system sensitivity in an automatic way.
5. CONCLUSIONS

5.1 Summary

Ubiquitous health care system is a new interdisciplinary field that aims to expand the health care services beyond the standard clinical environments. The implementation of these systems among patients has notable advantages, however, one of the remarkable features is the ability to provide a continuous care for patients, who are suffering from chronic diseases, such as the diabetes mellitus. The diabetes mellitus, which is known as losing the ability to regulate blood glucose, requires an extensive type of care in order to maintain a normal daily life. Although the treatment within diabetes has advanced greatly within the past years, there are still some other existed challenges, which prevents diabetic patient from living in a perfect regular lifestyle. These challenges require patients to maintain difficult tasks in regular bases, such as managing diabetic medication, monitoring body conditions and keeping follow-ups with diabetic practitioners regularly. With the capability of ubiquitous technologies, such as smart devices, cloud computing and wearable systems, we believe that overcoming some of these challenges is till manageable. There are multiple types of applications and software, which have the potential to ease the medication tasks for diabetic patients. Furthermore, most smart devices are now having the capability to read body condition through either embedded sensors or exchanging data with wearable sensors. Finally, communication among users has advanced greatly then early days; this can be utilized to smooth the communication between patients and practitioners and improve the diabetic consultation. Within this research, we are focusing on improving the management of the diabetes mellitus through the utilization of ubiquitous technologies. We are approaching this research through two cases, which considered major challenges within the
diabetes mellitus. The first case is related to the management of diabetic medication, which focuses specifically on the insulin therapy through the multiple daily injections (MDI) practices. The other case focuses on the detection of Hypoglycemia episodes through wearable systems and ubiquitous computing.

The first study focused on patients, who were mainly rely on insulin as part of their diabetic treatment. Insulin therapy is administered through two well-known types of method, insulin injection and insulin pumping. MDI therapy is currently the most common practice for insulin injection. The instrument for injecting insulin started with regular syringes initially. In 1976, a new instrument has been introduced for insulin injection known as insulin pen. The main purpose was to create a more practical instrument, which can ease carrying it around and minimize the effort for dose administration. Due to its simplicity and accuracy, insulin pen has become currently the most common instrument for insulin injection, especially within MDI practices. Nevertheless, the involvement of technology within MDI has remained limited for the past couple of years. On the other hand, insulin pumps have evolved rapidly through the utilization of technologies. Latest development of insulin pumps has managed to overcome many of the challenges, which is still existed within MDI routines. Both methods are still having their own positive and negative sides. Nevertheless, in order to elevate the insulin pen instrument into a new standard, a number of new technological solutions have been introduced known as intelligent insulin pen technology. Intelligent insulin pen technology is an attempt to overcome some of the common issues within MDI, such as missing daily doses. The technology is still far from the insulin pumping capability, but they can be considered as the first step toward smart solutions for MDI practices.
As the technology of intelligent insulin pens still recent and not standardized among insulin dependent patients, we conducted some assessment studies for this technology among a group of insulin dependent patients and diabetic practitioners as well. The studies were conducted first through online community, and then, through specialized clinics. The studies included some additional information related to the management of diabetes mellitus. Overall the technology received positive views from patients and practitioners as well. Nevertheless, after observing diabetic management behavior and current issue among our participants, we found the technology could be a good alternative for current instrument, which could offer some useful functions, such as keeping records for doses. On the other hand, there are still some difficulties within the diabetic management, which current technology of intelligent insulin pens cannot overcome, such as calculation for carbohydrate ratio. So the technology itself is still not critical, which makes it less justifiable among the majority of diabetic patients. Nevertheless, switching the MDI instrument from a mechanical base mechanism into a total technological solution would be a good step toward modernizing MDI routines. MDI practices might able to overcome many of the existed challenges through the utilization of modern technology, such as ubiquitous computing. To emphasize the importance of the previous claim, we conducted a series of pilot studies following the previous assessment study. The pilot studies focused on testing a smart system composed of intelligent insulin pen technology and smartphones. The proposed system was a smart reminder system, which can control the alarms and administration of doses in an automated way. For the experiments, we recruited a group of patients in order to observe their adherence to the insulin basal doses before and after using the reminder system. The results from the pilot studies showed that the system had the potential to provide a more reliable method to remind patients about their basal doses. The majority of participants had positive views about
using the system, however, there were some of negative views, which were related mainly in the
difficulty in using advanced technologies. Overall, the results encouraged adopting more similar
solution for MDI practices in the future, which can enhance the practice furthermore.

Another study was conducted under different area related to the one of the major challenges within the diabetes mellitus. The study focused on the detection of Hypoglycemia episodes using wearable systems and ubiquitous computing. Hypoglycemia symptoms are usually associated with a number of symptoms, which occur within three stages of Hypoglycemia episode. Previous researches used several types of wearable sensors trying to detect different types of Hypoglycemia symptoms. The conducted experiments showed that this method had the potential in detecting Hypoglycemia at early stagers; however, the method were suffering from some inaccuracy within the detected results, and it could not be considered a total reliable method. Most of the previous researches focused on detecting the symptoms only, however, they did not put consideration some other data like insulin onset behavior, conducted exercise or mealtime. We believe by using knowledge from ubiquitous computing, such as context awareness and machine learning, we might able to increase the validity of the detected results. We proposed a conceptual design for a hypoglycemia detection system. The proposed system is mainly divided into three main functions. The first function collects information about patient’s diabetic data for validation purposes. The second function focuses on collecting and analyzing the data from the wearable sensors. And the final part focuses on tracking the accuracy for the detected episodes in order to make an automatic adjustment for the threshold values. The proposed system is still subject to testing and validation. The system requires some simulation testing to validate the action mechanism, and then it requires some other testing through experiments to validate the actual work of the system.
5.2 Contributions

For the first study concerning the MDI routines for insulin therapy, we noticed that the use of technologies within MDI was relatively limited compared to its counterpart the insulin pumping method. We hope by highlighting on the capability of advance technologies within this research, it would expand the development and utilization of advanced technologies even further. For example, we showed how we could expand the intelligent insulin pen technology through the communication with smart devices. This kind of approach cannot be achieved through current of MDI routines, such as regular insulin pens and basic glucometer.

On the other hand, the study showed the low level of awareness among MDI patients as per the technology usage. For example, there was little awareness about the use of smart devices or the availability of advanced technology like the intelligent insulin pens. We hope that this study would trigger the interest in how to raise the awareness of using technology, and how to facilitate the shifting from the usual practices into more advanced solutions.

Lastly, we noticed that the technological development were focusing into modernizing the MDI routines by digitizing former practices, however, these developments have little interest in how to apply smart functions that would ease the MDI management itself. For example, within our pilot experiments, we showed how could we use the collected doses data and use them to acknowledge issued remainder alarms. So rather than keeping the collected data only as references, we tried them to utilize them for other smart functions. We hope that future development would focus on approaching the same way that would aim to simplify the diabetic management itself.
For the study concerning the detection of Hypoglycemia through its symptoms, we pointed out that previous researches focused on detecting the symptoms only, however, there were no direction toward validating the detected results through other knowledge, such as context awareness or machine learning. We highlighted how current technologies can keep track of diabetic daily routines; the attempted detection method can utilize these diabetic data to raise the accuracy of the detected results. We hope that our conceptual design would create new approaches in handling these researches in the future.

5.3 Limitation

A per the assessment study for the intelligent insulin technology, the sample size for the participants was relatively small. We could not consider the result representative for the insulin dependent population. If we would like to have a proper evaluation regarding the intelligent insulin pens technology, we need to obtain a larger sample size that would be sufficient for statistical analysis. Additionally, the usability tests conducted among the group of patients were short types of studies, which were mainly for observing the patients’ impression and gain some information. If we need to observe the impact on the patients’ glycemic level, we need to conduct longer types of studies, which can also shade all the positive and negative outcomes for using this technology.

For the proposed reminder system pilot studies, the constructed system was based on the Wizard of Oz prototyping method. It was sufficient to examine the potential within the system and observe the users’ interaction with the system. Moreover, due the period of the pilot study
was also short and cannot conclude any information regarding the glycemic control. Future studies should focus on using a full prototype system in order to test its reliability among the insulin dependent patients. Also, future experiments should planned for at least 3 months of period in order to observe the changes within the patients’ glycemic values. These types of experiments can help to prove whether advanced technologies have the capability in enhancing the diabetic management among patients.

For the proposed Hypoglycemia detection system, the analysis for the proper threshold values and system validation, require collecting actual vital signs and then implement them within the system. At the current moment, in order to approach with these analyses, there is a need to collaborate with specialized sectors in these filed in order to obtain the required information. Experimenting with wearable technology might require supervision from the capable practitioners to minimize the risks and obtain more accurate results. At the current situation using simulation techniques can be used for refining the system mechanism, however, it would be sufficient for testing the reliability of the system.

5.4 Future Work

For the study related to modernizing MDI routines, future studies should focus on conducting a longer period of the proposed system. This kind of study might require collaboration with specialized sectors, which have similar interest. The target period should be about 3 months at least in order to see the changes within the glycated hemoglobin (A1C) value. This would require close follow up from practitioners and careful supervision. Through
this setup, we can determine the effectiveness of applying these kinds of systems within the MDI practices. Moreover, the system was using the Wizard of Oz concept for experimenting purposes. In the future, based on the obtained results, we can proceed with an actual prototype system in order to test the system reliability among its users. A full prototype system might require building additional module to expand the dosing instrument to achieve the required functions. It also requires building a dedicated cloud based interface between the instrument and reminder system for data exchange and processing.

For the proposed Hypoglycemia detection system, future study might focus on conducting a couple of experiments to collect some vital data during different conditions. The vital data can be used to build a simulated version from the proposed system. These experiments might require collaborating with specialized practitioners for supervision and recommendations purposes. The simulated system can be used later to construct an actual prototype for the system. The main purpose from this step is to validate the concept before testing an actual prototype system.
REFERENCES


APPENDIX A. Survey of Assessment Study of the Intelligent Insulin Pens

Smart Insulin Pen Survey
If you are a diabetic patient who are under insulin therapy or someone who is taking care of a diabetic patient under insulin therapy, kindly, please help us by filling this survey. This survey was made to test the importance of smart insulin pens within diabetic management. The main objective from this research is to see how we can expand the current technologies to be part of the "Ubiquitous Health Care Systems". Your contribution will help other patients struggling with diabetes mellitus. We do appreciate your help and support, and thank you in advance.

Notes:
Please acknowledge that:
1- This survey does not cover diabetic patients who are not under insulin therapy.
2- The survey results will be used for academic purposes only.
3- The presented materials within this survey are meant for illustration and research purposes only. 4- The presented materials within this survey are not meant for sales or advertisement purposes.

* Required

Participant Information
1- Full name or (Nickname) of the person who is filling this survey? *

---

2- You are helping us today by filling this survey because you are: *
Mark only one oval.

☐ I am a diabetic patient who is under insulin therapy
☐ I am taking care of a diabetic patient who is under insulin therapy
☐ Other: ____________________________________________

Patient’s Personal Information
3- Patient’s age? *
Mark only one oval.

☐ Under 10 Yrs
☐ 10 - 19 Yrs
☐ 20 - 29 Yrs
☐ 30 - 49 Yrs
☐ Over 50 Yrs
4- Patient's gender *  
*Mark only one oval.*

☐ Male
☐ Female

5- Patient's current job status *  
*Mark only one oval.*

☐ Not Working
☐ Student
☐ Working
☐ Retired

6- Patient's current location (country)? *

________________________________________________________________________

7- Do you use smart devices (e.g. iPhone, iPad) ? *  
(i.e. either the patient or his (or her) caring person)  
*Mark only one oval.*

☐ Yes
☐ No   Skip to question 8

Personal Information

Do you use your smart device to manage your Diabetes? *  
*Mark only one oval.*

☐ Yes
☐ No

If no, why not? If yes, list the apps?

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________
Diabetic Personal Information

8- How long has the patient been diagnosed with diabetes? *
   Mark only one oval.
   ☐ Less than 5 years
   ☐ 5 - 10 years
   ☐ 11 - 15 years
   ☐ More than 15 years

9- Which type of diabetes the patient was diagnosed with? *
   Mark only one oval.
   ☐ Type 1 (aka. Insulin Dependent or Juvenile Diabetes )
   ☐ Type 2
   ☐ Not Sure

10- Is the patient under insulin therapy right now? *
    Mark only one oval.
    ☐ Yes
    ☐ No  Stop filling out this form.

Insulin Therapy

11- How many types (or brands) of insulin is the patient currently using? *
    (e.g.)
    Mark only one oval.
    ☐ One only
    ☐ Two only
    ☐ More than two
12- Could you please name the insulin types (or brands) that the patient is currently using?  
(e.g. Fast-acting Regular, Long-acting Glargine, Sanofi Lantus, Lilly Humalog, Novo Mixtard, etc) 


13- How does the patient take insulin doses? *  
Mark only one oval.  

☐ With syringes  
☐ With insulin pens  
☐ I use both regular syringes and insulin pens  
☐ Other: ____________________________________________

Image courtesy of Blausen Medical

14- How regularly do you have Insulin dosage or consumption mistakes? *  
(e.g. double doses, inaccurate doses, missing doses)  
Mark only one oval.  

☐ Frequent (A couple of times during a month)  
☐ Sometimes (One time or two times within a long period)  
☐ Barely (Almost never had such a thing)
Diabetic Management

15- Does the patient measure and give insulin doses by himself (herself)? *
Mark only one oval.

☐ Yes
☐ No

16- Does the patient measure his (her) meal calories by himself (herself)? *
Mark only one oval.

☐ Yes
☐ No

17- Are you keeping regular records of daily blood tests for the patient? *
(i.e. written in in notebooks or saved in digital files)
Mark only one oval.

☐ Yes
☐ No

If no, please write the reason for not keeping daily blood test records

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

18- Are you keeping regular records of the patient’s daily carbohydrates consumption? *
(i.e. written in in notebooks or saved in digital files)
Mark only one oval.

☐ Yes
☐ No
If no, please write the reason for not keeping track of the daily amount of consumed carbohydrates

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

19- Are you keeping regular records of daily insulin dosages for the patient? *
(i.e. written in in notebooks or saved in digital files)
*Mark only one oval.*

☐ Yes
☐ No

If no, please write the reason for not keeping daily insulin dosages

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

20- If you want to keep track of the patient’s records, what is the best format for you? *
*Mark only one oval.*

☐ Paper format (Write them down or print them from devices)
☐ Digital format (Type them or Download them from devices)
☐ Both digital and paper
☐ Other: ____________________________

21- Does the patient go for regular HbA1c tests? *
(HbA1c: Average of glucose level within three months)
*Mark only one oval.*

☐ Yes
☐ No

22- When was the last time the patient did HbA1c test?
*Mark only one oval.*

☐ Less than 6 months
☐ 6 - 12 months
☐ More than 12 months
23- What was the value of the last HbA1c test if you know it?

Hypoglycemia and Hyperglycemia

24- How regular does the patient have Hypoglycemia episodes per month? *
(i.e. Low blood glucose less than 70 mg/dl or 3.9 mmol/l)
Mark only one oval.

☐ Less than 3 times per month
☐ Between 3 to 7 times per month
☐ More than 7 times per month

25- What is the main reason behind the patient’s Hypoglycemia episodes? *
Mark only one oval.

☐ Taking double insulin doses or extra amount of insulin by mistake
☐ Insufficient amount of carbohydrates
☐ Too much exercise
☐ Other: ________________________________

26- How regular does the patient have Hyperglycemia episodes per month? *
(i.e. High blood glucose more than 250 mg/dl or 13.9 mmol/l)
Mark only one oval.

☐ Less than 3 times per month
☐ Between 3 to 7 times per month
☐ More than 7 times per month

27- What is the main reason behind the patient’s Hyperglycemia episodes? *
Mark only one oval.

☐ Missing insulin doses or taking insufficient amount of insulin by mistake
☐ Extra amount of carbohydrates
☐ No enough exercise
☐ Other: ________________________________
Smart Insulin Pen

28- Have you ever heard about or used smart insulin pens? *
(e.g. Pendiq Intelligent Insulin Pen, NovoPen® 5, Lilly HumaPen® Memoir )
Mark only one oval.

☐ Yes
☐ No       Skip to next page

Please write which brand of smart insulin pens you have used or heard about before, and what is your opinion about it

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Smart Insulin Pens Introduction:
Currently, few numbers of smart electronic pens have been introduced by a couple of specialized companies. These pens are offering several useful functions that can ease the process of taking insulin doses.

In the next section, we will present the current available functions within the latest smart pens models. Kindly, please go through them, and then evaluate the importance of each function for diabetic management field.

Original Designs:
Pendiq GmbH
Novo Nordisk A/S
Eli Lilly and Company

Image resources:
www.pendiq.com
www.prestoimages.net/store/rd648/648_pd2004603_1.jpg

Current Smart Insulin Functions:
This is a list of some functions available within a couple of smart pens introduced already into the market. Kindly, please go through this section, and then evaluate the importance of each function for diabetic management field at the end of the presented materials.
Current smart pens technologies can keep tracks of doses and record several types of data (time, date and dosage amount).

35 units injected
12 or more hours ago

Image resources:
www.pendiq.com
Some current technologies have a precise dosage adjustment (0.1 U scale) capability; with this, the patient can have more accurate dosages.

Some pens allow to pre-program daily frequent dosages for a different time segments. For example, if you are taking a 18 U of basal insulin everyday, you do not need to readjust your pen every time you want to take your dose.
Some pens now allow you to transfer the recorded data into PCs or smartphones through USB connection. The USB connection can also do the battery recharging function at the same time.

Some pens now have the ability to alarm about insulin blockage, low insulin residual or countdown for dose administration, etc. Pens operated with rechargeable battery can also alarm about low battery level.)
Even under the out-of-battery cases, these pens have been designed to be easily switched to a manual operating mode (i.e. no battery) in order to take your doses without worrying about battery operation.

Image resources:

www.pendiq.com
29- Which of the features above do you think would help with the diabetic management? *
Please choose only two items at most from the list below?
Check all that apply.

☐ Dosage Auditing System (Records of Date, time and dosage amount)
☐ Precise Dosage Adjustment (0.1 U Increment)
☐ Pre-programming Frequent Dosages
☐ Transferring Data to PC
☐ Alarming System (Battery, Dose administration, etc)
☐ Switching between Digital and Manual modes
☐ Other: ____________________________________________

30- What kind of improvements would you like to achieve with the use of a digital pen? *
Please choose only two items at most from the list below?
Check all that apply.

☐ Less Hypoglycemia and Hyperglycemia episodes for the patient
☐ help to avoid missing or doubling doses
☐ help to keep regular records about taken doses
☐ help to achieve more accurate insulin doses and proper dosing administration
☐ Other: ____________________________________________

31- What would be the top reasons for you not to obtain this kind of smart insulin pens? *
Pick your top two reasons
Check all that apply.

☐ High prices (in the case of the absence of healthcare insurance)
☐ Complicated Interface and control
☐ Compatibility with your current insulin brand
☐ Availability within your country
☐ Other: ____________________________________________

32- How important do you think that this kind of pens for diabetic patients are? *
Important = Better than traditional instrument Useless = I prefer traditional instrument
Mark only one oval.

    1  2  3  4  5
Useless  -------------------- Important
Communication with Smart Devices

Within this research, we are aiming to expand the smart pen technology in order to be part of the current "Ubiquitous Healthcare Systems". This means that we might have the ability make a continues communication between the smart pens and smart devices. This communication will allow us to do a continues data processing and exchange, and with this we might able to achieve the following kinds of functions (and hopefully more):

Image resources:
www.pendiq.com
www.apple.com
33- Which one of the functions above might help you better with your diabetic management? *
Mark only one oval.

- ☐ Reminders about doses
- ☐ Warning for certain actions
- ☐ Automation of data collection
- ☐ Interactive interface
- ☐ None of the above
- ☐ Other:

34- How important do you consider that this kind of communication between smart devices and pens? *
Important = Better than traditional instrument Useless = I prefer traditional instrument
Mark only one oval.

<table>
<thead>
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<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Useless</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

Note: The above presented materials are meant for illustration purposes only.

Original designs:

Pendiq GmbH
Apple Inc.

Optional Information

35- Please provide us with any suggestion or comment if you have any? (Optional)
APPENDIX B. Pendiq® Intelligent Insulin Pen – Quick Manual

1. **Introduction:**

   Pendiq® Intelligent Insulin Pen is a digital insulin delivery pen for insulin dependent patient. The pen has small increments of 0.1 U. It allows reviewing the history of injection through the memory function (date, time and delivered amount). The full manual available in [www.pendiq.com](http://www.pendiq.com)

2. **Pendiq® Components:** (Adopted from Pendiq® Official manual)

   ![Pendiq® Components Diagram]

3. **Operation Button:** (Adopted from Pendiq® Official manual)

   - **(ACT) button is used**
     - to turn on the pen
     - to confirm an operation or settling
     - to inject dose
     - to return to home screen
   - **(M) button is used**
     - to enter the menu
     - to review memory
     - to cancel an operation or setting (display returns to home screen)
   - **(+ button is used**
     - to increase number
     - to prime
     - to track forward in injection memory
     - to drive the plunger forward
   - **(-) button is used**
     - to decrease number
     - to track back in injection memory
     - to rewind the plunger
4. **Display Symbols:** (Adopted from Pendiq® Official manual)

![Display Symbols Diagram]

5. **Highlighted Features**

- Memory Function: 195 injections with date, time and delivered dose
- Software Manager DIABASS® or SiDiary®
- Dose time pre-programming
- Switching to Manual mode
- Micro dosages in increments of 0.1 U
- USB for data transfer
- Chargeable Battery through USB
- Alarm for low battery, blockage and low insulin residual
- Digital motor driven 2U / Sec
- Compatible with common insulin cartridges (excluding Novo Nordisk A/S)
- Large and readable display
- Easy operation and handling
6. Technical Information

<table>
<thead>
<tr>
<th>Product name</th>
<th>pendiq®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>Diamesco Co., Ltd., Daejeon, 305-500, Korea</td>
</tr>
<tr>
<td>Length</td>
<td>182mm</td>
</tr>
<tr>
<td>Weight</td>
<td>46g (without insulin cartridge and pen-needle)</td>
</tr>
<tr>
<td>Infusion rate</td>
<td>2.0U/sec</td>
</tr>
<tr>
<td>Cartridge Storage Volume</td>
<td>3ml (300.0U)</td>
</tr>
<tr>
<td>Increments</td>
<td>0.1U</td>
</tr>
<tr>
<td>Dosage range per Injection</td>
<td>0.5 - 60.0U</td>
</tr>
<tr>
<td>Battery</td>
<td>3.7V, 90mAh, Lithium-Ion-Polymer battery, rechargeable up to 300x (80% capacity)</td>
</tr>
<tr>
<td>Memory</td>
<td>195 last injections (date, time and amount delivered)</td>
</tr>
<tr>
<td>Alarm</td>
<td>low battery, blockage, low residual amount of insulin in the cartridge (20.0 U or lower)</td>
</tr>
<tr>
<td>Acoustic signals</td>
<td>end of injection (alarm sounds on/off optional)</td>
</tr>
<tr>
<td>Data transfer</td>
<td>data transfer through USB</td>
</tr>
<tr>
<td>USB Current Rating</td>
<td>USB 5V, 500mAh</td>
</tr>
</tbody>
</table>
| Storage          | Temperature: -10 – 40°C / 14°F – 104°F  
                  | Humidity: 10 – 90% RH            
                  | Atmospheric Pressure: 680 –1060 mbar |
| Operating conditions | Temperature: 0 – 40°C / 32°F – 104°F  
                      | Humidity: 20 – 70% RH            
                      | Atmospheric Pressure: 680 –1060 mbar |
| Warranty         | 2 years                          |
| Duration of battery | 7 days                           |
| Type of protection against electric shock | Class II equipment with internally powered equipment |
| Degree of protection against electric shock | Type BF applied part |
| Degree of protection against the ingress of water | IPX0 (no special protection) |
| Mode of operation | Continuous operation             |
| Maximum pressure | 1.5 kg/cm²                       |
| Blockage pressure | 1.0 kg/cm²                       |
| Allowable maximum volume per 1 time | 60.0 U                           |
| Allowable minimum volume per 1 time | 0.5 U                            |
| Injection rate   | 2.0 U/sec.                       |
| Display turns itself off (when no button is pressed) after | 60 seconds                       |
| To turn on screen, press (ACT) button for | 3 seconds                        |
| Countdown after injection | 15 seconds                      |
| Dosage increments | 0.1U                             |
| Display of units in | U (≈0.01 ml)                     |
| Cartridge volume | 3ml (300.0U)                     |

pendiq® is a registered trademark of pendiq GmbH.
pendiq GmbH
Baerler Strasse 100
47441 Moers, Germany

Manufacturer
Diamesco Co., Ltd
Migun Techno World II #305, 533-1, Yongsan-dong Yuseong-gu, Daejeon, 305-500, Korea
diamesco@naver.com
www.diamesco.com
## APPENDIX C. List of Research Achievements

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
</table>