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(54) **Title:** SYSTEM FOR MONITORING AND DELIVERING MEDICATION TO A PATIENT AND METHOD OF USING THE SAME TO MINIMIZE THE RISKS ASSOCIATED WITH AUTOMATED THERAPY

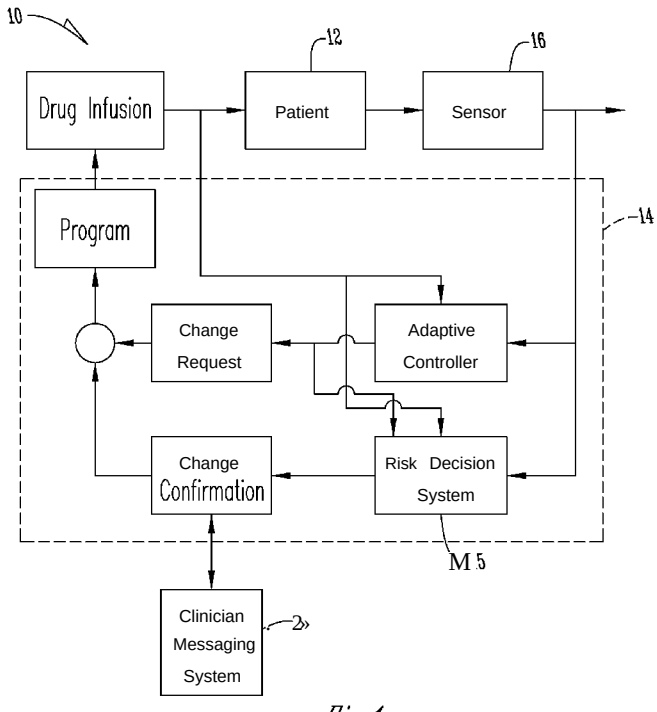

Fig. 1

(57) **Abstract:** A system and method for monitoring and delivering medication to a patient includes a controller that has a control algorithm and a closed loop control that monitors the control algorithm. A sensor is in communication with the controller and monitors a medical condition. A rule base application in the controller receives data from the sensor and the closed loop control and compares the data to predetermined medical information to determine the risk of automation of therapy to the patient. The controller then provides a predetermined risk threshold where below the predetermined risk threshold automated closed loop medication therapy is provided. If the predetermined risk threshold is met or exceeded, automated therapy adjustments may not occur and user/clinician intervention is requested.

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TITLE: SYSTEM FOR MONITORING AND DELIVERING MEDICATION TO A PATIENT AND METHOD OF USING THE SAME TO MINIMIZE THE RISKS ASSOCIATED WITH AUTOMATED THERAPY

BACKGROUND OF THE INVENTION

This invention relates to a system for monitoring and delivering medication to a patient. More specifically, the present invention is directed toward a device that monitors the risk to a patient of allowing an automated therapy decision and allows a clinician to customize rules that determine whether an automated change in therapy is to be allowed or whether user/clinician intervention should be required based upon the risk of automation and the customized rules.

Diabetes is a metabolic disorder that afflicts tens of millions of people throughout the world. Diabetes results from the inability of the body to properly utilize and metabolize carbohydrates, particularly glucose. Normally, the finely tuned balance between glucose in the blood and glucose in bodily tissue cells is maintained by insulin, a hormone produced by the pancreas which controls, among other things, the transfer of glucose from blood into body tissue cells. Upsetting this balance causes many complications and pathologies including heart disease, coronary and peripheral artery sclerosis, peripheral neuropathies, retinal damage, cataracts, hypertension, coma, and death from hypoglycemic shock .

In patients with insulin-dependent diabetes the symptoms of the disease can be controlled by administering additional insulin (or other agents that have similar effects) by injection or by external or implantable insulin pumps. The correct insulin dosage is a function of the level of glucose in the blood. Ideally, insulin administration should be

continuously readjusted in response to changes in blood glucose level. In diabetes management, insulin enables the uptake of glucose by the body's cells from the blood. Glucagon acts opposite to insulin and causes the liver to release glucose into the blood stream. The basal rate is the rate of continuous supply of insulin provided by an electronic medication (insulin) delivery device (pump). The bolus is the specific amount of insulin that is given to raise blood concentration of the insulin to an effective level when needed (as opposed to continuous).

Presently, systems are available for continuously monitoring blood glucose levels by inserting a glucose sensitive probe into the patient's subcutaneous layer or vascular compartment or by periodically drawing blood from a vascular access point to a sensor. Other measurement systems provide a continuous or periodic glucose measurement by noninvasively interfacing a patient with an optical or electromagnetic system. Such probes measure various properties of blood or other tissues including optical absorption, electrochemical potential, and enzymatic products. The output of such sensors can be communicated to a hand held device that is used to calculate an appropriate dosage of insulin to be delivered into the blood stream in view of several factors such as a patient's present glucose level and rate of change, insulin administration rate, carbohydrates consumed or to be consumed, steroid usage, renal and hepatic status, and exercise. These calculations can then be used to control a pump that delivers the insulin either at a controlled basal rate or as a periodic or one-time bolus. When provided as an integrated system the continuous glucose monitor, controller, and pump work together to provide continuous glucose monitoring and insulin pump control.

Such systems at present require intervention by a patient

or clinician to calculate, control and confirm the amount of insulin to be delivered. However, there may be periods when the patient or clinician is not able to adjust insulin delivery or confirm recommended therapy decisions. For example, when the patient is sleeping, he or she cannot intervene in the delivery of insulin - yet control of a patient's glucose level is still necessary. A system capable of integrating and automating the functions of glucose monitoring and controlled insulin delivery would be useful in assisting patients in maintaining their glucose levels, especially during periods of the day when they are unable to intervene .

Alternately, in the hospital environment an optimal glucose management system involves frequent adjustments to insulin delivery rates in response to the variables previously mentioned. However, constant intervention on the part of the clinician is burdensome and most glucose management systems are designed to maximize the time interval between insulin updates . A system capable of safely automating low-risk decisions for insulin delivery would be useful in improving patient insulin therapy and supporting clinician workflow.

Since the year 2000 at least five continuous or semi-continuous glucose monitors have received regulatory approval . In combination with continuous subcutaneous insulin infusion (CSII), these devices have promoted research toward closed loop systems which deliver insulin according to real time needs as opposed to open loop systems which lack the real time responsiveness to changing glucose levels. A closed loop system, also called the artificial pancreas, consists of three components: a glucose monitoring device such as a continuous glucose monitor (CGM) that measures subcutaneous glucose concentration (SC); a titrating algorithm to compute the amount of analyte such as insulin and/or glucagon to be

delivered; and one or more analyte pumps to deliver computed analyte doses subcutaneously . Several prototype systems have been developed, tested, and reported based on evaluation in clinical and simulated home settings. This concerted effort promises accelerated progress toward home testing of closed loop systems .

Similarly, closed loop systems have been proposed for the hospital setting and investigational devices have been developed and tested, primarily through animal studies. In addition, several manufacturers are either in the process of developing or have submitted to the FDA automated glucose measurement systems designed for inpatient testing. Such systems will accelerate the development of fully automated systems for inpatient glucose management.

The primary problem with closed loop control or full automation of insulin therapy is that a computerized system makes decisions that may be high risk in terms of potential consequences if the patient's condition changes or differs from the assumptions behind the computerized decision system. As a result of the automation these high risk decisions are not uncovered until the risk is realized and the patient displays an unacceptable medical condition. Second, in scenarios in which frequent glucose measurements are automatically collected but automation is not desired, it is undesirable to update the infusion at the same frequency as glucose measurements are collected. Third, when user intervention is required it may be undesirable or difficult for a clinician to respond at the bedside. For example, if the patient is in an isolation room but is observable, the clinician may desire to update the infusion rate without entering the room.

Thus, a principle object of the present invention is to provide an improved system for monitoring and delivering

medication to a patient that makes risk determinations of an automated therapy decision and action before providing or continuing to provide automated therapy.

Yet another object of the present invention is to provide a system for monitoring and delivering medication to a patient that minimizes the risk to a patient based on automation of therapy .

Yet another object of the present invention is to provide a system for monitoring and delivering medication that is able to selectively request user intervention based upon a risk of automation of therapy.

Yet another object of the present invention is to provide a system for monitoring and delivering medication that allows a user to define an acceptable level of risk of automated therapy .

Yet another object of the present invention is to provide a system for monitoring and delivering medication that allows a user to define an unacceptable level of risk of automated therapy at or above which manually intervention is required.

These and other objects, features, or advantages of the present invention will become apparent from the specification and claims .

BRIEF SUMMARY OF THE INVENTION

A system for monitoring and delivering medication to a patient and the method of using the same includes a controller that has an adjustment or control algorithm and an automation risk monitor that monitors the control algorithm. More specifically, the present invention is directed toward a system and method that monitors the risk to a patient of an automated therapy decision and allows a clinician to customize rules that determine whether an automated change in therapy or continuation of automated medication delivery therapy is to be

allowed or whether user/clinician intervention should be required based upon the risk of automation and the customized rules. The customized rules may be established by the supplier of the system or by the user of the system. Thus, the risk of potential adverse consequences to the patient if the patient's condition changes or differs from the assumptions behind the computerized or automated decision system can be minimized.

A sensor in communication with the controller monitors a medical condition to provide data to a rule based application in the controller. In addition, the rule based application receives data, which may include monitored, measured or calculated values, from the closed loop control and compares the data to predetermined medical information to determine the risk of therapy automation to the patient. When the risk is below a predetermined risk threshold, medication or automated therapy adjustments are allowed to occur in an automated manner according to a closed loop algorithm. Alternatively, when the risk is above the predetermined risk threshold, the controller triggers a request for user intervention or reduces the degree of automated therapy allowed.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a schematic diagram of a closed loop control system augmented with the automation risk monitor of the present invention;

Fig. 2 is an example messaging diagram for the present invention ;

Fig. 3 is a schematic diagram showing the architecture of a semi automatic glucose management system; and

Fig. 4 is a schematic diagram of an automation risk monitor system.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

Fig. 1 provides a system 10 for monitoring and delivering medication, such as insulin, to a patient 12. The system 10 includes a controller 14 that utilizes a control algorithm and an automation risk monitor 15 all presented in a closed loop. A sensor 16 is in communication with the controller 14 and monitors a medical condition of the patient 12. A rule based application 18 in the control receives data from the sensor 16 and compares the data to predetermined medical information to determine the risk to the patient 12 to automate the delivery of medication. The rule based application 18 in one embodiment includes physician or clinician entered conditions of when automation is acceptable. The system 10 is thus in communication with a clinician messaging system 20 that communicates to a clinician when the risk of automation is unacceptable. In a preferred embodiment the messaging system is remote from the system 10.

The rule based application 18 in one embodiment can include a risk profile wherein a clinician implements a risk profile according to a metric that may be qualitative (low, medium or high) or quantitative (1-10 where 10 is the highest risk) and a threshold defining when intervention is required. In either case, a quantitative metric is internally calculated and compared to a quantitative threshold. For example, in the case of low, medium or high each qualitative measurement is assigned a quantitative value such as 2, 5 and 7 respectively. Consequently, a risk scale is specified and a threshold is defined at or above which intervention is requested. The rule based application 18 can also include a risk matrix that is developed to enable a determination of risk. Although the matrix is ultimately stored internally, it can be parameter itized by the user. One example of the risk matrix is shown below:

Glucose Range (mg/dL)	Glucose Change (derivative)	Calculated Change in Insulin	Risk Level
0-70	Increasing	Increasing	High
0-70	Increasing	Decreasing	Low
0-70	Decreasing	Increasing	High
0-70	Decreasing	Decreasing	Low
70-90	Increasing	Increasing	Medium
70-90	Increasing	Decreasing	Low
70-90	Decreasing	Increasing	High
70-90	Decreasing	Decreasing	Low
90-120	Increasing	Increasing	Medium
90-120	Increasing	Decreasing	Low
90-120	Decreasing	Increasing	High
90-120	Decreasing	Decreasing	Low
120-180	Increasing	Increasing	Low
120-180	Increasing	Decreasing	Low
120-180	Decreasing	Increasing	Medium
120-180	Decreasing	Decreasing	Low
180-250	Increasing	Increasing	Low
180-250	Increasing	Decreasing	High
180-250	Decreasing	Increasing	Medium
180-250	Decreasing	Decreasing	Low
Above 250	Increasing	Increasing	High
Above 250	Increasing	Decreasing	Low
Above 250	Decreasing	Increasing	Low
Above 250	Decreasing	Decreasing	Medium

Specifically, the second column is the calculated or requested insulin level from the closed loop controller. The table is an example of how the treatment condition is mapped to a risk level. There are numerous other methods for implementing this information which may include continuous mapping functions, fuzzy logic, probabilistic models (e.g., Bayesian networks), probability calculations and the like.

A second way to provide this type of system is to employ an insulin/glucose pharmacokinetic/pharmacodynamic model as shown below which predicts the future glucose level and current insulin-on-board . The clinician can then use a predicted value and/or the anticipated insulin effect rather than or in addition to glucose level and a derivative.

$$\dot{G}(t) = -p_G G(t) - S_I(t) \cdot G \cdot \frac{Q(t)}{1+\alpha_G Q(t)} + \frac{P(t) + EG_{P-CNS}}{V_G}$$

$$\dot{I}(t) = -n\frac{I(t)}{1+\alpha_I I(t)} + \frac{u_{ex}(t)}{V_I} + \frac{u_{en}(t)}{V_I}$$

$$\dot{P}_1(t) = -d_1 P_1(t) + P_e(t)$$

$$\dot{P}_2(t) = -\min\left(d_2 P_2(t), P_{\max}\right) + d_1 P_1(t)$$

$$P(t) = \min\left(d_2 P_2(t), P_{\max}\right) + P_N(t)$$

$$\dot{G}(t) = -p_G(t)G(t) - S_I(t)G(t)\frac{Q(t)}{1+\alpha_G Q(t)} + \frac{Pit)}{V_G} \quad (1)$$

$$\dot{Q}(t) = -kQ(t) + kI(t) \quad (2)$$

$$\dot{I}(t) = -n\frac{I(t)}{1+\alpha_I I(t)} + \frac{u_{ex}(t)}{V_I}$$

In Equations (l)-(3), $G(t)$ [mmol/L] denotes the total plasma glucose concentration, and $I(t)$ [mU/L] is the plasma insulin concentration. The effect of previously infused insulin being utilized over time is represented by $Q(t)$ [mU/L], with k [1/min] accounting for the effective life of insulin in the system. Exogenous insulin infusion rate is represented by $u_{ex}(t)$ [mU/min], whereas $P(t)$ [mmol/L min] is the exogenous glucose infusion rate. Patient's endogenous glucose removal and insulin sensitivity through time are described by $p_G(t)$ [1/min] and $S_I(t)$ [L/mU min], respectively. The parameters V_I [L] and V_G [L] stand for insulin and glucose distribution volumes, n [1/min] is the first order decay rate of insulin from plasma. Two Michaelis-Menten constants are used to

describe saturation, with α_I [L/mU] used for the saturation of plasma insulin disappearance, and α_G [L/mU] for the saturation of insulin-dependent glucose clearance.

Thus, the rule base application 18 determines the risk of therapy automation to a patient 12 by referencing or comparing the monitored, measured, or determined present or future condition to a predetermined risk threshold. Below the predetermined risk threshold, because a low risk condition is detected, the system 10 can move forward in an automated fashion and provide medication as required. If the risk is determined to meet or exceed (i.e., be at or above) the predetermined risk threshold, the controller triggers a request for user intervention by contacting the clinician, for example via a clinician messaging system 20, instead of moving forward with automation .

In operation, the system 10 monitors a control algorithm of a controller 14 to receive data. The controller 14 additionally receives continuous data from a sensor 16 regarding a medical condition such as a glucose level . The controller 14 then compares the data from the control algorithm and the sensor 16 to predetermined medical information so that the controller 18 can determine whether a predetermined risk threshold of automating the delivery of medication has been met or exceeded. Then, based on the data, if a risk of automated therapy is below a predetermined threshold, automation is permitted and a command or request for medication or insulin is provided to the electronic insulin pump and the insulin delivery rate is automatically updated. Therefore the insulin delivery rate is automatically updated according to the algorithm model or closed loop controller used. Alternatively, if the risk is above a predetermined threshold, a request for user intervention is triggered sending a message to the clinician, for example via

a clinician messaging system 20, so that a user may intervene to make a determination regarding whether the medication should be provided. The request for intervention is generated and sent directly to the user through a messaging system that is bi-directional. The message system 20 provides information and requests a user response. When the response is related to a change in therapy an authentication step is included.

The response to a request is provided by the user directly through the user interface of the system. Alternatively, the response can be returned through an authenticated messaging system involving a unique identifier specific to a positive or negative response .

During the course of normal operation glucose measurements may be received that generate a change in the recommended insulin. However, the change may not be significant enough to provide a therapeutic advantage to the patient versus the burden of requesting confirmation from the nurse. Consequently, a rule based system is provided which evaluates therapy changes to trigger a request for an automatic update or nursing intervention. The input to the rule based system includes the blood glucose level, the change in glucose, the insulin infusion, the recommended change in insulin infusion, the estimated insulin on board, and the predicted glucose in the future. Rules involving comparisons to thresholds, regression equations, and calculations are created which trigger a therapy update based on the inputs.

Thus, the present system can be used to make determinations of treatment decisions requiring user intervention based upon a diagnostic value, the change in diagnostic value, the current drug infusion rate, the updated drug infusion rate, and the treatment target range. In addition, the system notifies a clinician that intervention is required and receives the implementing clinician instruction

in response to the notification.

An additional advantage is presented because the system 10 determines when clinician intervention is necessary and unnecessary. Specifically, system 10 is independent of an adaptive control algorithm or a computerized protocol. The system 10 functions as a safety supervisor that watches the performance of the closed loop system. Consequently, data from the closed loop system and diagnostic sensor 16 are provided to a rules database that uses a matrix to produce a quantitative level of risk of automation. The risk is compared to a particular risk threshold to either generate and/or provide an "okay" to proceed with automated therapy or to trigger a request for user intervention. The risk threshold can be selected or customized based on the desires of the user or the healthcare facility or organization.

This operation differs from current systems that do not determine risk of automation. Instead prior art systems allow automation to occur regardless of potential risk and then when sensors indicate a patient is experiencing an unacceptable medical condition a clinician is alerted. Therefore the system 10 provides an advantage of preventing the unacceptable medical condition from occurring in the first place as a result of monitoring the automation process, predetermining risks of automation, and comparing the risk of automation to a predetermined risk of automation threshold. The user can customize or select what factors are used to determine the risk of automation, as well as the predetermined threshold of automation risk that they are willing to accept without triggering a request for user intervention and preventing automated therapy. Thus, at the very least all of the stated objectives have been met.

What is claimed is:

1. A system for delivering medication to a patient, the system comprising:

a controller having a control algorithm and an automation risk monitor that monitors the control algorithm;

an electronic medication delivery device controlled by the controller;

a sensor in communication with the controller and the automation risk monitor and monitoring a medical condition;

a rule based application in the automation risk monitor that receives data from the sensor and the closed loop control and compares the data to predetermined medical information to determine a risk of therapy automation to the patient; and

wherein the controller controls the medication delivery device to deliver medication to the patient based on a comparison of the risk to a predetermined risk threshold.

2. The system of claim 1 wherein when the risk is below the predetermined risk threshold additional automated medication delivery therapy is provided and when the risk at or above the predetermined risk threshold the controller triggers a request for user intervention.

3. The system of claim 2 wherein triggering a request for user intervention causes the closed loop control to function as an open loop.

4. The system of claim 2 wherein the additional automated medication delivery therapy includes delivering insulin.

5. The system of claim 1 wherein the medical condition is a glucose level of the patient.

6. The system of claim 1 wherein the predetermined medical information includes a risk matrix.

7. The system of claim 6 wherein the risk matrix includes information pertaining to glucose ranges, glucose change, insulin change and risk level.

8. The system of claim 1 wherein the predetermined medical information includes information determined using continuous mapping functions, fuzzy logic or probability calculations.

9. The system of claim 1 wherein the predetermined medical information includes information determined using a mathematical model.

10. The system of claim 9 wherein the mathematical model is defined by one of a pharmacokinetic and a pharmacodynamic model.

11. The system of claim 2 wherein the request for user intervention is sent to the user through a messaging system.

12. The system of claim 6 wherein a portion of the risk matrix is user customizable.

13. The system of claim 12 wherein the user customizable portion of the risk matrix includes a plurality of user-defined risk levels and respective actions are associated with the risk levels and wherein at least two of the respective

actions are different.

14. The system of claim 13 wherein the plurality of user-defined risk levels includes at least three risk levels comprising high, medium and low risk levels.

15. A method for monitoring and delivering medication to a patient comprising:

monitoring a control algorithm of a controller for delivering medication from an electronic medication delivery device with an automation risk monitor;

receiving data at the controller from a sensor regarding a medical condition;

comparing the data from the control algorithm and sensor to predetermined medical information to determine a risk of therapy automation to the patient;

comparing the risk of therapy automation to a predetermined risk threshold; and

delivering medication to the patient as automated medication therapy based on the comparison of the risk of therapy automation to the predetermined risk threshold.

16. The method of claim 15 further comprising the step of providing additional automated medication delivery therapy when the risk is below the predetermined risk threshold.

17. The method of claim 16 wherein the automated medication delivery therapy includes delivering insulin.

18. The method of claim 15 further comprising the step of triggering a request for user intervention when the risk is at or above the predetermined threshold to cause a closed loop control to function as an open loop.

19. The method of claim 15 wherein the medical condition is a glucose level of the patient.

20. The method of claim 15 wherein the predetermined medical information includes a risk matrix.

21. The method of claim 20 wherein the risk matrix includes information pertaining to glucose ranges, glucose change, insulin change and risk level.

22. The method of claim 15 wherein the predetermined medical information includes information determined using continuous mapping functions, fuzzy logic or probability calculations.

23. The method of claim 15 wherein the predetermined medical information includes information determined using a mathematical model.

24. The method of claim 23 wherein the mathematical model is defined by one of a pharmacokinetic and a pharmacodynamic model.

25. The method of claim 15 wherein the request for user intervention is sent to the user through a messaging system.

26. The method of claim 20 wherein a portion of the risk matrix is user customizable and includes at least three risk levels comprising high, medium and low risk levels with respective actions associated therewith and at least two of the respective actions are different.

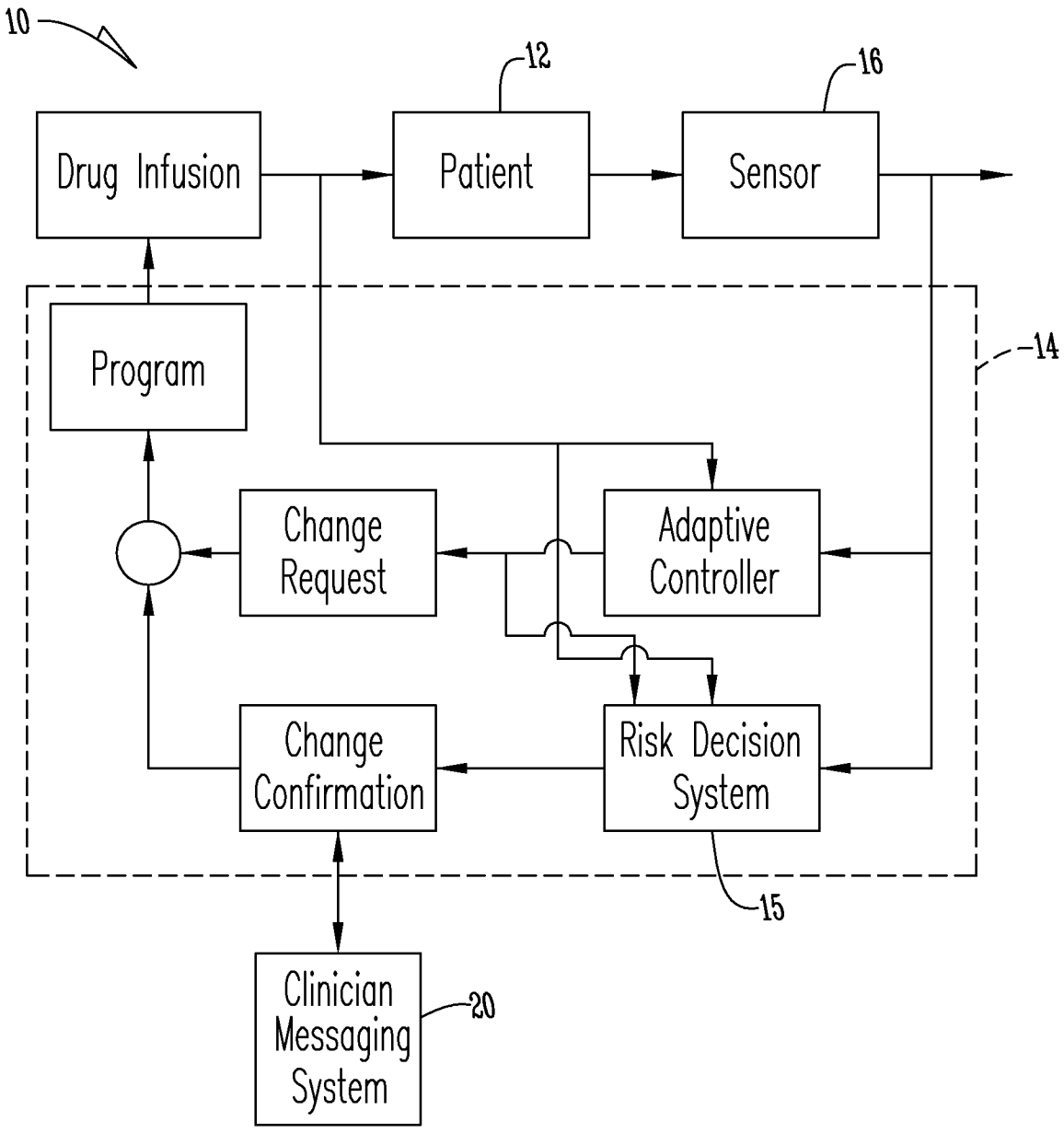
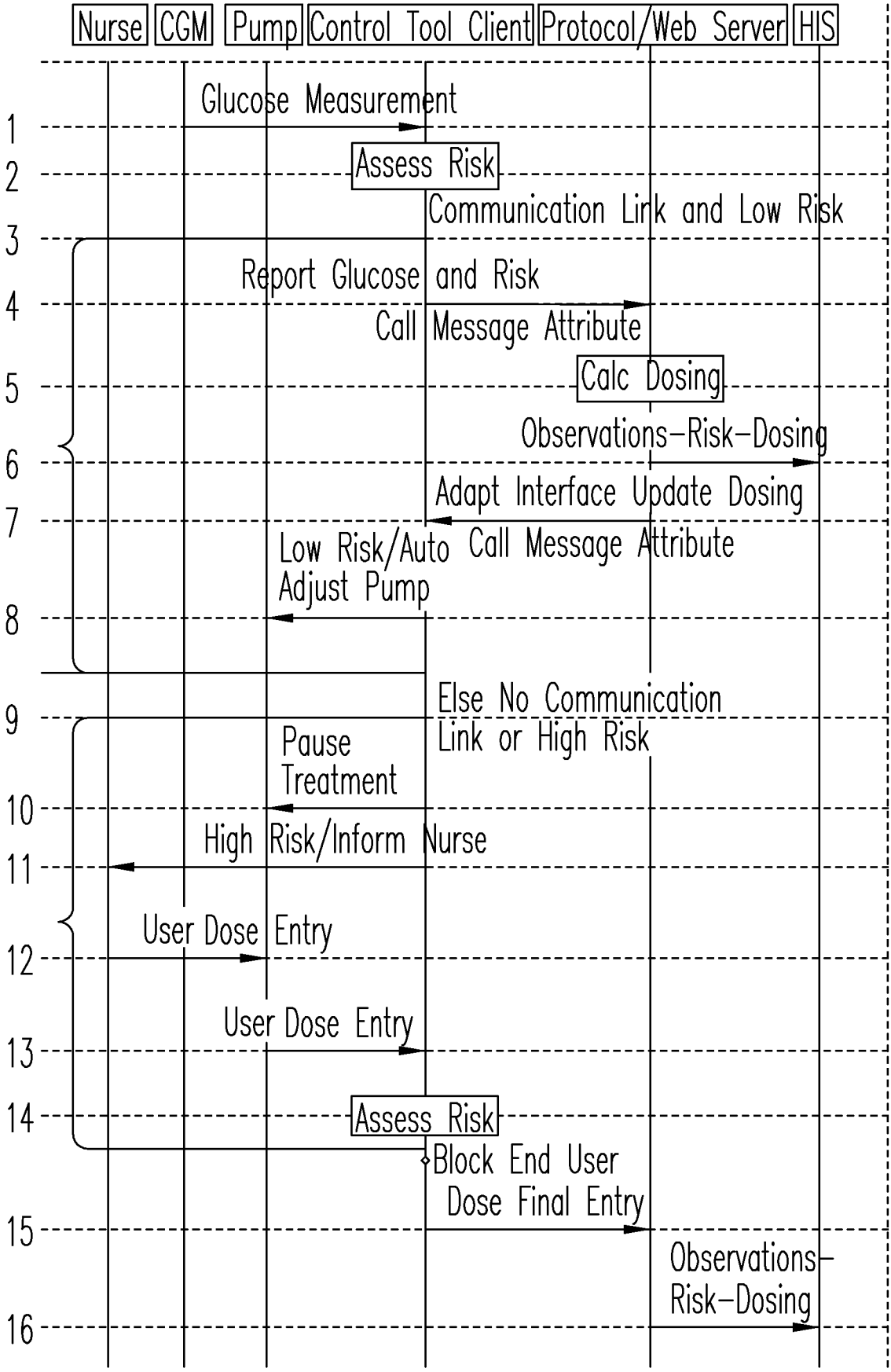

10
12
16
Drug Infusion
Patient
Sensor
Program
14
Change Request
Adaptive Controller
Change Confirmation
Risk Decision System
15
Clinician Messaging System
20

Fig. 1

Fig.2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Pump
Control Tool Client
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Assess Risk
2
Communication Link and Low Risk
3
Report Glucose and Risk
4
Call Message Attribute
Calc Dosing
5
Observations-Risk-Dosing
6
Adapt Interface Update Dosing
7
Low Risk/Auto Call Message Attribute
Adjust Pump
8
Else No Communication
9
Link or High Risk
Pause
Treatment
10
High Risk/Inform Nurse
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12
User Dose Entry
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14
Block End User
Dose Final Entry
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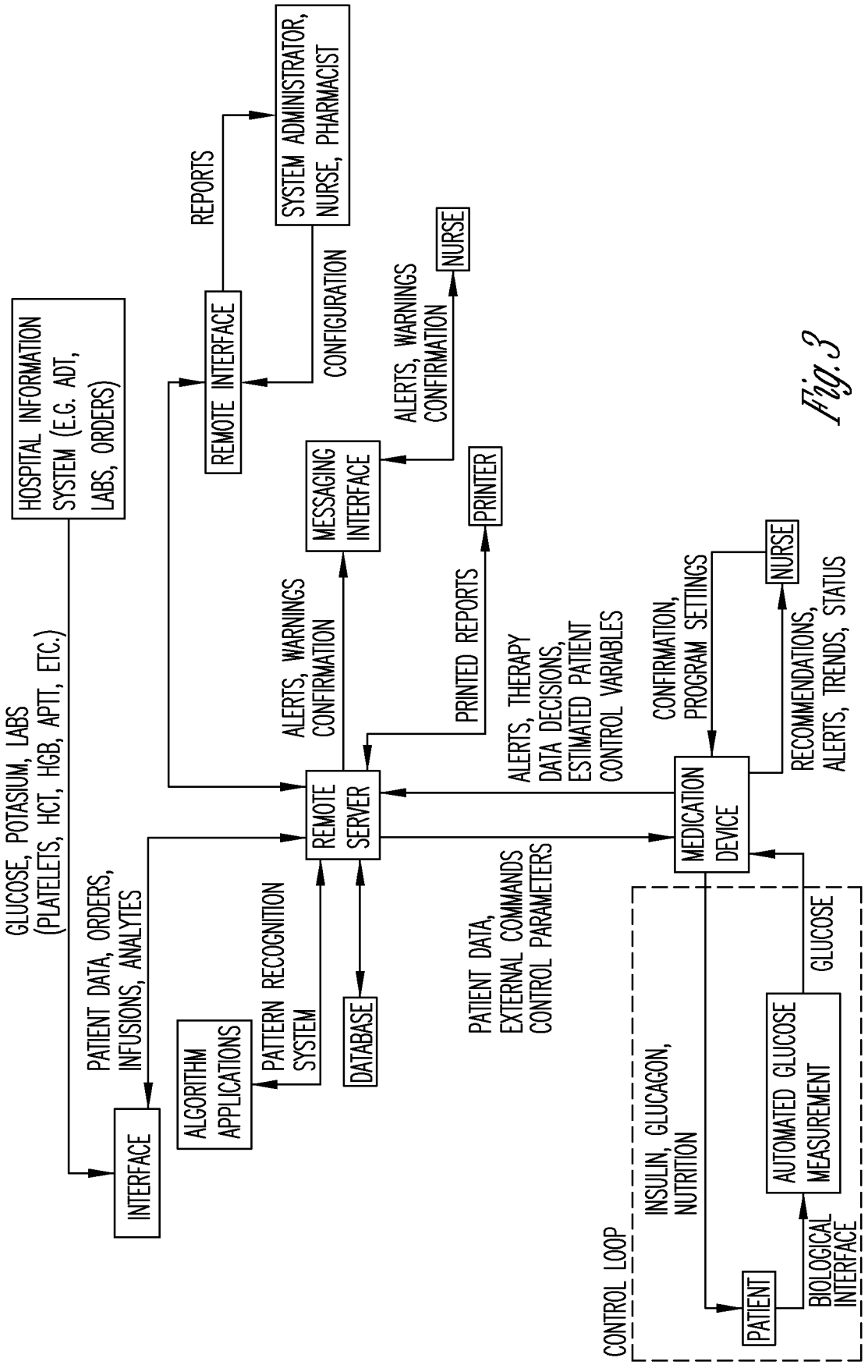
Risk-Dosing
16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GLUCOSE, POTASIUM, LABS (PLATELETS, HCT, HGB, APTT, ETC.)
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INTERFACE
ALGORITHM APPLICATIONS
PATTERN RECOGNITION SYSTEM
DATABASE
REMOTE SERVER
REMOTE INTERFACE
REPORTS
SYSTEM ADMINISTRATOR, NURSE, PHARMACIST
CONFIGURATION
MESSAGING INTERFACE
ALERTS, WARNINGS CONFIRMATION
NURSE
PRINTER
PRINTED REPORTS
ALERTS, WARNINGS CONFIRMATION
ALERTS, THERAPY DATA DECISIONS, ESTIMATED PATIENT CONTROL VARIABLES
PATIENT DATA, EXTERNAL COMMANDS CONTROL PARAMETERS
CONFIRMATION, PROGRAM SETTINGS
MEDICATION DEVICE
NURSE
RECOMMENDATIONS, ALERTS, TRENDS, STATUS
CONTROL LOOP
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PATIENT
BIOLOGICAL INTERFACE
AUTOMATED GLUCOSE MEASUREMENT
GLUCOSE

Fig. 3

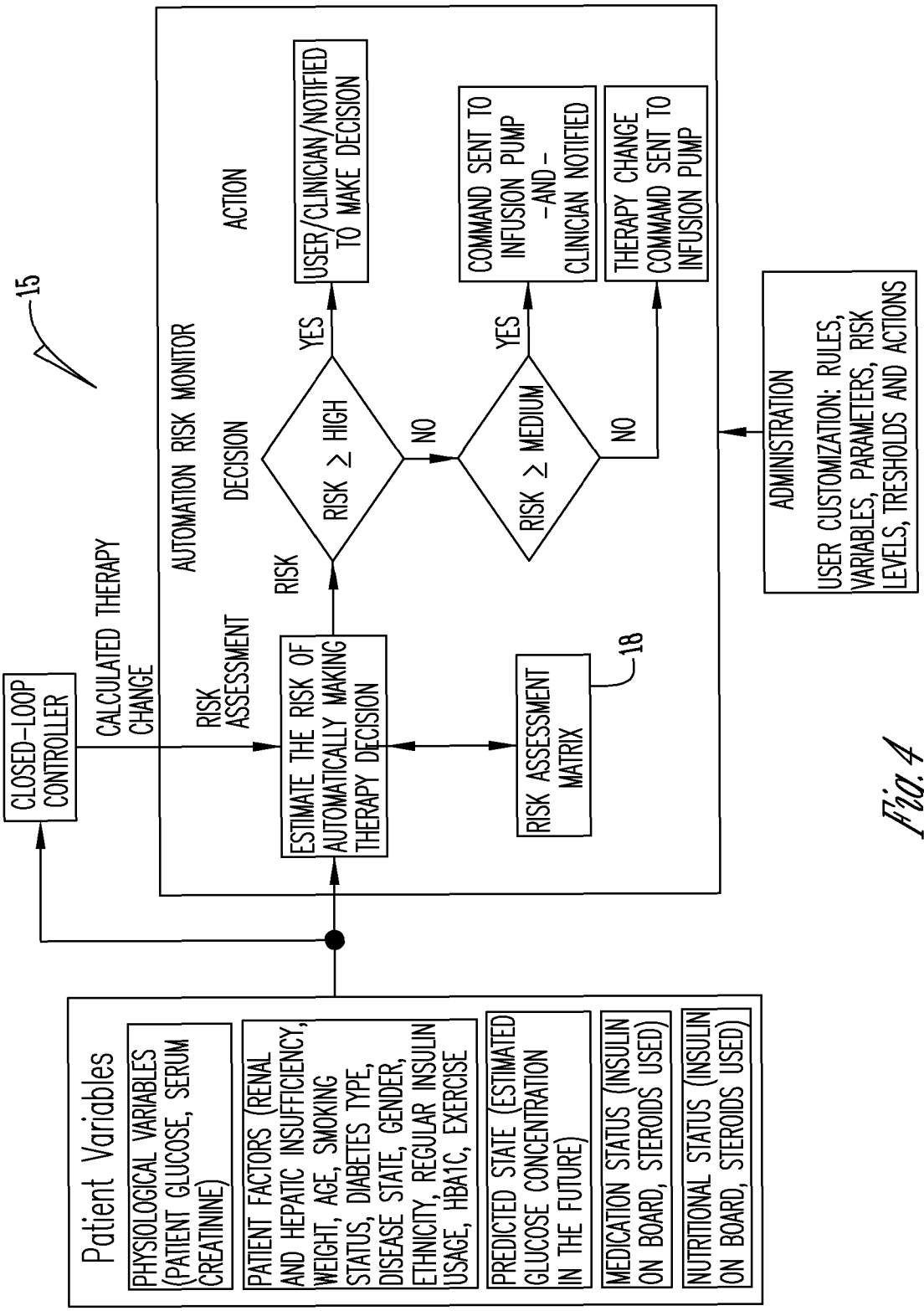
15
AUTOMATION RISK MONITOR
CLOSED-LOOP CONTROLLER
CALCULATED THERAPY CHANGE
RISK ASSESSMENT
ESTIMATE THE RISK OF AUTOMATICALLY MAKING THERAPY DECISION
RISK ASSESSMENT MATRIX
18
RISK
DECISION
RISK ≥ HIGH
YES
NO
RISK ≥ MEDIUM
YES
NO
ACTION
USER/CLINICIAN/NOTIFIED TO MAKE DECISION
COMMAND SENT TO INFUSION PUMP -AND- CLINICIAN NOTIFIED
THERAPY CHANGE COMMAMD SENT TO INFUSION PUMP
ADMINISTRATION
USER CUSTOMIZATION: RULES, VARIABLES, PARAMETERS, RISK LEVELS, TRESHOLDS AND ACTIONS
Patient Variables
PHYSIOLOGICAL VARIABLES (PATIENT GLUCOSE, SERUM CREATININE)
PATIENT FACTORS (RENAL AND HEPATIC INSUFFICIENCY, WEIGHT, AGE, SMOKING STATUS, DIABETES TYPE, DISEASE STATE, GENDER, ETHNICITY, REGULAR INSULIN USAGE, HBA1C, EXERCISE
PREDICTED STATE (ESTIMATED GLUCOSE CONCENTRATION IN THE FUTURE)
MEDICATION STATUS (INSULIN ON BOARD, STEROIDS USED)
NUTRITIONAL STATUS (INSULIN ON BOARD, STEROIDS USED)

Fig. 4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 12/69730

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - G05B 13/02 (2013.01)
USPC - 700/32
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8): G05B 13/02 (2013.01)
USPC: 700/32

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 600/300; 702/177 (keyword limited; terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase; Google Scholar; Google Patents; FreePatentsOnline. Search terms used: deliver-medication patient-medication control-deliver-medication deliver-insulin deliver-therapy patient-therapy, controller control-algorithm control-equation closed-loop-control, sensor sense sample, automate adapt dynamic, risk risk-matrix custom-risk-matrix risk-arra

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 2010/0298765 A1 (BUDIMAN et al.) 25 November 2010 (25.11.2010) entire document, especially Abstract; para [0009], [0024], [0053], [0061], [0070], [0078], [0080], [0085], [0090], [0108], [0110], [0111], [0114], [0117], [0119], [0123], [0129]	1-5, 9-11, 15-19, 23-25 ---------- 6-8, 12-14, 20-22, 26
Y	US 2003/0060688 A1 (CIARNIELLO et al.) 27 March 2003 (27.03.2003) entire document, especially Abstract; para [0013], [0064], [0127]	6, 7, 12, 13, 20, 21, 26
Y	US 2006/0200007 A1 (BROCKWAY et al.) 07 September 2006 (07.09.2006) entire document, especially Abstract; para [0007], [0059], [0060]	8, 22
Y	US 2008/0009684 A1 (CORSETTI et al.) 10 January 2008 (10.01.2008) entire document, especially Abstract; Figs. 10, 11; para [0007], [0169]	14
A	US 2010/0212675 A1 (WALLING et al.) 26 August 2010 (26.08.2010) entire document	1 - 26
A	US 2005/0038680 A1 (MCMAHON) 17 February 2005 (17.02.2005) entire document	1 - 26

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 January 2013 (29.01.2013)	28 FEB 2013

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774