Journal of Diabetes Science and Technology
Volume 2, Issue 5, September 2008

PERSPECTIVES on
Diabetes Information Technology

Definition of Information Technology Architectures for Continuous Data Management and Medical Device Integration in Diabetes

M. Elena Hernando, Ph.D.,[1] Mario Pascual, Ph.D.,[2] Carlos H. Salvador, Ph.D.,[2]
Gema García-Sáez, M.S.,[1] Agustín Rodríguez-Herrero, M.S.,[1] Iñaki Martínez-Sarriegui, M.S.,[1]
and Enrique J. Gómez, Ph.D.[1]

Abstract

The growing availability of continuous data from medical devices in diabetes management makes it crucial to define novel information technology architectures for efficient data storage, data transmission, and data visualization. The new paradigm of care demands the sharing of information in interoperable systems as the only way to support patient care in a continuum of care scenario. The technological platforms should support all the services required by the actors involved in the care process, located in different scenarios and managing diverse information for different purposes. This article presents basic criteria for defining flexible and adaptive architectures that are capable of interoperating with external systems, and integrating medical devices and decision support tools to extract all the relevant knowledge to support diabetes care.

J Diabetes Sci Technol 2008;2(5):899-905

Introduction

The growing availability of continuous data coming from glucose sensors and subcutaneous insulin infusion pumps makes it crucial to define new information technology (IT) architectures for the efficient management of data storage, data transmission, and data visualization. Health care professionals must become involved in the exhaustive evaluation of these new technologies before adopting them in routine clinical practice. The complexity of evaluation is increased because clinical experiments require registering a huge amount of information that is not supported by the current clinical information systems, and their adaptation cannot be performed rapidly.

A fast approach to achieving access to continuous data is to use the proprietary software solutions provided by the device manufactures, either as personal computer or

Author Affiliations: [1]Bioengineering and Telemedicine Group, Polytechnic University of Madrid, Spain, and CIBER-BBN: Networking Research Centre for Bioengineering, Biomaterials and Nanomedicine, Spain, and [2]Department of Telemedicine and Information Society of Health Institute "Carlos III," Madrid, Spain

Abbreviations: (DICOM) Digital Imaging and Communications in Medicine, (EHR) electronic health record, (HL7) Health Level Seven, (IHE) Integrating the Healthcare Enterprise, (IMS) IP Multimedia Subsystem, (IP) internet protocol, (IT) information technologies, (NGN) Next Generation Networks, (PDA) personal digital assistant, (RIA) Rich Internet Applications, (SOA) service-oriented architecture, (XML) Extensible Markup Language

Keywords: diabetes, continuous data management, device interoperability, software architecture

Corresponding Author: M. Elena Hernando, Grupo de Bioingeniería y Telemedicina, ETSI Telecomunicación, Ciudad Universitaria s/n, 28040 Madrid, Spain; email address elena@gbt.tfo.upm.es

Web-based user applications. This approach obviously accelerates the evaluation of a new technology, but can have several harmful consequences in long-term usage. On the one hand, information from different vendors is dispersed, unlinked to the patient electronic health record (EHR). Researchers miss the opportunity to combine the clinical information in order to perform multiparametric studies that will surely accelerate the progress of medical knowledge. On the other hand, the health care organization becomes captive to the proprietary technology and loses autonomy to use other medical devices that are not compatible with those external information systems. The current situation is just the opposite of the open solutions that have succeeded in other medical technology applications with the adoption of standards [i.e., Digital Imaging and Communications in Medicine (DICOM) standard for medical imaging storage and communication].

The evolution of IT technologies is also driven by the need for existing eHealth services to cope with the evolving paradigms of health care as recommended in the continuum of care model concept defined by the World Health Organization.[1] The new paradigm of care promotes novel types of interactions between actors (patient and health care professionals working at different levels) based on the sharing of information in a technology-enabling framework. In this respect, interoperable information systems are the only way to support patient care in a continuum of care scenario.

Several international initiatives are working to solve interoperability problems, enabling the sharing of clinical data among health care information systems in order to avoid the behavior of medical information systems as isolated islands.

One viewpoint of interoperability is to support the health care process across institutional boundaries, resulting in a more consistent continuity of care and contributing to the quality of care.[2] The key to success is achieving semantic interoperability using a two-level modeling paradigm that separates the information model from the knowledge model.[3] In this way, the information systems will be future proof, as the software is independent from the clinical concepts that change over time. The main examples that follow this two-level paradigm are Health Level Seven (HL7) v3.0[4] and the Comitée Européen de Normalisation (European Committee for Standardization) EN13606 norm,[5] both dealing with EHR communication. Semantic interoperability is achieved through codified attributes and archetypes that are bound to terminologies and ontologies (i.e., Systematized Nomenclature of Medicine—Clinical Terms).

Another viewpoint of interoperability relates to the integration of commercial devices for either monitoring or insulin delivery. Nowadays, no international standard specifically solves the problem of medical device integration in home or in ambulatory telemonitoring scenarios. The family of standards International Organization for Standardization 11073/Institute of Electrical and Electronics Engineers 1073,[6] also referred to as Point of Care medical device communication, covers the communication of medical devices at the point of care, but additional efforts are needed to extend those standards to support ambulatory monitoring.[7] Another international initiative is Integrating the Healthcare Enterprise (IHE), which promotes the coordinated use of established standards such as DICOM and HL7 to address specific clinical needs in support of optimal patient care.[8] IHE is not a standard in itself, but provides recommendations through the definition of "integration profiles" for common interoperability problems. Although the companies most active in IHE belong to the field of medical imaging systems, there exists a growing interest on the part of hospital information system companies to be compliant with IHE Cross Enterprise Document Sharing profiles, and there are several initiatives to define IHE profiles for specific health care applications (i.e., home monitoring devices). In addition, the Continua Health Alliance in the United States also works toward the implementation of interoperability of health care services, as well as end-user devices and sensor systems from different manufacturers.[9]

Information and communication technologies have been used for remote monitoring in diabetes care in the past. From the point of view of functional components, a system for diabetic patients' follow-up requires managing self-monitoring data and at least has to include blood glucose transmission capabilities and asynchronous expert feedback. The simplest architectures are the point-to-point ones that support the transmission of home glucose monitoring values by telephone, sending data directly from the glucose meter to a server using a modem or a mobile terminal. Some reviews can be found elsewhere.[10,11]

In some instances, the expert feedback has been delivered synchronously using a phone[12] or videoconference,[13] but the tendency is to send the expert feedback asynchronously using Web-based applications,[14] short messages with mobile phones,[15] or personal digital assistants (PDA).[16]

Currently, Web applications are commonly used because the adoption of Internet protocols (IP), and Web protocols reduce the problems of software installation and maintenance at the patient's home and professionals' workplaces. The most common solution used to support remote monitoring and ubiquitous care scenarios is the integration of Web applications and mobile terminals, such as mobile phones or PDAs, allowing the transmission of health care information and the reception of expert feedback in a short time.

The latest generation of telemedicine platforms is implemented as distributed architectures spreading the users' interactions mechanisms, for example, with a videoconference[13] or multiaccess portable devices.[17] Patients are provided with electronic diaries implemented in Web applications,[14,18] mobile phones,[15] or smart personal assistants[19] to register blood glucose, insulin, continuous glucose monitoring, diet, physical exercise, and so on.

The main advantage of the electronic management of data is that health care professionals and patients can benefit from decision-making aids that exploit the multiparametric information either for graphical visualization or for automatic generation of warnings and reminders.[18,20] Currently, distributed telemedicine architectures can contribute to make the dream of an "ambulatory artificial pancreas" a reality, with the integration of portable control systems capable of closing the loop by modifying the pump insulin delivery.[21]

The aim of this article is to present some basic criteria for the definition of flexible and adaptive platforms, capable of interoperating with external systems, and integrating medical devices and decision support tools to extract all the relevant knowledge to support diabetes care.

Criteria for the Design of Efficient Architectures

The platform architecture is the technological core that allows the optimal management of information. The architectural design has to guarantee the interoperability between patient and professional environments and must assure that the information is available 24 hours a day. The availability of monitoring tools and automatic reporting services for platform audit is mandatory for the awareness of how services are operating.

The technological platforms have to support all the services required by the actors involved in the care process, located in different scenarios (i.e., the health professional in a corporative network, the patient at home, the third-party company that provides monitoring services), managing diverse information for different purposes (i.e., patient care, experimental evaluation studies, cost analysis studies).

Within this context, the architectural requirements are no different from those demanded by any company of a technological platform that supports its activity:

- Capacity for rapid evolution and adaptation to changes based on reusable components, and independence of the underlying technological infrastructure.
- Capacity for interoperability with other systems, with the ability to integrate heterogeneously distributed components from legacy systems and third parties.
- Transparency to users, who will perceive it as a medical care service integrated into the health care context.
- Capacity for scalability, with the ability to support research activities from reduced pilots to extensive multicenter interventions.
- Robustness, security, maintainability, and 24-hour availability.

The model that best matches the aforementioned requirements is a service-oriented distributed architecture based on concepts such as interoperability, portability, use of open standards, and ability to integrate different functional areas working in a coordinated and transparent way.

Open Source Software

The Global Observatory for eHealth, created in 2005 by the World Health Organization, emphasizes the development of open source eHealth tools and services.[22] Because the open-source license makes source code available with relaxed or nonexistent copyright restrictions, use of the software is not limited, making it possible to study the code in order to learn how it works and to adapt it to one's needs. Among others, the main benefits to users are easy evaluation and acquisition, adaptability and easy integration, code availability for quality inspection, independence of providers' survival, a tool for learning, and a good method to establish standards. However, the use of open source software is not possible in all situations. Specifically, the integration of commercial medical devices usually makes it necessary to develop ad-hoc nonstandard solutions to integrate proprietary software from the manufacturer.

We consider that a basic requirement for a service platform is to use software under open-source licenses.

Communication Standards and Networks

In a heterogeneous context, it is important to choose communication technologies that are able to achieve the uniformity of the interconnection among different components as a significant step toward the interoperability, scalability, and robustness of the whole system. Consequently, all the technologies based on IP protocols are suitable for implementing the platform communications. IP technologies also guarantee access to public networks, such as the internet, using different access networks (Asymmetric Digital Subscriber Line, General Packet Radio Service, Universal Mobile Telecommunications System, etc.). **Figure 1** shows a nonexhaustive evolution of internet, wireless, and mobile technologies in recent years.

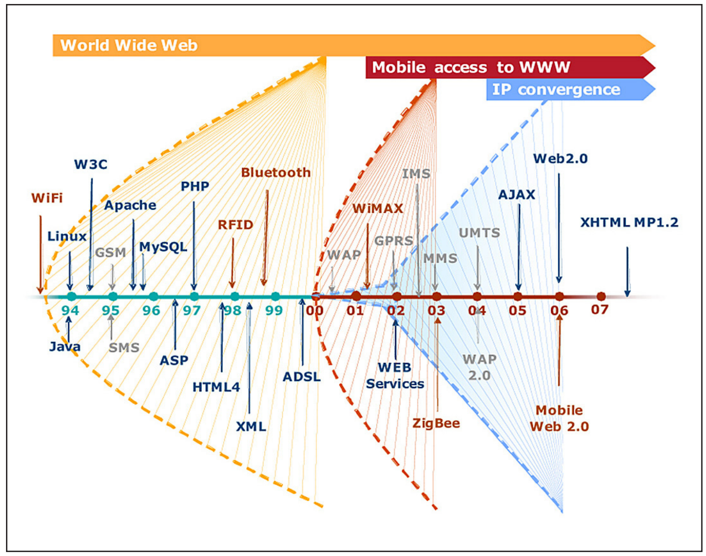

Figure 1. Evolution of internet and mobile technologies toward IP convergence. WiFi, Wireless Fidelity; GSM, Global System for Mobile; RFID, radio frequency identification; WAP, Wireless Application Protocol; WiMAX, Worldwide Interoperability for Microwave Access; GPRS, General Packet Radio Service; MMS, Multimedia Messaging Service; UMTS, Universal Mobile Telecommunications System; AJAX, Asynchronous JavaScript and XML; XHTML MP, Extensible Hypertext Markup Language Mobile Profile; SMS, Short Message Service; ASP, Active Server Pages; HTML, HyperText Markup Language; ADSL, Asymmetric Digital Subscriber Line; WAP, Wireless Application Protocol.

The Next Generation Networks (NGN) will enable the convergence between fixed and mobile networks by integrating current networks and services into a single all-IP-based architecture. An example of NGN is the new standard IP Multimedia Subsystem (IMS), which solves the limitations of the open IP networks independently of the access network. The IMS networks will speed up the development of end-user applications because they provide basic communications services or enablers (i.e., multivideoconferencing, presence, multimedia messaging, group list management, quality of service, access awareness, security, charging) that can be integrated directly within the applications.[23]

Platform Software and Services

Within a software platform, we could distinguish between services that have to interact with the external users (front-end services) and other services for data processing and for internal operation of the platform (back-end services). The conceptual separation of these two types of services allows service reuse and rapid adaptation to new requirements.

To implement the back-end services, the most appropriate approach is to follow service-oriented architecture (SOA).[24] Applications in SOA are built based on services that can be used by different applications or processes and can be implemented using different technologies, such as Remote Method Invocation, Distributed Component Object Model, Common Object Request Broker Architecture, or Web services. The term "Web service" specifically refers to clients and servers that communicate using Extensible Markup Language (XML) messages that follow the Simple Object Access Protocol standard.[25] In one report, the HL7-OMG Healthcare Services Specification Project proposed a SOA approach to develop clinical decision support systems as the most effective approach to enable their widespread adoption within the health care systems.[26]

To implement the front-end services, the most appropriate approach is to build Web-based applications. The Web clients are already available in personal computers and PDAs. Some mobile phones also have a Web client, but, if not, most of them have indirect access to the World Wide Web through the Wireless Application Protocol.

The time response for page refresh is one of the disadvantages of Web applications. When high interactivity is required, the Web technology is moving to Rich Internet Applications (RIA) running on the client side, that is to say, the user Web navigator. One of the Web 2.0 programming technologies that supports RIA is "Asynchronous JavaScript and XML," which achieves an increased responsiveness of Web pages by exchanging small amounts of data with the server and the rest of the layout does not need to be redrawn on each page update.

In the context of distributed services, where information comes from different sources, the evolution of Web applications is the so-called "mashup." In technology, a mashup is a hybrid Web application that combines data from more than one source into a single integrated tool. We can consider mashups as the evolution of Web portals. A mashup for clinical applications should be focused on data aggregation and presentation and should also add collaborative functionality, making the end result suitable for an integrated view of the patient EHR.

Figure 2 shows the proposed mashup–SOA architecture that could integrate the platform front-end and back-end services.

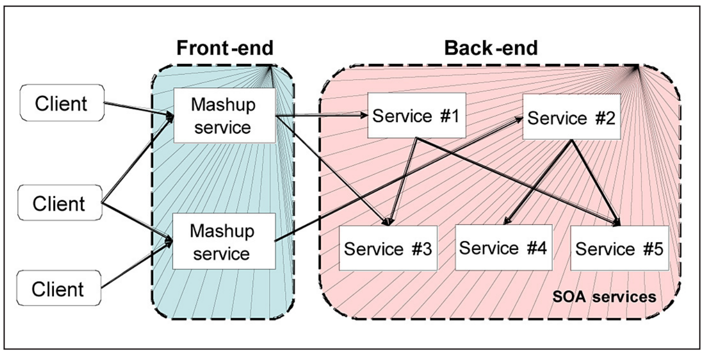

Figure 2. Proposed mashup–SOA architecture.

Each end user accesses the system through a different mashup service that presents the information according to the user role and privileges. In the back end, the SOA services implement well-defined functionalities (i.e., messaging, information search, access to terminology sources, drug interaction queries) that can be reused within different end-user applications. The authors have already implemented the proposed architecture in a follow-up service for hypertensive patients that has been tested successfully in a randomized controlled trial.[27]

Interoperability with Medical Devices

Most of the medical devices suitable for diabetes care (i.e., glucose meters, insulin pumps, subcutaneous glucose sensors, weight scales, pedometers) not only display the information to the user, but also have an internal memory to record previous values and are able to transmit this information to a computer. The ideal picture is to integrate these medical devices into our IT platform, avoiding any manual transcription of data. However, the information transmitted by the medical device is received, processed, and stored by proprietary software provided by the manufacturer. The communications protocols and data formats are not usually public and, thus, the integration requires a close collaboration with the manufacturer, which has to open the product to the platform developers.

When information on communication protocols is provided, we can develop an ad-hoc SOA service to integrate the device into the proposed architecture in a user-transparent way; otherwise the integration requires developing middleware software that encapsulates the manufacturer software and converts it into a SOA service, but users still have to interact with the third-party software. In any case, manufacturers tend to change the communication procedures upon the introduction of any new device version and, consequently, our communication services have to be modified. The adoption of standards by manufacturers should minimize the current efforts to integrate medical devices.

Security

The selection of a model of architecture based on distributed services increases the complexity of security aspects due to the implicit dispersion of the resources. The degree of complexity depends on different aspects, such as the legal framework and the specific user requirements. Some major issues that should be considered are as follows.

- Secure access to both physical and telematic platforms. Access control should take into account different user roles and privileges, the use of firewalls, and strategies of network segmentation, service filtering, and so on.

- Secure data storage, covering aspects such as data encryption, privacy, data integrity, and access logging.

- Secure data transmission. Any information transfer through public networks must be encrypted. Some common technical approaches involve the use of Hypertext Transfer Protocol secure/Secure Sockets Layer or virtual private networks over IP security.

- Secure platform integrity and 24-hour availability, providing hardware redundancy such as clusters of servers, data storage with redundant arrays of independent disk level 5, redundant power systems, uninterruptible power supply, backup strategies, and so on.

Analysis and Visualization of Continuous Data

The complexity of data analysis in diabetes implies the need for complementary approaches that go from statistical analysis to time series analysis, model-based techniques, or artificial intelligence methods. Statistical analysis is useful in extracting basic information that can be used in further analysis, but is usually insufficient for summarizing the patient's status because it does not take into account the temporal structure of data. The definition of advanced mathematical indexes can extract data on the dynamic characteristics to assess patients' metabolic control.[28–30] Analysis based on physiological models can simulate the patient and disease course and can be used for diagnostics, therapy planning, and education.[31] Analysis based on artificial intelligence approaches is useful for data interpretation, diagnostics, diet planning, and insulin dosage adjustment.[32–34] Automated tools can also generate automatic alarms to notify patients and/or professionals after detecting risky situations.[35]

The analysis and the presentation of continuous information have yet to be well defined. Continuous data analysis demands a lot of time on the part of the professionals and, in the case of the patients, requires skills and knowledge that they usually do not possess. Therefore, it is necessary to define multiparametric analytical methods and decision support tools able to extract all the relevant knowledge from data in order to evaluate the effectiveness of therapy, to detect erroneous behaviors or hazardous situations, to assess patient risk, and to prognosticate the disease course over time.

Discussion

The management of continuous data in diabetes is becoming increasingly common, and the availability of new medical devices for therapy and monitoring is growing fast. For an optimal management of information, we require flexible and adaptive platforms able to keep up with the rapid evolution of user needs. In addition, the new paradigm of care demands the sharing of information in interoperable systems as the only way to support patient care in a continuum of care scenario. The technological platforms should support all the services required by the actors involved in the care process, located in different scenarios and managing diverse information for different purposes.

The adoption of IP and Web protocols reduces the problems of software installation and maintenance at the patient's home and professionals' workplaces. The use of Web applications and mobile terminals, such as mobile phones or PDAs, are the best solutions to support remote monitoring and ubiquitous care scenarios, allowing the transmission and visualization of health care information and the reception of expert feedback in a short time.

The complexity of data analysis in diabetes implies the need for complementary approaches that go from statistical analysis to time series analysis, model-based techniques, or artificial intelligence methods. The analysis and the presentation of multiparametric continuous information are ways to enhance health care professionals' and patients' decision making.

The authors propose a service-oriented architecture paradigm combined with mashup applications accessible from all-IP networks to fulfill all the requirements for continuous data management and medical device integration in diabetes.

Nevertheless, in contrast with the standardized scenario of software platforms and networks, the integration of medical devices is still an unsolved problem. In fact, communication with insulin pumps, continuous glucose sensors, glucose meters, pedometers, and so on is not standardized at all. The integration of any new device into the information system requires new developments and the collaboration of manufacturers in replication of the communication protocols. Users should form an alliance to demand common solutions from the industry that will speed up the evaluation and penetration of new technologies in routine patient care in diabetes.

Funding:

This work was partially supported by a Spanish FIS grant from the Ministry of Health and Consumer Affairs "ADVISING"-FIS PI060437 and the MOBIS Research Programme funded by Fundación Vodafone España and Instituto de Salud Carlos III.

References:

1. Pruitt S. Innovative care for chronic conditions: building blocks for action: global report. Geneva: World Health Organization; 2002. Report No.: WHO/MNC/CCH/0201.
2. van Servellen G, Fongwa M, D'errico EM. Continuity of care and quality care outcomes for people experiencing chronic conditions: a literature review. Nurs Health Sci. 2006;8(3):185-95.
3. Beale T. Archetypes: constraint-based domain models for future-proof information systems [cited 2008, Apr 4]. Available from: http://www.oceaninformatics.biz/publications/archetypes_new.pdf.
4. Health Level Seven, Inc. Health Level Seven Standard for clinical records [cited 2008, Apr 4]. Michigan: Available from: http://www.hl7.org.
5. Health informatics, Electronic healthcare record communication, Part 1: Extended architecture. 2007. Report No.: CEN ENV 13606-1.
6. Health informatics. Point-of-care medical device communication. 2004. Report No.: ISO11073/IEEE1073.

7. de Toledo P, Galárraga M, Martínez I, Serrano L, Fernández J, del Pozo F. Towards e-Health device interoperability: the Spanish experience in the telemedicine research network. Proc. of the 28th Ann Int Conf IEEE Eng Med Biol Soc.; 2006 Aug 30-Sept 3; New York City. 2006.

8. IHE: Integrating the healthcare enterprise. IHE International [cited 2008, April 4]. Available from: http://www.ihe.net/.

9. Continua Health Alliance [cited 2008, April 4] . Oregon: VTM Inc. Available from: http://www.continuaalliance.org.

10. Wojcicki JM. Analysis: transfer of the data collected by the patient to the health care providers: problems and solutions. Diabetes Technol Ther. 2005;7(2):248-52.

11. Farmer A, Gibson OJ, Tarassenko L, Neil A. A systematic review of telemedicine interventions to support blood glucose self-monitoring in diabetes. Diabet Med. 2005;22(10):1372-8.

12. Liesenfeld B, Renner R, Neese M, Hepp KD. Telemedical care reduces hypoglycemias and improves glycemic control in children and adolescents with type 1 diabetes. Diabetes Technol Ther. 2000;2(4):561-7.

13. Starren J, Hripcsak G, Sengupta S, Abbruscato CR, Knudson PE, Weinstock RS, Shea S. Columbia University's Informatics for Diabetes Education and Telemedicine (IDEATel) project: Technical implementation. J Am Med Inform Assoc. 2002;9(1):25-36.

14. Cho J, Chang S, Kwon H, Choi Y, Ko S, Moon S, Yoo S, Song K, Son H, Kim H, Lee W, Cha B, Son H, Yoon K. Long-term effect of the Internet-based glucose monitoring system on HbA1c reduction and glucose stability: a 30-month follow-up study for diabetes management with a ubiquitous medical care system. Diabetes Care. 2006;29(12):2625-31.

15. Farmer AJ, Gibson OJ, Dudley C, Bryden K, Hayton PM, Tarassenko L, Neil A. A randomized controlled trial of the effect of real-time telemedicine support on glycemic control in young adults with type 1 diabetes (ISRCTN 46889446). Diabetes Care. 2005;28(11):2697-702.

16. Rigla M, Hernando ME, Go´mez EJ, Brugue´s E, Garci´a-Sa´ez G, Torralba V, Prados A, Erdozain L, Vilaverde J, de Leiva A. A telemedicine system that includes a personal assistant improves glycemic control in pump-treated patients with type 1 diabetes. J Diabetes Sci Technol. 2007;1(4):505-10.

17. Bellazzi R, Arcelloni M, Bensa G, Blankenfeld H, Brugue´s E, Carson E, Cobelli C, Cramp D, D'Annunzio G, De Cata P, De Leiva A, Deutsch T, Fratino P, Gazzaruso C, Garci`a A, Gergely T, Go´mez E, Harvey F, Ferrari P, Hernando E, Boulos MK, Larizza C, Ludekke H, Maran A, Nucci G, Pennati C, Ramat S, Roudsari A, Rigla M, Stefanelli M. Design, methods, and evaluation directions of a multi-access service for the management of diabetes mellitus patients. Diabetes Technol Ther. 2003;5(4):621-9.

18. Kim C, Kim H, Nam J, Cho M, Park J, Kang E, Ahn C, Cha B, Lee E, Lim S, Kim K, Lee H. Internet diabetic patient management using a short messaging service automatically produced by a knowledge matrix system. Diabetes Care. 2007;30(11):2857-8.

19. Rigla M, Hernando ME, Gomez EJ, Brugues E, Garcia-Saez G, Capel I, Pons B, de Leiva A. Real-time continuous glucose monitoring together with telemedical assistance improves glycemic control and glucose stability in pump-treated patients. Diabetes Technol Ther. 2008;10(3):194-9.

20. Hernando ME, Garcia G, Gomez EJ, del Pozo F. Intelligent alarms integrated in a multi-agent architecture for diabetes management. Trans Inst Measurement Control. 2004;26(3):185-200.

21. Gomez E, Hernando ME, Vering T, Rigla M, Bott O, Garcia-Saez G, Pretschner P, Brugues E, Schnell O, Patte C, Bergmann J, Dudde R, de Leiva A. The INCA system: a further step towards a telemedical artificial pancreas. IEEE Trans Inform Technol Biomed. In press 2008.

22. eHealth tools and services: Needs of the member states. World Health Organization; 2006. Report No.: Report of the WHO Global Observatory for eHealth.

23. Russell T. The IP Multimedia subsystem (IMS): session control and other network operations. McGraw-Hill Osborne Media; 2007.

24. Earl T. Service-oriented architecture: concepts, technology and design. Prentice Hall; 2006.

25. Alonso G, Casati F, Kuno H, Machiraju V. Web services: concepts, architectures and applications. Springer Verlag; 2004.

26. Kawamoto K, Lobach DF. Proposal for fulfilling strategic objectives of the U.S. roadmap for national action on decision support through a service-oriented architecture leveraging HL7 services. J Am Med Inform Assoc. 2007;14(2):146-55.

27. Pascual MM, Salvador CC, Sagredo PP, Marquez-Montes JJ, Gonzalez MM, Fragua JJ, Carmona MM, Garcia-Olmos LL, Garcia-Lopez FF, Munoz AA, Monteagudo JJ. Impact of patient-general practitioner short messages based interaction on the control of hypertension in a follow-up service for low-to-medium risk hypertensive patients. A randomized controlled trial. IEEE Trans Inform Technol Biomed. In press 2008.

28. Schlichtkrull J, Munck O, Jersild M. The M-value, an index of blood sugar control in diabetics. Acta Med Scand. 1965;177(0001-6101):95-102.

29. Wojcicki JM. "J"-index. A new proposition of the assessment of current glucose control in diabetic patients. Horm Metab Res. 1995;27(1):41-2.

30. Kovatchev BP, Clarke WL, Breton M, Brayman K, McCall A. Quantifying temporal glucose variability in diabetes via continuous glucose monitoring: mathematical methods and clinical application. Diabetes Technol Ther. 2005;7(6):849-62.

31. Berger MP, Gelfand RA, Miller PL. Combining statistical, rule-based, and physiologic model-based methods to assist in the management of diabetes mellitus. Comput Biomed Res. 1990;23(4):346-57.

32. Hernando ME, Go´mez EJ, Corcoy R, Del Pozo F. Evaluation of DIABNET, a decision support system for therapy planning in gestational diabetes. Comput Methods Programs Biomed. 2000;62(3):235-48.

33. Montani S, Magni P, Bellazzi R, Larizza C, Roudsari AV, Carson ER. Integrating model-based decision support in a multi-modal reasoning system for managing type 1 diabetic patients. Artif Intell Med. 2003;29(1-2):131-51.

34. Petot GJ, Marling C, Sterling L. An artificial intelligence system for computer-assisted menu planning. J Am Diet Assoc. 1998;98(9):1009-14.

35. Hernando ME, Garcia G, Gomez EJ, del Pozo F. Intelligent alarms integrated in a multi-agent architecture for diabetes management. Trans Inst Meas Control. 2004;26(3):185-200.