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Management of Patients with Diabetes Through Information Technology: Tools for Monitoring and Control of the Patients' Metabolic Behavior

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ABSTRACT

Background: The junction of telemedicine home monitoring with multifaceted disease management programs seems nowadays a promising direction to combine the need for an intensive approach to deal with diabetes and the pressure to contain the costs of the interventions. Several projects in the European Union and the United States are implementing information technology-based services for diabetes management using a comprehensive approach. Within these systems, the role of tools for data analysis and automatic reminder generation seems crucial to deal with the information overload that may result from large home monitoring programs. The objective of this study was to describe the automatic reminder generation system and the summary indicators used in a clinical center within the telemedicine project M^{2}DM, funded by the European Commission, and to show their usage during a 7-month on-field testing period.

Methods: M^{2}DM is a multi-access service for management of patients with diabetes. The basic functionality of the technical service includes a Web-based electronic medical record and messaging system, a computer telephony integration service, a smart-modem located at home, and a set of specialized software modules for automated data analysis. The information flow is regulated by a software scheduler, called the Organizer, that, on the basis of the knowledge on the health care organization, is able to automatically send e-mails and alerts notifications as well as to commit activities to software agents, such as data analysis. Thanks to this system, it was possible to define an automatic reminder system, which relies on a data analysis tool and on a number of technologies for communication. Within the M2DM system, we have also defined and implemented a number of indexes able to summarize the patients' day-by-day metabolic control. In particular, we have defined the global risk index (GRI) of developing microangiopathic complications.

Results: The system for generating automatic alarms and reminders coupled with the indexes for evaluating the patients' metabolic control has been used for 7 months at the Fondazione Salvatore Maugeri (FSM) in Pavia, Italy. Twenty-two patients (43 ± 16 years old, 12 men and 10

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women) have been involved; six dropped out from the study. The average number of monthly automatic messages was 29.44 ± 9.83, *i.e.,* about 1.8 messages per patient per month. The number of monthly alarm reminders generated by the system was 16.44 ± 4.39, so that the number of alarms per patient was about 1. The number of messages sent by patients and physicians during the project was about 13 per month. The GRI analysis shows, during the last trimester, a slight improvement of the performance of the FSM clinic, with a decrease in the percentage of badly controlled values from 33% to 27%. Finally, we found the presence of a linear increasing correlation between the mean GRI values and the number of alarms generated by the system.

Conclusions: A telemedicine system may incorporate features that make it a suitable technological backbone for implementing a disease management program. The availability of data analysis tools, automated messaging system, and summary indicators of the effectiveness of the health care program may help in defining efficient clinical interventions.

INTRODUCTION

Diabetes mellitus is reaching epidemic proportions in western countries. It is estimated that the prevalence of diabetes is of about 5.2% in the regions affiliated with the International Diabetes Federation, and that such prevalence will progressively rise in the next few years, mainly because of the population's aging and to the behavioral changes in diet and lifestyle.[1] Diabetes mellitus has unfortunately a large social and economic impact, being related to the development of major micro- and macrovascular complications.[2–4] North American and European studies have shown that the costs for management of patients with diabetes are staggering: The majority of costs are related to hospitalization due to diabetes-related complications.[5–8] It is therefore becoming mandatory to define suitable programs in order to improve the overall disease management process, including support for metabolic control optimization and guidelines for the screening and prevention of complications. Recent studies and reviews have shown that the so-called "multifaceted" organizational interventions may have a strong impact in terms of clinical outcomes. Such interventions usually represent a paradigm shift in the management of disease: They involve general practitioners, specialists, and patients in a comprehensive program that comprises education, use of clinical guidelines, feedback for patients, and second opinion consultations for general practitioners. The capability to communicate is an essential feature of this programs: Faxes, e-mails, telephones, and educational material distributed using the surface mail are, systematically or not, used and recommended during those interventions.[9,10]

Rather interestingly, diabetes mellitus is the chronic disease for which the largest number of telemedicine studies has been reported in the literature.[11] The main reason is related to the peculiar characteristics of the disease treatment: Patients with diabetes must often (depending on the kind and severity of the disease) self-monitor their blood glucose levels, and in relation to the measurements' values, they are educated to change their daily therapy, following therapeutic protocol and lifestyle guidelines defined by the health care managers. All the data collected during self-monitoring, comprising blood glucose readings, ketonuria analysis, and meal intakes, are reported into diaries, which can be on paper or also electronic. A telemedicine system, designed to allow the patients to transmit the data collected to a medical center, may enable the care manager to give promptly advices to patients, to better patients' education, and finally to improve the metabolic control level. A meta-analysis of telemedicine applications in diabetes management has confirmed such intuition, although the improvement reported is not highly significant from a clinical viewpoint.[12]

The junction of telemedicine home monitoring with multifaceted disease management programs seems nowadays a promising direction to combine the need of an intensive approach to deal with diabetes and the pressure to contain the costs of the interventions. To this end, the U.S. Health Care Financing Administration (Medicare and Medicaid) has recently funded with a $28 million grant the IDEATEL project,[13,14] which aims to evaluate the cost-effectiveness of telemedicine-based disease management in diabetes. IDEATEL is designed to provide a telemedicine service to manage patients with diabetes in rural or urban underserved areas. The European Commission has funded several projects in the area of diabetes management since the early 1990s, too. Within the V framework funding (1998–2002) seven projects dealt with the application of information technology to the management of diabetes.[15] Some of those projects were targeted to test specific technological solutions, while some others have been oriented to cope with specific aspects of the disease, such as diabetic retinopathy. Among them, the project M^{2}DM (Multi-Access Services for Managing Diabetes Mellitus patients) represents a technological and organizational advanced solution for dealing with complex telemedicine interventions.[16] M^{2}DM was devoted to designing and testing a platform for managing patients with all types of diabetes. The basic concept of M^{2}DM is to define a service for disease management with remote monitoring capabilities relying on multi-access technologies: A central database server can be accessed through the Web, through the phone, or through dedicated software for data downloading from the glucose measurement instrument (glucometer). Depending on the different communication systems used, different services are provided to the users: An electronic patient record, a multimedia messaging system, a guideline-based expert system, a statistical analysis package, and a mathematical simulation package are some examples of the available functionalities.[17] Among the different research objectives that were pursued in the project, the capability of the telemedicine system to deal with the information overload was investigated. To this end, we have worked on the definition of technological instruments for data analysis, reminder generation, and data summarization at the patient and at the center level. In this paper we describe the experience that was carried on within the M^{2}DM project by one of the clinical centers involved, the Fondazione Salvatore Maugeri Hospital (FSM), Pavia, Italy, in the definition of tools for long-distance monitoring and control of the patients' metabolic behavior.

SUBJECTS AND METHODS

The M^{2}DM project was funded in the years 2000–2002. Nine European partners have been involved, including universities, technical companies, and five hospitals. The project design, implementation, and results have been reported elsewhere[16]; the final clinical assessment of the results is still underway.[17] The basic technical service includes a Web-based electronic medical record and messaging system, a computer telephony integration (CTI) service based on an interactive voice response system, and a smart-modem located at home. A distinguishing feature of M^{2}DM is to exploit technology for managing the knowledge available to patients and physicians. To this end, the information flow is regulated by a software scheduler, called the Organizer, that, on the basis of the knowledge on the health care organization, is able to automatically send e-mails and alerts notifications, as well as to commit activities to specialized software modules, such as data analysis.

Within the project, a specific project has been carried on at the IRCCS FSM with the following goals:

1. Define a strategy for generation of automatic reminders based on rules predefined by physicians.
2. Define overall indicators at the patient and at the medical center level in order to have a dynamic picture of the patients' metabolic control.

Concerning the first issue, the technical implementation of the reminder system has been made possible thanks to the flexibility of the overall architecture of the M^{2}DM system; in particular, the software modules devoted to generation of reminders implemented at the FSM are described in Figures 1 and 2. The patient may send the data (Fig. 1) by resorting to a smart-modem (Acculink Modem™, Roche Diagnostics, Indianapolis, IN), which enables di-

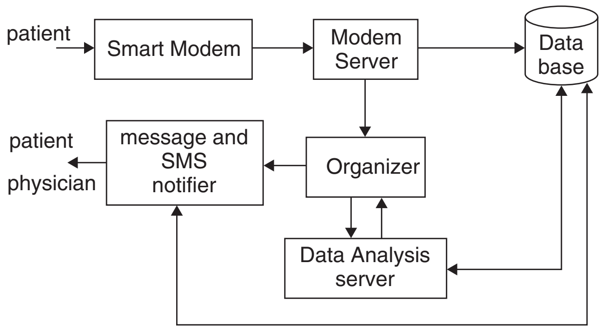

FIG. 1. The M2DM system components involved in the reminder generation based on automatic data analysis results.

rect data downloading from the glucometer and data transmission to the M2DM service. A specialized server puts the data into the M2DM database and notifies the Organizer of the data transmission. The Organizer triggers the data analysis server, which analyzes the data and stores the data analysis results in the M2DM data base, together with a self-generated reminder. At the end of the analysis, the data analysis server notifies the Organizer both of the completion of the data analysis process and of the reminder generation. The Organizer, finally, activates a messaging server that sends the reminder to the physician (and optionally to the patient) as an SMS and as a message of the M2DM Web and CTI services. As a consequence of the data analysis results, the physician may then change the therapy plan (Fig. 2). When the physician saves the new therapy plan through the Web electronic medical record application, a notification is sent to the Organizer that triggers the messaging server in order to generate the reminder for the patient. Such a reminder is sent via SMS, and is available in the Web and CTI services. Let us note that in our system the reminders are subdivided into standard reminders, such as the list of patients who sent the data or educational messages for patients, and alarms, reporting metabolic conditions that may be critical for the patient. The rules for alarm definition are based on the analysis of the data sent from home.[18] The main statistical analysis performed is related to the so-called patient's modal day. In summary, since the glucose metabolism has a circadian variability, the blood glucose readings are grouped together depending on their measurement time period, *e.g.*, before breakfast, before lunch, etc. In this way, for each time period of the day it is possible to count the number of values belonging to predefined clinical ranges: In our case, five clinical ranges have been considered (strong hypoglycemia, mild hypoglycemia, normoglycemia, mild hyperglycemia, strong hyperglycemia). The numerical ranges associated can be changed depending on the specific patient's characteristic. On the basis of simple statistics on the modal day distributions, a reminder is generated by the system. Currently, an "alarm" reminder is generated when the number of blood glucose values in the strong hypo- and hyperglycemic range is higher than a certain threshold. In all other cases, a reminder that reports a summary of the collected data is sent to the physician through the Web service and the CTI one. This system allows a great flexibility within a disease management program: It is possible to define goals and plans for a certain patient, and to dynamically change the reminder thresholds depending on the achievement of the results. Moreover, the type of reminders and the communication media may be tailored to the specific patient and the specific physician.

The problem of coping with information overload at the center level has been solved by resorting to the definition of a set of summary indexes of metabolic control. Such indexes have then been made available to physicians for an informed decision-making activity. In particular, while hemoglobin A1c has been widely recognized as an index of mid-term metabolic control, there is not a single standardized summary index that takes advantage of the day-by-day monitoring capabilities of a telemedicine system. However, several glyce-

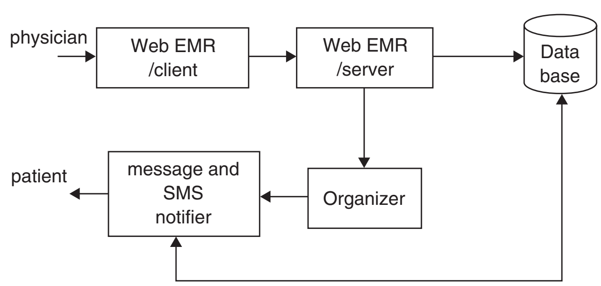

FIG. 2. The M2DM system compnents involved in the patient's notification after a therapy modification.

mic indexes have been found to be related to diabetes complications: Mean blood glucose, mean fasting glucose, mean postprandial blood glucose, M value, and mean amplitude glucose excursion (MAGE) are the most important ones. In order to merge them into a single summary index useful in a telemedicine setting, each of those glycemic indexes have been transformed through a logistic equation into a single risk index (SRI), that is, an index that is related to the risk of developing microangiopathic complications. In the case of the *i*-th index, we can write:

$$\mathrm{SRI}_i = \frac{1}{1 + e^{-k_i(I_i - I_{0i})}} \qquad (1)$$

where I_i is an index of the set given above, *e.g.*, the mean blood glucose, and I_{0i} and k_i are suitable constants. In order to determine the values of the constants I_{0i} and k_i, the values of I_i corresponding to a low (0.01) and a high SRI_i (0.99) have been defined. This allows us to obtain a system of two equations with two unknowns with a unique solution for I_{0i} and k_i. The average of each SRI_i allows us to obtain a global risk index (GRI), which represents a global normalized indicator of the quality of metabolic control, with being 0 the best control and 1 the worst. GRI is defined as:

$$\mathrm{GRI} = \frac{1}{N}\sum_{i=1}^{N} \mathrm{SRI}_i \qquad (2)$$

where N is the number of indexes considered.

Within the project, we have exploited the indexes that could be automatically calculated on the basis of the home monitoring data: the mean blood glucose, the M value of blood glucose level (BGL) ($M = \frac{1}{M}\sum_{j=1}^{M} |10 \log \frac{\mathrm{BGL}_j}{90}|^3$), the standard deviation of blood glucose, and the MAGE.

The M^{2}DM system with the above-mentioned reminder functionalities has been exploited in the last 7 months of the project. Twenty-two patients were originally involved, but six dropped out from the study. The average age of the patients was 43 ± 16 years, with 12 men and 10 women. If we consider the patients who ended the study, five patients were workers, four were students, four were pensioners, and one was a housewife. Regarding educational level, five patients had attended the primary school only, nine got a secondary school diploma, and two had a degree. All patients were given for free a Web TV, an Acculink modem, and all access functionalities (Web, CTI, data downloading, and SMS).

The hardware for the implementation of the M^{2}DM system at the FSM includes two different servers that support all the required functionalities: a Sun Solaris Server and a Windows server. The Solaris server has Solaris version 5.8 as the operating system. This server holds the Database Management System (Oracle Database 8i), the Web server (Apache Web server), and the Servlet container (Tomcat). The Windows server has Windows 2000 Professional as the operating system. This server holds the Organizer, the modem server, and the CTI service and the software modules for data analysis, alarm and reminder generation, and messaging server.

The Web application relies on PL/SQL dynamic pages and on Java applets and Servlets. The Organizer has been developed in Delphi, and the CTI system has been implemented through the Infovox software on Dialogic boards. Since FSM has a Hospital Information System for managing administrative data, as well as for patients' referrals, we implemented an middle layer for data integration based on XML interchange files.

RESULTS

The M^{2}DM system has been tested for 1 year, while the automatic messaging functionalities have been used only in the last 7 months of the test. In this section we will describe the usage of the system, and we will depict the metabolic control reached by the patients using the GRI introduced in Subjects and Methods. Figure 3a shows the Web interface of the M^{2}DM system, which enables the physician to have a summary of the messages sent by patients and of the ones automatically generated by the system. It is possible to note that the automatic messages contain in the subject an "A:" before the message. Moreover, the messages with a red subject are alarms.

Figure 3b shows the content of a message automatically generated after the data analysis

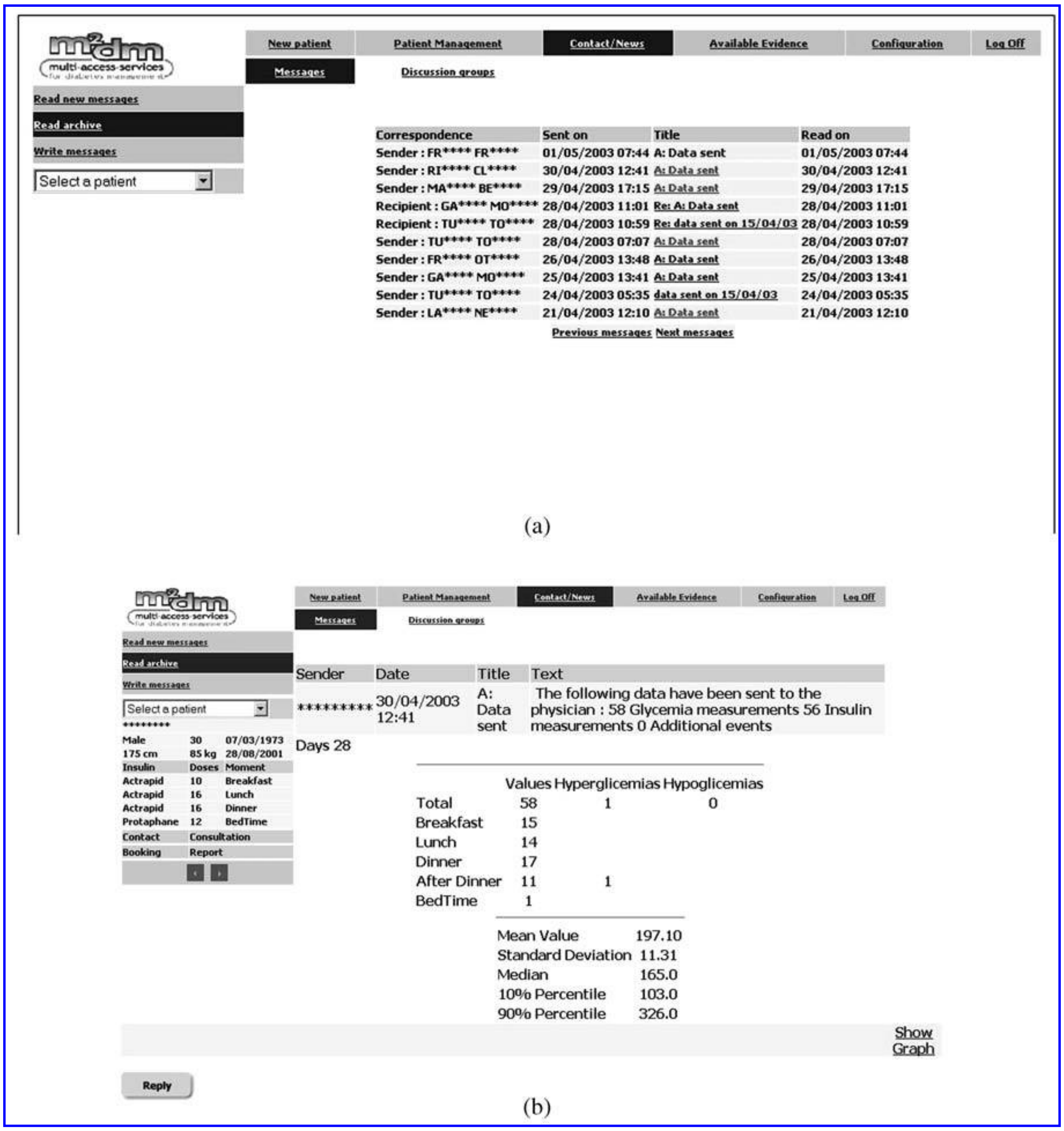

FIG. 3. The Web page for the physicians' access displaying the messages (**a**) and a sample automatic message generated by the system (**b**). The message summarized the main features of the blood glucose readings.

performed by the system. A brief summary of the metabolic control is reported, with the number of measurements collected, the distribution in the different times of the day, and the number of episodes of hypo- and hyperglycemia. Moreover, a set of descriptive statistics is reported in the bottom part of the message window.

Figure 4a shows the number of automatic messages for patients and physicians generated by the system. The average number of monthly automatic messages is 29.44 ± 9.83, *i.e.*, about 1.8 messages per patient per month. The time course of the messages does not show any significant trend; on the contrary, the behavior seems nearly constant. The number of alarm reminders (Fig. 4b) generated by the system was 16.44 ± 4.39, with a sudden increase at month 4 and a decreasing trend over the last 4 months. The number of alarms per patient per month was about 1.

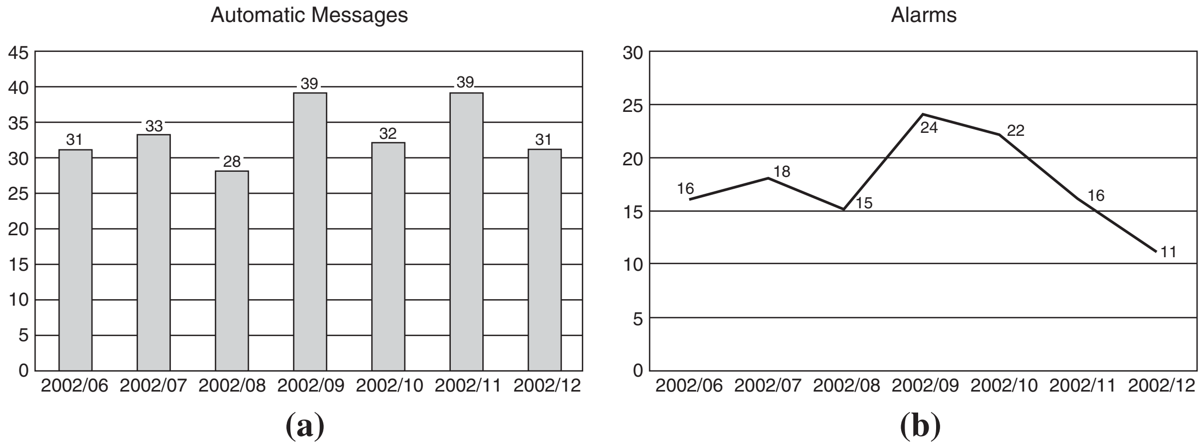

FIG. 4. The number of automatic messages (**a**) and the number of alarms (**b**) generated by the M^2DM system in the monitoring period corresponding to the last 6 months of the project.

Figure 5 shows the number of messages sent by patients and physicians during the project. It is possible to note that, after the first 2 months, corresponding to the initial phases of the project, the number of messages oscillates around a value of 13 messages per month for both patients and physicians.

Figure 6 shows the GRI of one patient calculated over the entire monitoring period of the M^2DM telemedicine study. It is possible to note that the daily GRI has strong fluctuations, while its running average over 15 days (red thick line) depicts the long-term curve behavior. The GRI is a sort of short-term summary indicator of the patient's metabolic control, which takes jointly into account the mean blood glucose level and its dispersion around the mean.

Figure 7 shows the performance of the FSM over the entire year of the M^2DM on test. The GRIs are evaluated on all patients in the different trimesters. The lightest area shows the proportion of patients with GRI corresponding to a good metabolic control (0–0.35), the

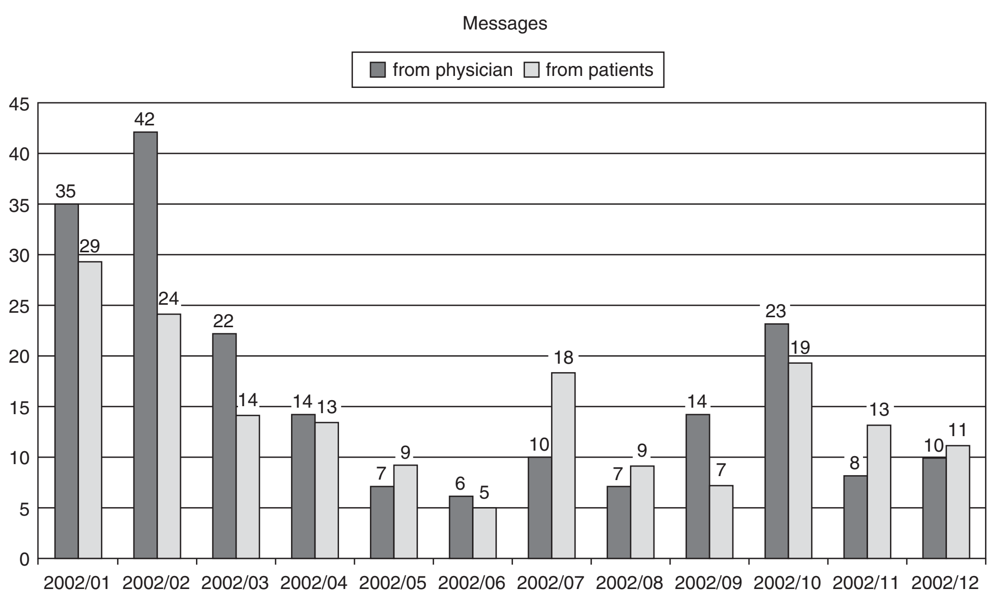

FIG. 5. The number of messages sent by physicians and patients during the project.

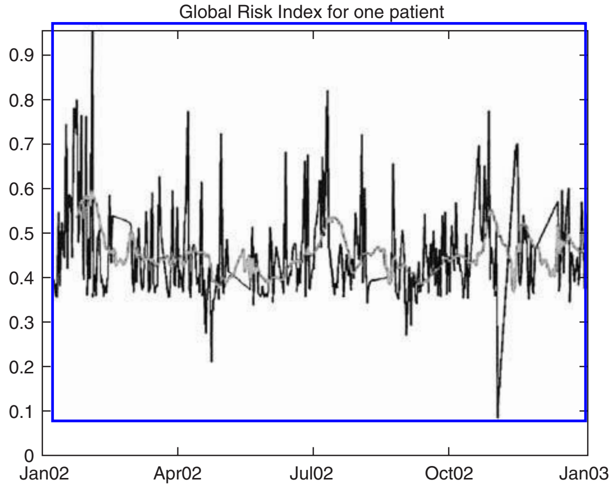

FIG. 6. The GRI of one patient. The values calculated on the basis of the daily blood glucose level measurements are shown, while the gray line shows the running average of the curve calculated over 15 days.

medium shaded area corresponds to a metabolic control of average quality, while the dark shaded area shows the proportion of patients with GRI corresponding to a bad metabolic control (0.7–1). The GRI analysis shows an initial decrease of the performance at the center level, with the number of patients with average control increasing from 27% to 33%, with a corresponding decrease of the proportion of good metabolic control data (from 40% to 34%). During the last trimester the performance of the FSM clinic improved, with a decrease of the percentage of badly controlled values from 33% to 27%. The lower left panel of Figure 7 also shows the GRIs of all patients over the 6-month monitoring period.

Figure 8 shows the presence of a linear increasing correlation between the mean GRI val-

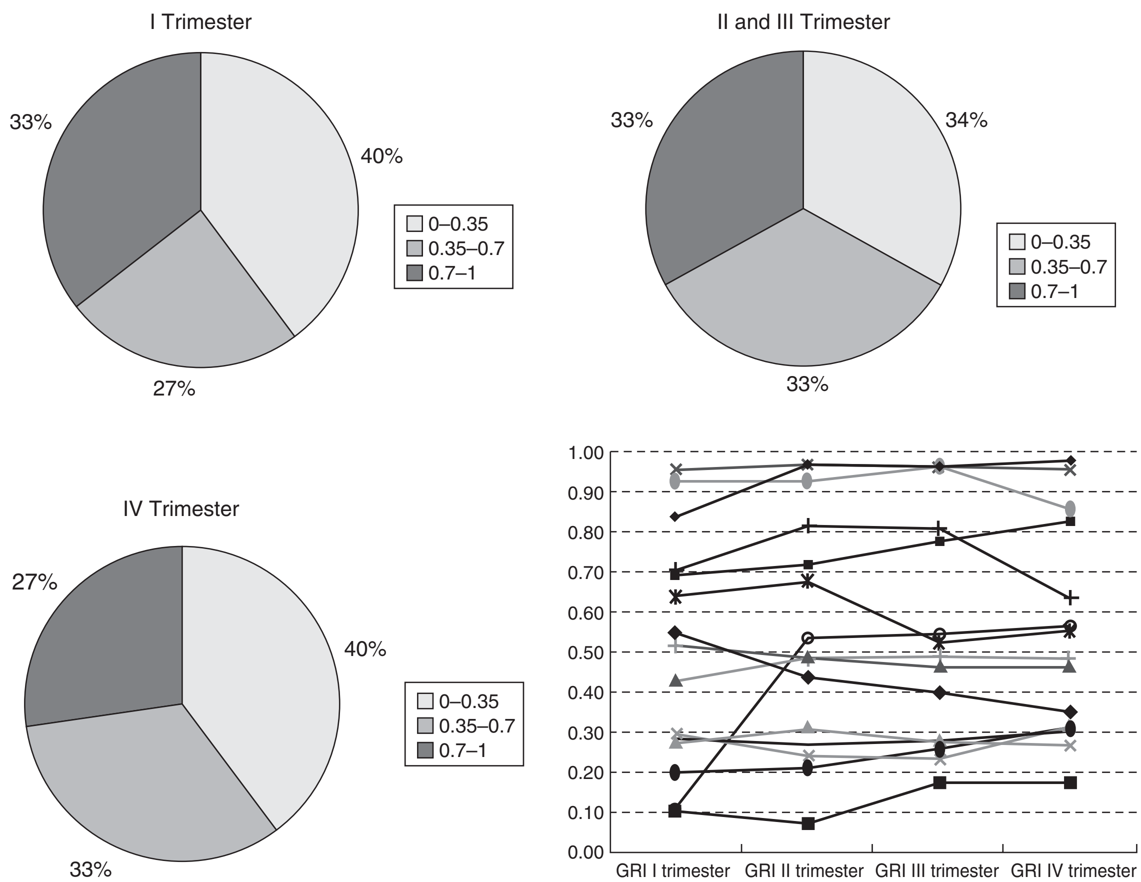

FIG. 7. The GRI calculated at the center level. The overall performance of the intervention improved from the first to the last trimester, with a slight reduction in the percentage of badly controlled patients, which went from 33% to 27%. In the **lower right panel** the GRI of each patient over the four 3-month study intervals is shown.

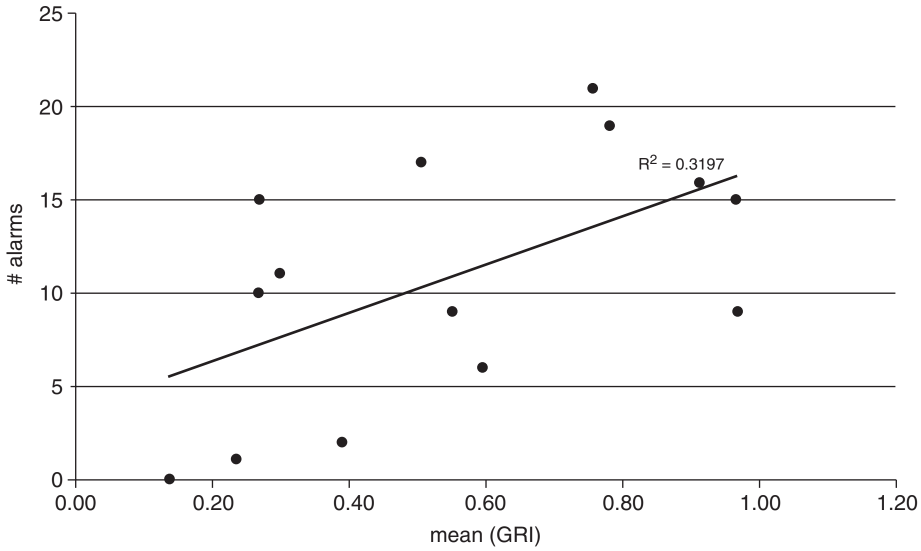

FIG. 8. The correlation between the number of alarms and the mean GRI calculated in the period from June 2002 to March 2003. Each point corresponds to one patient. The linear regression shows that the GRI correlates well with the number of alarms sent by the system.

ues and the number of alarms generated by the system. As expected, the number of alarms is a function of the metabolic control, which is well described by the mean GRI level.

DISCUSSION AND CONCLUSIONS

In this paper we have shown how a telemedicine system may incorporate features that make it a suitable technological backbone for implementing a disease management program. The practical use of such features has been shown, together with the relationships between the automatic generation of reminders and the level of metabolic control. The availability of data analysis tools, automated messaging system, and summary indicators of the effectiveness of the health care program may help in defining efficient clinical interventions. The system presented in this paper allows us to obtain a multifaceted clinical profile of the patient; such a profile can be synthesized through mathematical indexes, as shown here, or simply made available to health care providers in order to fully exploit all the available information for the assessment of the therapy and its further optimization. Moreover, the telemedicine-based approach presented in the paper has the potential to establish a "permanent" link between the patients and the health care organizations, improving patients' empowerment and education.

The technical solutions and results shown are part of a larger telemedicine system, which was implemented within a European-funded project. This system must be assessed within the framework of the international research on telemedicine in diabetes care. In a recent editorial, Klonoff[19] has pointed out that four requirements must be fulfilled by a telemedicine system, with particular reference to diabetes care: technological soundness, effectiveness, cost-effectiveness, and practicality. Concerning the soundness of a telemedicine system, Klonoff has focused attention on: (1) the accurate collection of clinical data; (2) the use of a secure electronic record; (3) the presence of protocols for distant analysis; (4) the presence of communication tools between specialists and patients; and (5) the automated flagging capabilities of a system. M^2DM fulfilled all those requirements. In particular, we have shown in this paper that the conjunction of an automated system for data analysis and of summary indicators of the patient's behavior may lead to the design and implementation of a knowledge-based flagging system, which relies on all available communication tools to make the disease management process efficient. We think that this aspect is particularly crucial in the area of telemedicine-supported disease management, where information technology solutions are used as instruments to implement a complex multifaceted program. The application of knowledge-based flagging and alarming system may transform a potentially cumbersome system into a practical tool for disease management. This aspect is also related to the last requirement, *i.e.,* practicality. The use of a multi-access and open technology coupled with a knowledge-based approach is definitely the way to improve the practicality of complex systems. In particular, within M^2DM we have exploited two different knowledge types:

- Domain knowledge on diabetes management. Such knowledge has been used to implement the reminder system and also a set of decision support tools.
- Organizational knowledge. Such knowledge has been used to define the information flows and the number and kind of messages to be generated to the different users.

Rather interestingly, the M^2DM architecture is so flexible that it could be possible to use also contextual knowledge, such as the knowledge on the technological preferences and the psychological behavior of the patient; this enables, for example, the tailoring to the patient's needs the particular kind of messages and alarms to be sent.

In order to complete the requirements of Klonoff's editorial, the critical issues of effectiveness and cost-effectiveness have to be faced. A survey carried on by Hersh *et al*.[11] has stated that "there is only a small amount of evidence that interventions provided by telemedicine result in clinical outcomes are comparable to or better than face-to-face care." The conclusion of that survey is that sound randomized control trials (RCTs) are needed to clearly demonstrate the advantage of telemedicine solutions. It must be noted that the relative low numbers of class I RCTs on telemedicine are mainly due to the difficulties of telemedicine evaluation: Telemedicine is not a drug, it is an organizational intervention.[20] As a matter of fact, when it is possible to clearly isolate the telemedicine intervention from the hospital organizational settings, and where the outcomes can be observed on a short-term basis, telemedicine proves to be effective and cost-effective. For example, the study of Riegel *et al*.[21] in the area of telecardiology and the study of Chase *et al*.[22] in the area of diabetes have clearly shown the effectiveness of long-distance monitoring to prevent re-hospitalization or simply to avoid too frequent face-to-face visits. In contrast, within the area of disease management and of diabetes management in particular, the impact on the health care organization is typically very strong. In this case, not only the way in which patients are treated is changed, but also the way in which physicians and nurses are working, and, in general, the ways in which health care is delivered by an institution are modified.[20] Therefore, the clinical outcomes could only be measured after years and only if organizational changes are performed. This makes very complex the design of a RCT. However, the evidence that disease management programs are effective is already available. Sperl-Hillen *et al*.[23] have reported the results of an observational study of the impact of a multifaceted diabetes management strategy in 18 primary care clinics that manage 170,000 adults. The intervention comprised the maximized use of information technology, such as e-mails, electronic prompt reminders, and electronic guidelines. The study showed a significant improvement in all metabolic control indicators. Moreover, a recent meta-analysis carried on by Weingarten *et al*.[10] on controlled studies showed that disease management programs with reminders for both patients and physicians had a significant impact in disease control in the area of diabetes management. Finally, concerning M^2DM, a multicenter (Italy, Spain, and Germany) controlled study has been executed, with clinical, organizational, economic, usability, and users' satisfaction outcomes. The results showed a significant improvement of metabolic indicators.[17,24]

The technological solutions presented in this paper, therefore, represent a way to improve soundness and practicality of information technology-based disease management interventions, which are progressively demonstrating their effectiveness and cost-effectiveness in clinical practice. The junction of clinical, technical, and organizational innovations is a promising a direction for defining and implementing interventions with a strong impact on the care of patients with chronic disease.

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