Chapter

State of Art of Telemonitoring in Patients with Diabetes Mellitus, with a Focus on Elderly Patients

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Abstract

Since the beginning of the 1990s, several telemedicine projects and studies focused on type 1 and type 2 diabetes have been developed, including very few elderly diabetic patients. Several of these projects specifically concerned elderly subjects (n = 4). Mainly, these projects and studies show that telemonitoring diabetes results in improved blood glucose control—a significant reduction in HbA1c, improved patient ownership of the disease, greater patient adherence to therapeutic and hygiene-dietary measures, positive impact on comorbidities (hypertension, weight, dyslipidemia), improved quality of life for patients, and at least good patient receptivity and accountability. To date, the magnitude of its effects remains debatable, especially with the variation in patients' characteristics (e.g., background, ability for self-management, medical condition), sample selection, and approach for treatment of control groups. Over the last 5 years, numerous telemedicine projects based on connected objects and new information and communication technologies (ICT) (elements defining telemedicine 2.0) have emerged or are still under development.

Keywords: elderly patient, telemedicine, telemonitoring, diabetes, artificial intelligence, information and communication technology, Web, heart failure, chronic disease

1. Introduction

Intensive glucose control has been shown to delay or prevent the development of micro- and macrovascular complications related to diabetes, even in elderly diabetic patients. However, it is estimated that 43.2–55.6% of diabetic patients with type 2 diabetes do not meet the reference target for glycemic control (hemoglobin A1c [HbA1c] < 7.0%) [1]. Factors that may contribute to suboptimal blood glucose (BG) control include inadequate home BG monitoring, nonadherence or noncompliance with medications or lifestyle changes (nutrition and sport), suboptimal patient education about the disease, and limited access to health professionals [1–3]. In the absence of timely and accurate data on home BG values, healthcare professionals may be reluctant, rightly so, to aggressively intensify oral hypoglycemic agents or insulin treatments for fear of hypoglycemia [4].

This is particularly true in the elderly, where hypoglycemia can have dramatic consequences, such as myocardial infarction (MI), falls, etc. These patients have a high mortality rate, with 20% of deaths occurring within 5 years after the first cardiovascular event. In this context, patients are often hospitalized, with prolonged and iterative hospitalization [2].

In practice, the main causes of diabetes required medical intervention are related to the following: nontherapeutic adherence and compliance, poor nutrition, and poor adherence to prescribed lifestyle changes and therapy, the decompensation of diabetic comorbidities and macrovascular complication, and community-based infections [2]. In this context, telemedicine may be an effective approach in solving problems of education, compliance, and monitoring and provider access [2, 5]. BG control could be safely improved by basing drug changes on home BG readings and transmitting them in near real time to providers, particularly in elderlies. In this setting, telemedicine may also be an effective solution to monitor the complications of the diabetes, especially macrovascular complications (e.g., MI, heart failure [HF], etc.) and comorbidities (e.g., arterial hypertension).

In this article, we review the literature in the field of telemonitoring (remote monitoring) of diabetic patients, with a focus on elderly diabetic patients.

2. First-generation telemedicine projects and studies in the field of diabetes

Since the early 1990s to the end of 2010, numerous telemedicine projects and studies have been developed in the field of diabetes [6–27]. Practically all of them have investigated *telemonitoring* or *telephone follow-up* (defined terms in **Table 1**), especially to monitor BG levels. For the majority of them, they were conducted on specific population of poor controlled type 1 and type 2 diabetic patients, including very few elderly diabetic patients. Several of these projects include specifically elderly diabetic patients (< 80 years old) (n = 1) [21, 27]. Mainly these projects have been developed in children and young people (n = 3), young or mild-age patients with intensified therapy (n = 2), young or mild-age patients under insulin pump therapy (n = 1), and patients with complicated or complex diabetes, including several elderly patients (n = 2) [6–27].

To our knowledge, to date, no project has been published on *tele-consultation* and *teleexpertise* (defined terms in **Table 1**) in the area of diabetes domain, as defined under European or French legislation [28]. Several of such projects have been developed, but no formal scientific conclusions are currently available about the usefulness of these telemedicine technologies [29].

It is worth bearing in mind that these projects and studies [6–27], particularly the earlier ones, more closely resembled as a telephone follow-up with care providers (such as a nurse) traveling to the diabetic patient's home rather than telemedicine use as we think of it nowadays with nonintrusive, automated, smart telemonitoring employing remote sensors via modern communication technology (e.g., smartphone) or even artificial intelligence (AI) (**Table 1**) [29]. Thus, they characterize in our opinion *first-generation* telemedicine projects and studies.

Using *PubMed* database and *Google Scholar*, we have identified more than 20 reports of first-generation telemonitoring studies in the field of diabetes, including type 1 and type 2 diabetic patients, involving the upload and direct transmission of BG data by diabetic patients to providers via cellular telephone, telephone landline, or a Web-based program [6–27]. The results of these studies were mixed, perhaps because many studies did not target diabetic patients with poor baseline BG control or the interval between glucose transmission and follow-up was delayed or unspecified or mainly with no therapeutic intervention (therapeutic inertia). None of these

-**Telemedicine**: provision of remote patient care and consultation using telecommunication technologies.
-**Telemonitoring**: this telemedicine practice allows a healthcare professional to remotely interpret the data necessary for the patient's medical follow-up in order to make decisions about his / her care. Remote data collection from a patient through a connected device or questionnaires to monitor his/her vital parameters and symptoms at home on a daily basis.
-**Teleexpertise**: this practice of telemedicine consists, for a medical professional, to seek the opinion of one or more medical professional experts regarding elements of the patient's medical file. Remote seeking by a health professional of a second medical opinion via sending of images (scanner, X-ray, eye fundus, etc.) and sometimes exchange by Internet-based videoconference.
-**Teleconsultation**: this telemedicine practice allows a medical professional to hold a consultation with a patient remotely. In the context of a teleconsultation, the patient can have at his/her side a health professional assisting the remote professional as well as a psychologist. Second opinion consultation by specialist.
-**Telemedicine 2.0**: over the last decade, the Internet has become increasingly popular and is now an important part of our daily life. The use of "Web 2.0" technologies in health/medicine care or in telemedicine is referred to as "Health 2.0" or "Medicine 2.0," and "telemedicine 2.0."
-**Artificial intelligence**: this concept makes it possible for machines to learn from experience, adjust to new inputs and perform human-like tasks. These processes include learning (the acquisition of information and rules for using the information), reasoning (using the rules to reach approximate or definite conclusions) and self-correction. Particular applications of AI include expert systems, speech recognition, and machine vision.

Table 1.
Glossary of terms and definitions in the field of telemedicine [29].

reports evaluated the intensity of intervention required to sustain achieved reductions in HbA1c after the implementation of home telemonitoring.

As with CHF, the results of these first-generation telemedicine projects differed from study to study, with fairly inconclusive results as to their potential clinical benefits in terms of balancing diabetes and the associated metabolic problems, re-hospitalization, and decreased morbidity or mortality, particularly regarding the statistical significance of the results [29, 30]. As a consequence, experts have shared now widely divergent opinions on the actual utility of telemedicine in diabetic patient management [29, 30].

To our knowledge, it should be emphasized that the first-generation studies and trials on telemedicine in diabetic patients were at times conducted with [29]:

- Inappropriate methodologies, involving unsuitable patient groups (such as well-balanced diabetic patients, diabetic patients without any complication) of small-sized patient samples and with very short follow-up periods (between 3 months and 1 year)
- Not well-structured follow-up organization, with nonspecialized staff to alarms, or without any association of patients' general practitioners, specialists of diabetes management, or endocrinologists nor any optimized management process or algorithm
- Several alarms arising too late, without therapeutic response (no specified therapeutic protocol available)
- No associated educational programs
- The absence of a human interface or contact between the telemedicine solution and the patients

Moreover, most of these studies were only based on glycemic control, without including other warning or monitoring parameters related to comorbidities or diabetic complication (e.g., tensiometer, heart rate, balance), with an underutilization

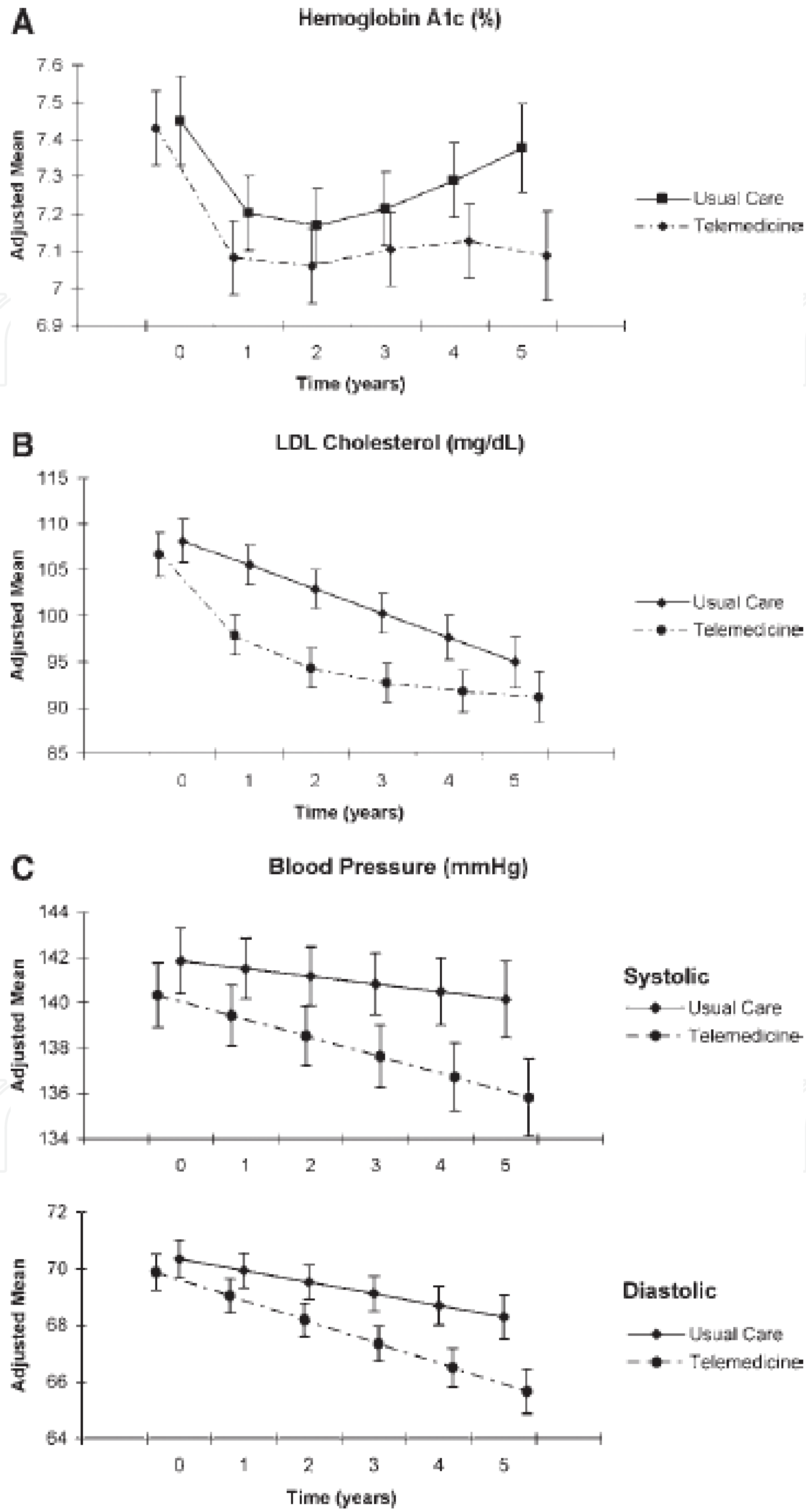

Figure 1.
Results of IDEAtel trial (n = 1665 diabetic elderly patients) (adapted from [21, 27]).

of the deployed device [29, 30]. Thus in our opinion, these facts explain that the demonstration of any benefits with these first-generation studies was "illusory," in particular in terms of statistical significance.

Besides these medical considerations, it is worth noting that an economical aspect must be investigated and consolidated in future telemedicine projects to promote the development of telemedicine in diabetes and legitimize it, especially in regard of the budgetary constraints affecting insurance and mutual health insurance companies. Things are less advanced than in the field of chronic heart failure telemonitoring [29]. To our knowledge, only Biermann's study is dedicated to this theme of economical aspect [11].

To date, none of the learned societies (e.g., *American Diabetes Association* [ADA], *European Society of Diabetes* [ESD]) involved in the topic of diabetes has, to our knowledge, made any formal recommendation as to whether or not telemedicine is of benefit to type 1 or type 2 diabetic patients. This is not the case in the setting of CHF, where factual data and medico-economic studies are more numerous, better documented, and consolidated (more mature field) [29]. In fact, the 2016 *European Society of Cardiology* (ESC) guidelines for the diagnosis and treatment of acute and chronic heart failure have recommended telemonitoring of heart failure patients with a recommendation grade of IIb and level of evidence B [31].

In the setting of diabetic patients, Shea et al. have conducted the first telemedicine study specifically dedicated to "elderly" diabetic patients (aged 55 years or greater) [21, 27]. It is a randomized, controlled trial comparing telemedicine case management to usual care, with blinding of those obtaining outcome data, in 1665 Medicare recipients with diabetes. In the intervention group (n = 844), mean HbA1c improved over 1 year from 7.35 to 6.97% and from 8.35 to 7.42% in the subgroup with baseline HbA1c ≥ 7% (n = 353) [21]. In the usual care group (n = 821), mean HbA1c improved over 1 year from 7.42 to 7.17%. Adjusted net reductions (1 year minus baseline mean values in each group, compared between groups) favoring the intervention were as follows (all principal criteria): HbA1c, 0.18% (p = 0.006); systolic and diastolic blood pressure, 3.4 (p = 0.001) and 1.9 mmHg (p < 0.001); and LDL cholesterol, 9.5 mg/dL (p < 0.001) (**Figure 1**). In the subgroup with baseline HbA1c ≥ 7%, net adjusted reduction in HbA1c favoring the intervention group was 0.32% (p = 0.002). Mean LDL cholesterol level in the intervention group at 1 year was 95.7 mg/dL. Mortality was not different between the groups, although power was limited. There were 176 deaths in the intervention group and 169 in the usual care group (hazard ratio 1.01 [0.82, 1.24]).

3. Second-generation telemedicine projects and studies in the field of diabetes

Over the last 10 years, *second-generation* telemedicine projects and studies have been developed in the setting of diabetes management, especially in the setting of telemonitoring [32–38], as defined in **Table 1**. These projects and studies have main objectives to evaluate the use of technology to implement medical and cost-effective healthcare management on a large scale for diabetes management. These projects include very few elderly patients. One project, the DiaTel study, was dedicated to elderly diabetic patients (<80 years old) [32]. Compared to the aforementioned project, most of the second-generation projects related to diabetes telemonitoring (for type 1 diabetic patients, n = 1; for type 2, n = 5) incorporate the following [32–38]:

- Self-administered medical questionnaires or forms on symptoms and signs of diabetes decompensation and BG levels

- Tools for medical education, particularly disease self-appropriation, food hygiene, and physical activity

- Tools for patient motivation

- Tools for therapeutic and hygiene observance

- Tool to remote comorbidities (e.g., arterial hypertension, obesity, dyslipidemia)

- Tools for interaction between the patient and healthcare professionals like telephone support centers, tablets, and Websites

3.1 The DiaTel study

The DiaTel study compared the short-term efficacy of home telemonitoring coupled with active medication management by a nurse practitioner with a monthly care coordination telephone call on glycemic control in veterans with type 2 diabetes [32]. The included patients were taking oral hypoglycemic agents and/or insulin for ≥1 year and had HbA1c ≥ 7.5%). Approximately one-third of the participants in both groups were aged 65 years. At enrollment, the patients were randomly assigned to either active care management (AMC) with home telemonitoring (HT) (ACM + HT group, n = 73) or a monthly care coordination telephone call (CC group, n = 77) [32]. Both groups received monthly calls for DM education and self-management review. ACM + HT group participants transmitted BG, blood pressure (BP), and weight to a nurse practitioner; the nurse practitioner adjusted medications for glucose, BP, and lipid control based on established ADA targets. Baseline characteristics of the patients in the DiaTel study were similar in both groups, with mean HbA1c of 9.4% in the CC group vs. 9.6% in ACM + HT group [32, 33]. Compared with the CC group, the ACM + HT group demonstrated significantly larger decreases in HbA1c (principal criterion) at 3 months (1.7 vs. 0.7%) and 6 months (1.7 vs. 0.8%; $p < 0.001$ for each), with most improvement occurring by 3 months (**Figure 2**).

3.2 The Utah Remote Monitoring Project

The Utah Remote Monitoring Project was a nonrandomized prospective observational pre- and post-intervention study [34]. The included patients were patients with uncontrolled type 2 diabetes and/or arterial hypertension. They have been enrolled from four rural and two urban primary care clinics and one urban stroke center participated in a telemonitoring program (n = 109). The primary clinical outcome measures were changes in HbA1c and BP. Other outcomes included fasting lipids, weight, patient engagement, diabetes knowledge, arterial hypertension knowledge, medication adherence, and patient perceptions of the usefulness of the telemonitoring program. The patients were randomized in two groups on telemonitoring delivery methods [34]. The first was a remote monitoring device for BP and heart rate. Patients used their own glucose meters to measure BG and were provided with an electronic digital scale to measure their weight. The device was programmed to sound an alarm at a pre-specified patient-referred time to prompt the patient to initiate a telemonitoring session. Patients were asked to enter data several times during the week. The device was programmed to ask how patients were feeling that day and whether they had taken their medications and then receive a prompt to take the measures. After, the patient received a series of education messages, focused on teaching patients about their diseases (diabetes, arterial

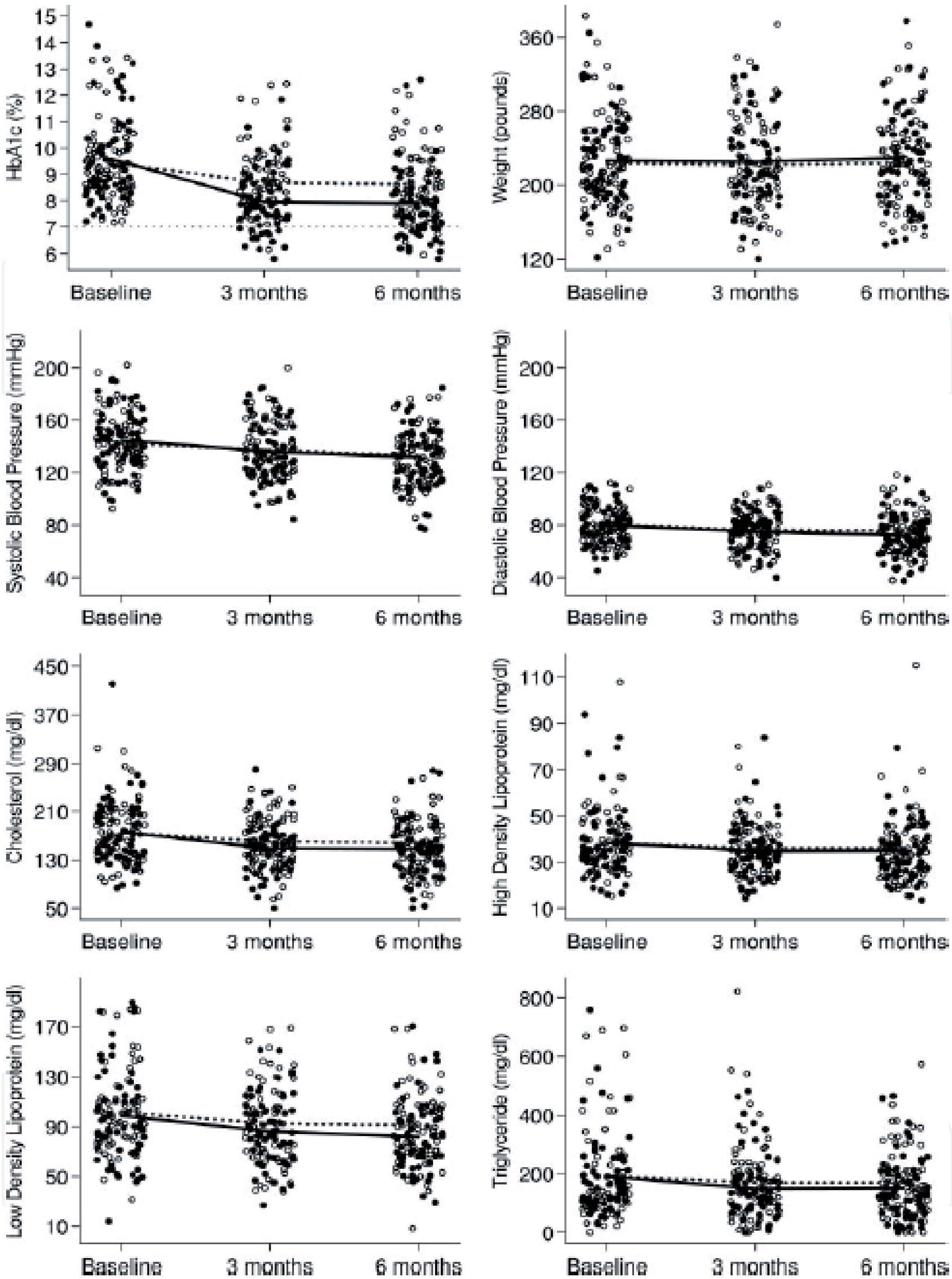

Figure 2.
Results of DiaTel study (n = 150 diabetic elderly patients) (adapted from [32]).

hypertension) and associated comorbidities. The second telemonitoring delivery method is the use of an interactive voice response (IVR) system. Patients were provided with a BP monitor and electronic digital scales, but they used their own BG meter. The patients have to use the same process described above, but received a call from the telemonitoring IVR service at a pre-specified. Medical providers were contacted either via a note in the electronic medical record (or immediately if there was a concern, in person or by telephone) if there was an out-of-range value (decided by individual providers or clinics as a value that was high or low). In this study, the mean HbA1c (principal criterion) decreased: 9.73% at baseline vs.

7.81% at the end of the program ($p < 0.0001$) [34]. Systolic BP (principal criterion) also declined significantly: 130.7 mmHg at baseline vs. 122.9 mmHg at the end ($p = 0.0001$). Low-density lipoprotein content decreased significantly: 103.9 mg/dL at baseline vs. 93.7 mg/dL at the end ($p = 0.0263$). Knowledge of diabetes and arterial hypertension increased significantly ($p < 0.001$ for both). Patient engagement and medication adherence also improved, but not significantly. Per questionnaires at study end, patients felt the telemonitoring program was useful.

3.3 Randomized trial on home telemonitoring for the management of metabolic and cardiovascular risk in patients with type 2 diabetes

This study evaluated whether a home telehealth (HT) system can improve metabolic control and overall cardiovascular risk in individuals with type 2 diabetes, compared with usual practice [35]. This study was a randomized, parallel-group, open-label, multicenter study conducted in general practice (29 general practitioners) including 302 patients, with a follow-up of 12 months. The HT system (for the telemedicine group of diabetic patients, n = 153) offers to the patient the possibility to monitor body weight, BG values, and BP values, associated with remote educational support and feedback to the general practitioner [35]. The use of the HT system was associated with a statistically significant reduction in HbA1c levels (principal criterion) compared with the control group: estimated mean difference of 0.33 ± 0.1 ($p = 0.001$) [35]. No difference was documented for body weight, BP, and lipid profile (all principal criteria). The proportion of patients reaching the target of HbA1c (HbA1c < 7.0%) was higher in the HT group than in the control group after 6 months, 33.0 vs. 18.7% ($p = 0.009$), and 12 months, 28.1 vs. 18.5% ($p = 0.07$). As for quality of life (evaluated with the 36-item short-form health survey), significant differences in favor of the HT group were detected as for physical functioning ($p = 0.01$) and mental health ($p = 0.005$). On an economic level, a lower number of specialist visits was reported in the telemedicine group: incidence rate ratio of 0.72 (95% confidence interval, 0.51–1.01; $p = 0.06$).

3.4 Study assessed the utility and cost-effectiveness of an automated Diabetes Remote Monitoring and Management System (DRMS)

This study assessed the utility and cost-effectiveness of an automated Diabetes Remote Monitoring and Management System (DRMS) in glycemic control versus usual care [36]. In this randomized, controlled study, patients with uncontrolled diabetes on insulin were randomized to use the DRMS or usual care. Participants in both groups were followed up for 6 months and had three clinic visits during the study period (at 0, 3, and 6 months [35]). The DRMS used text messages or phone calls to remind patients to test their BG and to report results via an automated system, with no human interaction unless a patient had severely high or low BG. The DRMS made adjustments to insulin dose(s) based on validated algorithms. Participants reported medication adherence through the Morisky Medication Adherence Scale-8, and diabetes-specific quality of life through the diabetes daily quality-of-life questionnaire. A cost-effectiveness analysis was conducted based on the estimated overall costs of DRMS and usual care. A total of 98 diabetic patients (60% of female) treated with insulin therapy were enrolled [36]. The mean age of the patients was 59 years. At the end, 87 patients (89%) have completed the follow-up. HbA1c was similar between the DRMS and control groups at 3 months, 7.60 vs. 8.10%, and at 6 months, 8.10 vs. 7.90% (p = ns) (principal criterion) [42]. Changes from baseline to 6 months were not statistically significant for self-reported medication adherence and diabetes-specific quality of life, except for the Daily Quality of Life-Social/Vocational Concerns subscale score ($p = 0.04$).

3.5 The Telescot Diabetes Pragmatic Multicenter Randomized Controlled Trial

The Telescot Diabetes is a randomized, parallel, investigator-blind controlled trial with centralized randomization in family practices in four regions of the United Kingdom [37]. This study included 321 patients with relatively well-controlled type 2 diabetes, with an HbA1c > 7.46%. In Telescot Diabetes, 160 people were randomized to the intervention group and 161 to the usual care group [37]. The supported telemonitoring intervention involved self-measurement and transmission to a secure Website of twice-weekly morning and evening glucose for review by family practice clinicians who were not blinded to allocation group. The control group received usual care, with at least annual review and more frequent reviews for people with poor glycemic or BP control. HbA1c assessed at ninth month was the primary outcome. The mean (SD) HbA1c at follow-up was 7.92% in the intervention group vs. 8.36% in the usual care group [37]. For primary analysis, adjusted mean HbA1c was 0.51% lower (95% CI 0.22% to 0.81%, (principal criterion) ($p = 0.0007$)). For secondary analyses, adjusted mean ambulatory systolic BP was 3.06 mmHg lower (95% CI 0.56–5.56 mmHg, $p = 0.017$) and mean ambulatory diastolic BP was 2.17 mmHg lower (95% CI 0.62–3.72, $p = 0.006$) among people in the intervention group when compared with usual care after adjustment. No significant differences were identified between groups in weight, treatment pattern, adherence to medication, or quality of life in secondary analyses. During the study, the number of telephone calls was greater between nurses and patients in the intervention compared with control group: rate ratio of 7.50 (95% CI 4.45–12.65, $p < 0.0001$), but no other significant differences between groups in the use of health services were identified between groups.

3.6 Educ@dom

Educ@dom is a multicenter, randomized, controlled, prospective study [38]. The primary objective of this study is to compare the efficacy of telemonitoring to standard monitoring in terms of changes in HbA1c after a 1-year follow-up period. The secondary objectives are clinical (changes in knowledge, physical activity, weight, etc.) and medical-economic. The Educ@dom study included 282 patients, 141 patients in each arm [38]. For patients in the intervention group, the device will be given to them for 1 year and then withdrawn during the second year of follow-up. The anticipated benefits of this research are an improvement in BG management in patients with type 2 diabetes by improving their lifestyle while rationalizing recourse to consultations in order to reduce the incidence of complications and cost in the long term. The results of this study are expected in 2019–2020.

4. New-generation projects and studies in diabetes

Over the last 5 years, new-generation telemedicine projects and studies have emerged in the setting of chronic diseases setting, especially in the setting of chronic heart failure, chronic obstructive pulmonary diseases, and type 1 and type 2 diabetes [29, 39–42]. They support transmission and remote interpretation of patients' data for follow-up and preventive interventions. These projects and studies have for main objectives to evaluate the use of technology to implement medical and cost-effective healthcare management on a large scale for diabetes management. Using *PubMed* database and *Google Scholar*, we have identified three of such projects and studies in the field of diabetes management: Telemonitoring and Health Counseling for Self-Management Support from Lindberg et al., TELESAGE, and DIABETe [39–42]. All these projects include elderly diabetic patients. Of note for the first time, one the telemedicine projects developed for chronic diseases management, the TIM-HF2 study [43], has recently demonstrated the usefulness of telemedicine in chronic heart failure, with statistical significance, in a prospective randomized study (the *gold standard* of evidence-based medicine [EBM]).

Between August 13, 2013, and May 12, 2017, 1571 patients (mean age of 70 years) were included in the TIM-HF2 study and randomly assigned to remote patient management (n = 796) or standard care (n = 775) [43]. At baseline, all patients exhibited a left ventricular ejection fraction of <45% and NYHA II or III while receiving treatment with diuretics. In TIM-HF2 study, the percentage of days lost due to unplanned cardiovascular hospital admissions and all-cause death was 4.88% (95% CI 4.55–5.23) in the remote patient management group vs. 6.64% (6.19–7.13) in the standard care group (ratio 0.80, 95% CI: 0.65–1) ($p = 0.0460$). The all-cause death rate was 7.86 (95% CI: 6.14–10.10) per 100 person-years of follow-up in the remote patient management group vs. 11.34 (95% CI: 9.21–13.95) per 100 person-years of follow-up in the standard care group (hazard ratio [HR] 0.70, 95% CI: 0.5–0.96) ($p = 0.0280$) (**Figure 3**). Cardiovascular mortality did not significantly differ between both groups (HR 0.671, 95% CI: 0.45–1.01; $p = 0.056$).

The TIM-HF2 study utilized a noninvasive, multiparameter telemonitoring system installed in the patient's home, comprising a three-channel ECG, BP-monitoring device, and weighing scales, by means of which the information was transferred remotely [43]. Patients received a mobile phone in order to contact the telemedical center in case of emergency. Patients were likewise followed via monthly phone interviews. For this TIM-HF2 care strategy, the key component was a well-structured telemedical center with physicians and HF nurses (*center of coordination*), available 24 hours a day and every day a week, able to act promptly according to the individual patient risk profile. The actions taken by the telemedical center staff included changes in medication and admission to hospital, as needed, in addition to educational activities.

In this setting, we believe that, thanks to technological innovations in connected health-monitoring devices, the telemonitoring of type 2 diabetic patients using

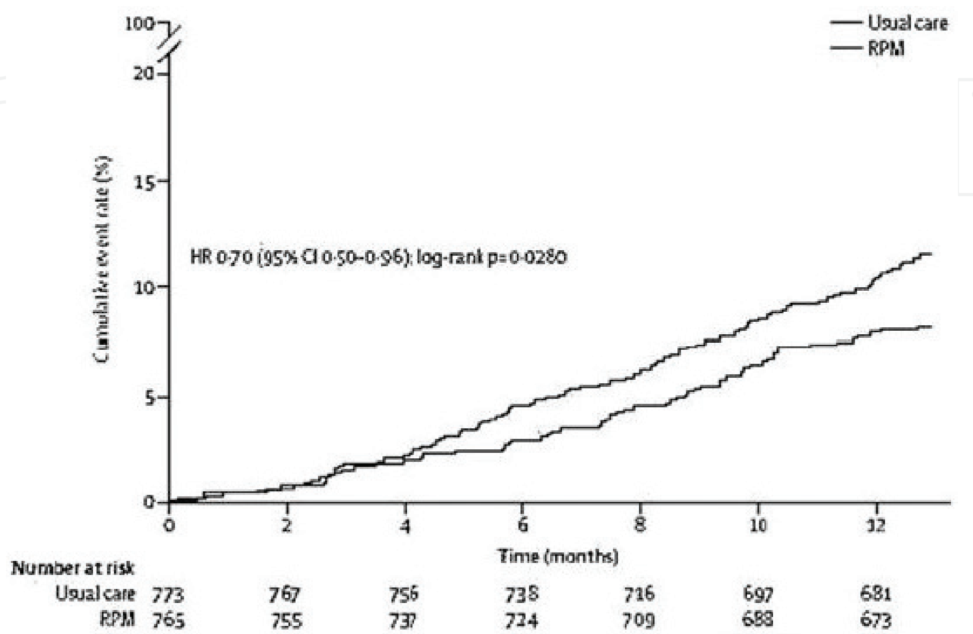

Figure 3.
TIM-HF2 trial. Rate of cumulative events in patients randomly assigned to remote patient management (n = 796) or usual care (n = 775) (adapted from [43]).

therapeutic educational tools is likely to help them adapt to their treatment and lifestyle habits and therefore improve BG management [29].

These new-generation telemedicine projects in diabetes (Telemonitoring and Health Counseling for Self-Management Support from Lindberg et al., TELESAGE, DIABETe) [39–42] are often known as *telemedicine 2.0* projects, given that they all utilize new information and communication technologies (ICT) and the Web (tools for the *e-Health 2.0*) (as defined in **Table 1**) [44].

Most projects and studies rely on the standard connected tools for monitoring type 1 and type 2 diabetes, such as glucose meters, BP, heart rate monitors, weighing scales, and pulse oximeters, which relay the collected information via Bluetooth, 3G, or 4G [29, 39–42]. Several projects also include continuous glycemic monitoring solution and often a video-call [29, 30]. Several of these telemedicine projects use machine learning, also called artificial intelligence (AI), in order to be able to:

- Adjust the BG level to the patient's activity (software Diabeo™ [see below]) [40, 41].

- Predict patient risks of diabetes decompensation [42, 45]. In this later situation, the cloud-based software aggregates, cleans, and analyzes patient data to allow for identifying patterns that may indicate potential risks and provide predictive insights on healthcare outcomes, as the software MyPredi™ (see below) [29, 42].

In the setting of chronic diseases, as in chronic heart disease or in diabetes, several informatics solutions or tools have been developed and used, such as artificial neural network (ANN) algorithms, data mining software, and ontology [45, 46]. In this context of AI, three clinical datasets are of particular interest: (1) patients' phenotype; (2) patients' electronic medical records containing physicians' notes, laboratory test results, as well as other information on diseases, treatments, and epidemiology that may be of interest for association studies and predictive modeling on prognosis and drug responses; and (3) literature knowledge including rules on diabetes management [46].

Besides these tools, it must be emphasized that diabetes telemonitoring may use, as for CHF telemonitoring, implantable invasive devices that send either sporadically or continuously data to the receiving physician (automatic telemonitoring) (*outside the scope of this paper*) [30]. In management of diabetes, implantable telemonitoring devices for multiparameters including mainly BG-insulin levels monitoring have recently proven to be an effective approach.

4.1 Telemonitoring and Health Counseling for Self-Management Support of Patients with Type 2 Diabetes

The objective of this study (Telemonitoring and Health Counseling for Self-Management Support) was to investigate whether the introduction of a health technology-supported self-management program involving telemonitoring and health counseling had beneficial effects on HbA1c, other clinical variables (weight, body mass index, BP, blood lipid profile), and health-related quality of life (HRQoL), as measured using the short-form health survey (SF-36) version 2 in patients with type 2 diabetes [39]. This was a pragmatic randomized controlled trial of patients with type 2 diabetes. Both the control (n = 79) and intervention groups (n = 87) received usual care [39]. The intervention group also participated in additional health promotion activities with the use of the Prescribed Healthcare Web application for self-monitoring of BG and BP. About every second month or when needed, the general practitioner or the DM nurse reviewed the results and the healthcare activity plan. Analyses of the data showed that there were no significant differences between the groups in the primary outcome HbA1c level ($p = 0.33$) and in the secondary outcome HRQoL as measured using SF-36 [39]. A total of 80% of the patients in the intervention group at the baseline and 98% of the responders after 19-month intervention were familiar with using a personal computer ($p = 0.001$). After 19 months, no responders reported significantly poorer mental health in social functioning and role emotional subscales on the SF-36 ($p = 0.03$ and $p = 0.01$, respectively).

4.2 TELESAGE study

TELESAGE (*Suivi A Grande Echelle d'une population de diabétiques de type 1 et de type 2 sous schéma insulinique basal bolus par la TELEmédecine* [large-scale follow-up of a population of type 1 and type 2 diabetics under basal insulin regimen bolus by telemedicine]) is a 6-month open-label parallel-group, multicenter study, including adult patients (n = 180) with type 1 diabetes (>1 year), on a basal-bolus insulin regimen (> 6 months), with HbA1c ≥ 8%, conducted in approximately 100 centers in France [40, 41]. These type 1 diabetic patients were randomized to usual quarterly follow-up (G1), home use of a smartphone recommending insulin doses (Diabeo™ software) with quarterly visits (G2), or the use of the smartphone with short teleconsultations every 2 weeks but no visit until point end (G3) [40, 41]. The primary objective of TELESAGE will be to investigate the effect of the Diabeo™ telemedicine system versus usual follow-up, with respect to improvements in the HbA1c levels (principal criterion) of diabetic patients with poorly controlled basal-bolus insulin levels (n = 696). The study will compare a control group (group 1 [G1], usual follow-up) with two Diabeo™ telemedicine systems: (1) physician-assisted telemedicine (group 2 [G2]) and (2) nurse-assisted telemonitoring and teleconsultations by a diabetologist's task delegation (group 3 [G3]). At 6 months, the mean HbA1c level is as follows: 8.41 ± 1.04% in G3 vs. 8.63 ± 1.07% in G2 vs. 9.10 ± 1.16% in G1 ($p = 0.0019$ for G1–G3 comparison) (**Figure 4**) [40, 41]. The Diabeo™ system gave a 0.91% (0.60–1.21) improvement in HbA1c over controls and a 0.67% (0.35–0.99) reduction when used without teleconsultation. There was no difference in the frequency of hypoglycemic episodes or in medical time spent for hospital or telephone consultations. However, patients in G1 and G2 spent nearly 5 h more than G3 patients attending hospital visits.

4.3 DIABETe project

The DIABETe project is scheduled to experiment a telemonitoring solution for at-home monitoring of type 1 and type 2 diabetic patients [29, 42]. The DIABETe telemonitoring project, conducted in Strasbourg (France), falls under the "telemedicine 2.0" category (as described above) [29, 44]. It has been developed and designed to optimize home monitoring of diabetic patients by detecting, via a telemonitoring 2.0 platform, situations with a risk of decompensation of diabetes and its complications (e.g., MI or CHF), the latter ultimately leading to hospitalization [29, 42]. The AI of the DIABETe platform (MyPredi™) automatically generates indicators of *health status* deterioration, i.e., *warning alerts* for any chronic disease worsening, particularly diabetes, its macrovascular complications, and cardiovascular comorbidities (e.g., arterial hypertension, chronic heart failure). For the patient, these situations may lead to hospitalization if not treated appropriately. To our knowledge, this is one of the first projects that use AI in addition to ICT. The platform comprises connected nonintrusive medical sensors (**Figure 5**), a touchscreen tablet connected by Wi-Fi, and a router or 3G/4G, rendering it possible to interact with the patient and provide education on treatment, diet, and lifestyle [29, 42].

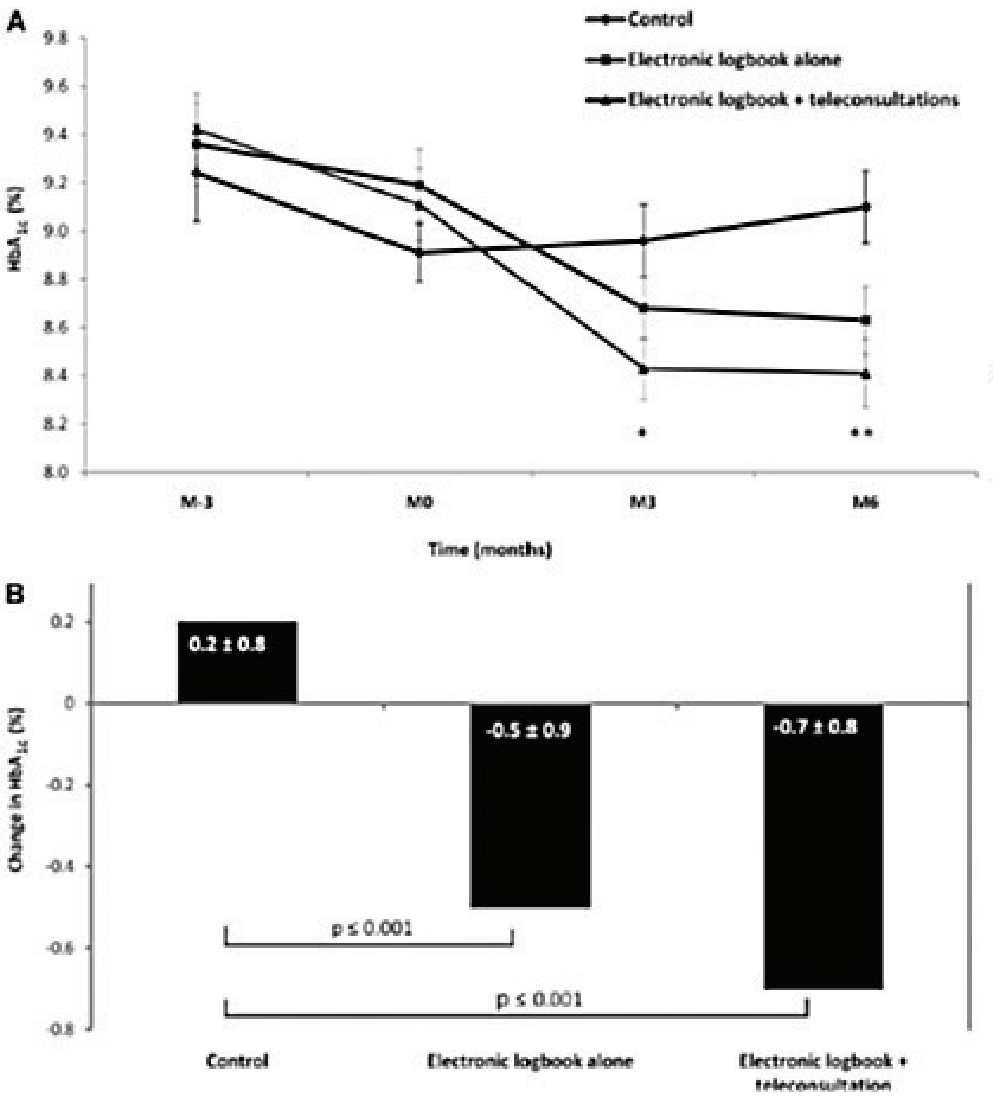

Figure 4.
Efficacy of the software Diabeo™ (adapted from [40]).

Figure 5.
DIABETe's connected nonintrusive medical sensors.

The system (**Figure 6**) involves a server that hosts the patient's data and a secure Internet portal to which the patient and hospital- and nonhospital-based healthcare professionals can connect (**Figure 7**) [29, 42].

DIABETe is based on a smart system comprising an inference engine and a medical ontology for personalized synchronous or asynchronous analysis of data specific to each patient and, if necessary, the sending of an AI-generated alert (MyPredi™) [29, 42].

DIABETe is run by a group bringing together the Strasbourg University Hospital (*Hôpitaux Universitaires de Strasbourg*), East Regional Health Agency (*Agence*

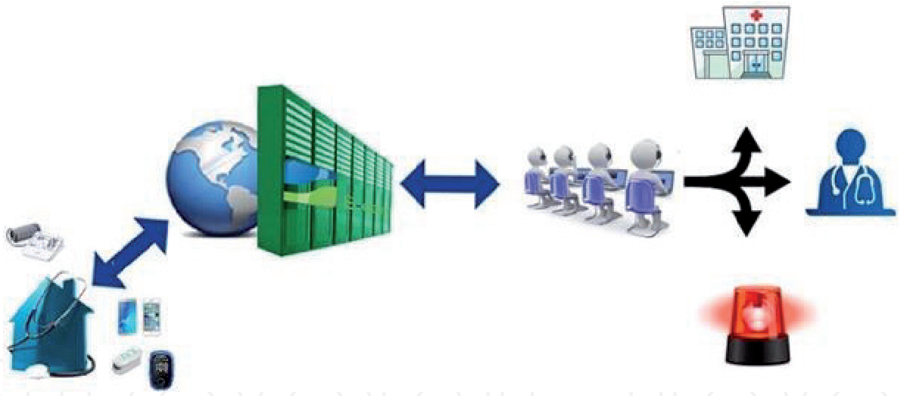

Figure 6.
DIABETe's platform.

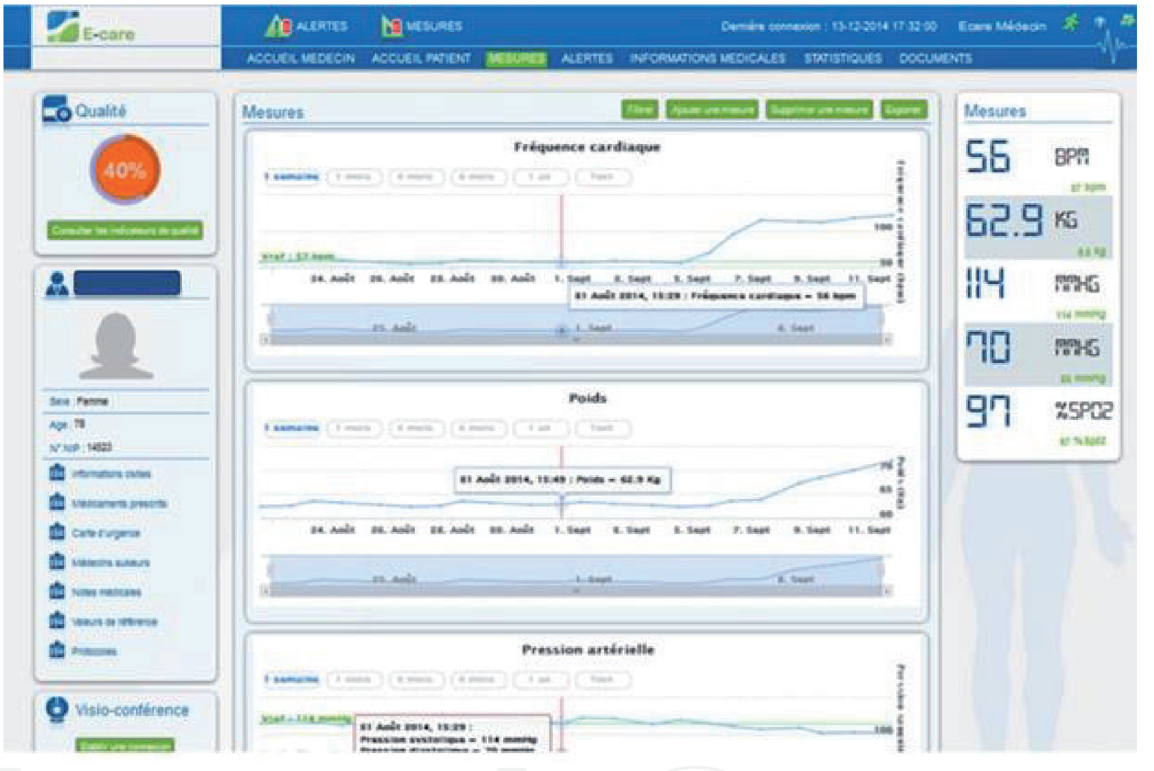

Figure 7.
DIABETe's Internet portal.

Régionale de Santé du Grand Est), Bas-Rhin branch of France's National Health Insurance (*Caisse Primaire d'Assurance du Bas-Rhin*), and *Predimed Technology* start-up [29, 42]. This project is likely allowing an in-depth study to be carried out designed to improve diagnosis by machine learning and detect abnormalities in diabetic patients at an early time point.

The telemonitoring platform used in DIABETe was first validated in a monocentric study conducted in the Strasbourg University Hospital, carried out as part of the E-Care project, primarily focused on the problem of CHF [47, 48]. Between February 2014 and April 2015, 175 elderly patients (mean age of 72 years) were included into the E-care project; 30% of these patients suffered from type 2 diabetes. During this period, the telemonitoring platform was used on a daily basis by patients and healthcare professionals, according to a defined protocol of use specific to each patient. During the study, 1500 measurements were taken, generating 700 alerts in 68 patients. One hundred seven subjects (61.1%) had no alerts upon follow-up. Analysis of the warning alerts in the 68 other patients showed that MyPredi™

detected any worsening of the "patient's health," with a sensitivity, specificity, as well as positive and negative predictive values of 100, 30, 89, and 100%, respectively. In this experimentation, both the healthcare professionals and patients, even the frailest, used the E-care system without difficulty until the end of the study.

The patients included in the DIABETe project were real-life type 1 and type 2 diabetic patients (n = 100) with (i) a "very high cardiovascular risk," when presenting a personal history of myocardial infarction or stroke, limb amputation, or cardiomyopathy and (ii) an "intensive" insulin therapy, with at least three injections per day or pump administration while offering them a personalized follow-up and education about their illness and its management [29, 42]. To date, several patients have been included. The results of this project are expected in late 2019–early 2020.

The DIABETe project is based on an intelligent platform that likely assists healthcare professionals by automatically processing the information obtained from nonintrusive medical sensors (BG meter, BP monitor, actimeter, connected scale, etc.) as well as the subjective information provided by the patient himself (questionnaires) and his/her behavior (compliance), enabling it to detect and report, at an early time, these situations at risk of hospitalization [29, 42]. Patient- and situation-adapted therapeutic education tools will be made available to the individual, and communication with the subject will likely occur via a touch pad. Alerts indicating a deterioration of the patient's condition will be generated by AI (new software version of MyPredi™ adapted for the management of diabetes) and transmitted to the health professionals in charge of the patient. The healthcare professional can thus anticipate the decompensation and initiate appropriate measures outside the emergency setting. An intermediate analysis is planned after the first 30 patients, possibly to set up a coordination cell with a nurse, as part of a delegation of tasks, as in TIM-HF2 [43]. Medical data can likewise be shared among health professionals, being part of a city-hospital network. Ultimately, an improvement in the patients' quality of life is to be expected.

DIABETe does not compete with Diabeo™ or other expert systems aimed at optimizing the glycemic balance, which is per se the main objective of diabetes management [41]. The DIABETe project focuses on the "global" management of diabetic patients through the detection of situations at risk of hospitalization: infection, cardiac decompensation, diabetic foot, as well as hypoglycemia and hyperglycemia episodes, potentially leading to hospitalizations [29, 42]. Regarding the remote monitoring platform used in DIABETe, an integration of or interfacing with expert systems such as Diabeo™ [41, 42] appears possible.

5. Perspectives regarding new developments in telemedicine

In the future, telemedicine projects will have to address some of today's medical issues (challenge for "tomorrow telemedicine") [29, 30]. Thus, the new solutions of telemedicine have to take into account the coexistence in the same individual of numerous chronic pathologies (e.g., diabetes, CHF, chronic obstructive pulmonary disease, chronic renal failure, etc.) and comorbidities (high BP, dyslipidemia, etc.). They have to offer complete and "global" management, including both social and medical dimensions. They have to resolve the specificities of elderly patients: no appetite for new technologies and new uses and their main problems (e.g., falls, malnutrition, mild cognitive impairment, etc.).

In this setting, the new developments in telemedicine are also to resolve the multiplicity of health professionals working with the same patient and the multiplicity of medical organizations (e.g., with or without human resources, telemedical center, etc.) [29, 30]. Today, the logistical obstacles to the implementation of

Overall mortality	Therapeutic education
Specific mortality of the considered chronic disease	Hygiene-dietary and therapeutic compliance
Number of hospitalization for the considered chronic disease	Optimization of food and sports hygiene
Number of re-hospitalization for the considered chronic disease	Patient self-management
Number of hospitalization days	Optimization of the care pathway for the considered chronic disease
Health costs	Structuring of the care pathway for the considered chronic disease
Management costs for the considered chronic disease	City-hospital relations
Number of days off work	Information sharing among health professionals
Quality of life	System use by health professionals

Table 2.
Potential parameters to be evaluated in a telemedicine project for chronic disease management.

telehealth are significant, as many health systems are not yet designed to integrate these technologies into existing information systems. It is therefore necessary to plan now for an interfacing of computer systems and the integration of future telemedicine solutions.

Considering the current problems of access to healthcare professionals, the new telemedicine solutions must be able to structure the patients' care pathways, a major medical topic that should interest our governments and authorities [28, 29]. Likewise, the E-care and DIABETe projects provide a means for healthcare professionals to exchange with each other, thereby facilitating patient access to medical resources. In this context, future research must also focus on the accessibility and practicality of telemedicine interventions.

Importantly, reimbursement remains a major concern and a barrier ("glass ceiling"). In fact, the healthcare delivered by telehealth is not covered by traditional fee-for-service payment models (e.g., in France, where all diabetic patients benefit from an integral treatment of their health expenses) [29]. The growth of value-based payment models may, however, provide incentives to implement telehealth as a strategy to provide high-quality, cost-effective, and coordinated care [29]. At country levels, variations in practice laws, restrictions on how telehealth can be delivered, and which patients should receive these services limit telemedicine's applicability as well [30].

Thus, to document the efficacy on the new telemedicine solutions, the future studies should integrate others objectives like potential targets to meet the needs and requirements of our societies, as listed in **Table 2**.

6. Conclusions

This review supports the efficacy of telemonitoring type 1 and type 2 diabetic patients. Several studies on diabetes telemonitoring, using diverse technologies, and transmitting different clinical, medical, and behavioral data were found. Significant impacts were observed, namely, at the behavioral, clinical, and structural levels. Minimal technical problems and cost-effectiveness analyses were reported. Four studies are dedicated specifically to elderly diabetic patients (all including <80-year-old patients).

Close management of diabetic patients, even elderly patients, through telemonitoring, showed the following: improvements in control of BG level and significant reduction in HbA1c, better appropriation of the disease by patients, greater adherence to therapeutic and hygiene-dietary measures, positive impact on comorbidities (arterial hypertension, weight, dyslipidemia), better patient's quality of life, and, at least, good receptiveness by patients and patient empowerment. Moreover, a cost-effectiveness analysis found a potential in medical economy. To date, the magnitude of its effects remains debatable, especially with the variation in patients' characteristics (e.g., background, ability for self-management, medical condition), sample selection, and approach for treatment of control groups.

To date, relatively few projects and trials in diabetic patients have been run within the "telemedicine 2.0" setting, using AI, ICT, and the Web 2.0. All these projects include real-life elderly diabetic patients. In this setting, it is the case of the project DIABETe. This project, as other projects listed in this review, is perfectly compatible with the care pathways being developed in chronic diseases by the authorities of industrialized countries, such as diabetes, chronic heart failure, and chronic obstructive pulmonary disease.

Further investigation of telemonitoring efficacy and cost-effectiveness over longer periods of time and larger samples is needed. Assessment of the attitude of providers is also important considering their heavy workload and issues of reimbursement.

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Competing interest

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Guarantor

EA.

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EA, LM and MH designed the paper and conducted the literature searches. EA, LM, AAZ, and MH drafted the results and parts of the discussion. ST, JD, JH, NJ, and AEHH provided critical analysis, revised the whole manuscript, and approved the final version for publication. EA is responsible for all revisions and remains in contact with the rest of the review team regarding status reports.

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