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Review

Digital diabetes: Perspectives for diabetes prevention, management and research

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A B S T R A C T

Digital medicine, digital research and artificial intelligence (AI) have the power to transform the field of diabetes with continuous and no-burden remote monitoring of patients' symptoms, physiological data, behaviours, and social and environmental contexts through the use of wearables, sensors and smartphone technologies. Moreover, data generated online and by digital technologies – which the authors suggest be grouped under the term 'digitosome' – constitute, through the quantity and variety of information they represent, a powerful potential for identifying new digital markers and patterns of risk that, ultimately, when combined with clinical data, can improve diabetes management and quality of life, and also prevent diabetes-related complications. Moving from a world in which patients are characterized by only a few recent measurements of fasting glucose levels and glycated haemoglobin to a world where patients, healthcare professionals and research scientists can consider various key parameters at thousands of time points simultaneously will profoundly change the way diabetes is prevented, managed and characterized in patients living with diabetes, as well as how it is scientifically researched. Indeed, the present review looks at how the digitization of diabetes can impact all fields of diabetes – its prevention, management, technology and research – and how it can complement, but not replace, what is usually done in traditional clinical settings. Such a profound shift is a genuine game changer that should be embraced by all, as it can provide solid research results transferable to patients, improve general health literacy, and provide tools to facilitate the everyday decision-making process by both healthcare professionals and patients living with diabetes.

Introduction

A total of 422 million adults worldwide were living with diabetes in 2014, which was four times more than in 1980 [1]. Diabetes imposes a heavy economic burden on both the global healthcare system and wider global economy. The global cost is estimated to be 825 billion US dollars per year, and is mostly driven by the costs of diabetes complications [2]. Yet, so far, there is still an unmet need for research into the health of people living with diabetes to improve their quality of life (QoL) and disease management, and prevent them from developing diabetes-related complications and premature mortality. Future research should now be driven by the fact that optimal diabetes control means both feeling and functioning better, which goes far beyond simply maintaining glycated haemoglobin (HbA_{1c}) levels within the normal range. Therefore, digital technologies and electronic healthcare (e-healthcare), along with the Big Data they generate and the artificial intelligence (AI) methods that analyze them, represent a major opportunity to rethink diabetes, as they are expected to have a major impact on all aspects of diabetes, from prevention to research, including diabetes care and management. However, these are still early days in the delivery of health services and information using the Internet and related technologies, such as smartphone apps and connected devices (often referred to as 'mHealth') [3], but also for social media, telemedicine [4] and e-health records that can completely change the diabetes landscape (Table 1).

The digitosome, an opportunity to fight diabetes

Data generated online and by digital technologies used by individuals – which may be grouped under the concept of 'digitosome' – constitute, by the quantity and variety of information

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Table 1
Overview of recent important achievements in diabetology related to the use of digital technology and artificial intelligence (AI).

Technology	Domain of application	Achievement	References	To be achieved in future
Mobile apps	Diabetes management	HbA_{1c} reduction in type 2 diabetes	[12]	Larger study sample populations Launch of large-scale real-life studies
AI-based algorithms	Personalized nutrition Prevention Diabetes management	Accurate personalized nutrition by predicting glycaemic responses	[14]	Inclusion in large-scale randomized trials and real-life studies
	Automated diagnosis	Accurate diagnosis of diabetic retinopathy and other eye diseases	[32–34]	Tested in everyday clinical practice Validated in various settings
	Virtual assistance for doctors	Prediction of optimal lines of treatment based on data from electronic health records	[37,38]	
Continuous/flash glucose monitoring, closed-loop systems	Diabetes management	Improved glycometabolic control Decreased frequency of hyper- or hypoglycaemia More time spent in range in type 1/type 2 diabetes requiring insulin Decreased risk of diabetes-related complications and mortality Identification of new clinically relevant metrics	[21–25,79]	Development of user-friendly data visualization tools Evidence-based guidelines for use of new metrics in clinical practice provided by learnèd diabetes societies
Social media, online communities	Peer support for patients Diabetes management Diabetes research	HbA_{1c} reduction Potential benefit for health-related quality of life, diabetes patients' knowledge and empowerment Epidemiological study of environmental and psychosocial risk factors	[49,54]	Integration of social-media data in traditional clinical and epidemiological research
Internet	Diabetes research	Launch of large-scale clinical or population-based e-cohorts	[56,57]	Development of methodologies to aggregate different types of data from various sources

they represent, a major potential to modify the way people with diabetes are monitored to identify new digital markers and patterns of risk that, ultimately, when combined with clinical data, can improve diabetes management and QoL, and also prevent complications. Compared with those who have other chronic conditions, patients with diabetes (whether type 1 or 2) self-monitor themselves the most, and are also the ones most willing to do so [5]. Indeed, people with diabetes, and especially those treated by insulin, regularly monitor their glucose levels and usually (or should) follow strict daily protocols. Such routines generate a strong potential for the use of e-health tools to efficiently track patterns of lifestyle factors and biomarkers of interest in everyday life. Digital medicine, digital research and artificial intelligence (AI) have the power to transform the field of diabetes through continuous and no-burden remote monitoring of patients' symptoms, physiological data and behaviours in social and environmental contexts [6,7], and the use of wearables, sensors and smartphone technologies.

Primary and tertiary diabetes prevention in the digital era

Self-tracking and e-coaching for healthy lifestyle changes

Type 1 diabetes (T1D) represents $<$ 1 in 10 diabetes cases, and effective methods of prevention are still sought. Type 2 diabetes (T2D) and its complications are preventable by changes in lifestyle and adequate disease management. In fact, changing lifestyle habits like physical activity and sleep is seen today as a priority for influencing trends in the evolution of chronic diseases as well as improving health-related QoL [8]. A landmark paper published in 2015 described wearable devices as "facilitators, not drivers, of health behaviour change" [9], and the currently available digital health technologies provide meaningful contributions to the design of healthy lifestyle interventions [10,11]. A recent meta-analysis calculated an average benefit of 0.49% in glycated haemoglobin (HbA_{1c}) levels for those using mobile apps for T2D management vs. controls [12]. However, it is important to bear in mind that these interventions were implemented in underpowered small-to-moderate sample populations [13]. In addition, no evidence-based predictive or system-alert tools to identify at-risk patterns through data from connected devices have been either implemented or independently validated so far. In fact, several barriers to the optimal use of digital tools for diabetes management have been identified: cost; insufficient scientific evidence; benefits limited to only some populations; data protection and security concerns; and regulatory legality issues [13].

More optimistically, personalized nutrition plans adapted to patients' glycaemic and microbiota profiles will soon be validated and incorporated into smartphone apps and other connected devices, and tested in real-life settings [14]. It is believed that such personalized AI-based lifestyle interventions will, one day, make it possible to help people prevent or efficiently delay the onset of T2D, and also improve everyday diabetes management while reducing the risk of long-term complications (Table 1).

Diabetes technology

Connected devices for management and monitoring

As 'smart' glucose and blood-pressure monitors, activity trackers and weighing scales become the most commonly used connected devices in the world of diabetes, more sophisticated tools are coming onto the market [15]. From 'smart' socks, which are supposed to monitor foot temperature to prevent inflammation and foot ulcers, to connected portable mini-electrocardiography (ECG) to track cardiovascular health, the increasing variety of devices for people living with diabetes should transform the way the disease is managed (Fig. 1). However, to make these tools accessible to the wider population, large-scale real-life studies are needed to assess their safety and usefulness, and to quantify their benefits compared with standard care. In addition, the multitude of smartphone apps to manage connected devices, but the lack of interoperability between them, may be a potential barrier to efficient diabetes management.

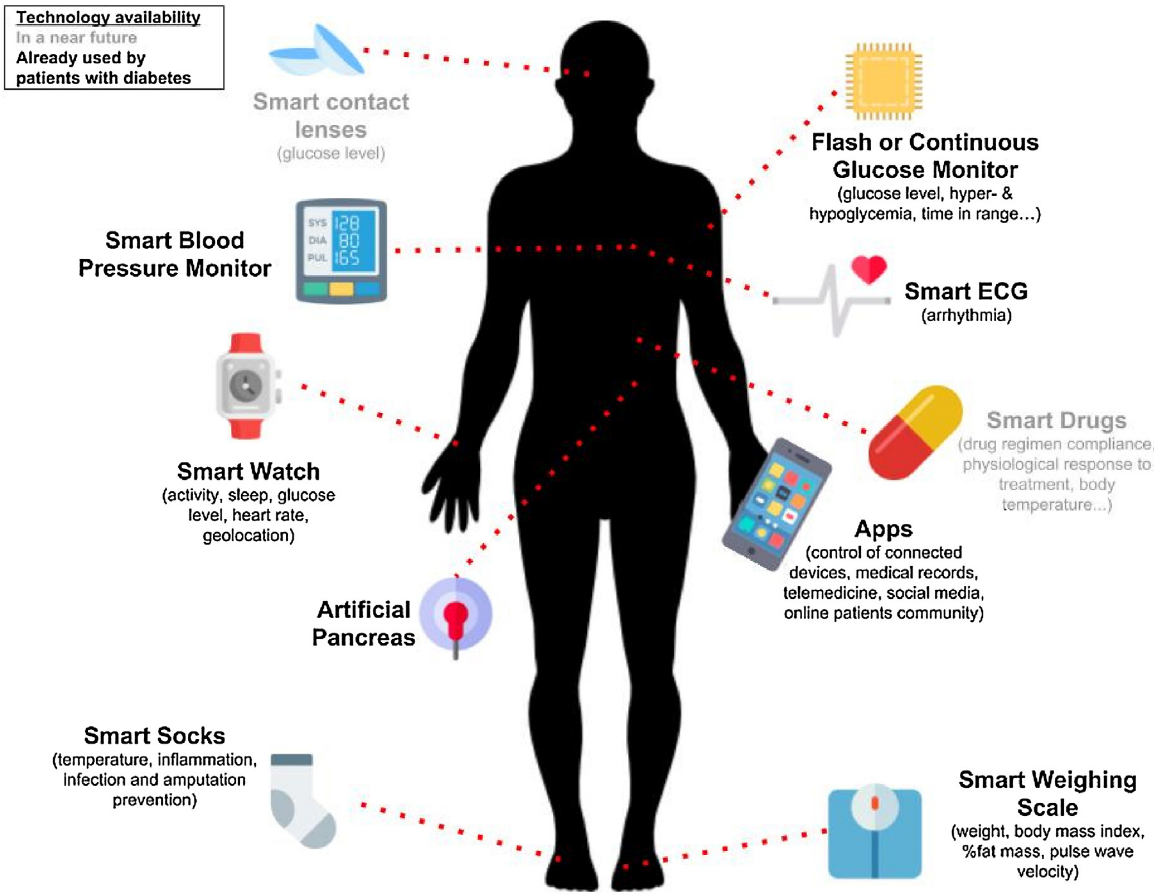

Fig. 1. Recent and future medical innovations to help people living with diabetes. ECG: electrocardiography. See high resolution here: https://docs.google.com/drawings/d/1wIF3AJKNFQINsWJJIHlxJCDy5et8zD6_wGJNhuvz6uU/edit?usp=sharing.

Flash and continuous glucose monitoring

It has increasingly been suggested that monitoring not only glycaemic levels, but also glycaemic variability, is of major interest [16]. Flash glucose monitors (FGMs) and continuous glucose monitors (CGMs) are recently available devices that can help patients manage their disease more effectively [17]. Originally used by people with T1D or insulin-requiring T2D [18], their use is expected to increase. Recent studies of connected CGM and/or FGM [19] such as the FreeStyle Libre (Abbott Diabetes Care, Alameda, CA, USA), a device that provides data on qualitative and quantitative changes in blood glucose over a 14-day period [20], have shown that their use for real-time evaluation of glycaemic fluctuations can help to better control short-term oscillations in blood glucose levels and also improve glycometabolic control, especially in people treated with multiple daily insulin injections [21]. Glucose fluctuations, as evaluated by mean amplitude of glycaemic excursions (MAGE) and postprandial incremental area under the curve (AUC), have already been associated with endothelial dysfunction, and greater risks of macro-vascular complications [22] and overall mortality [23]. Also, people with higher rates of FGM per day experienced more time within range and less time in hyper- and hypoglycaemia [24].

CGM has been found to perform even better than FGM in preventing hypoglycaemia and patients' fear of it [25,26]. In addition, the option of coupling a CGM system with an insulin pump now offers the possibility of a closed-loop insulin system such as Diabeloop technology (Diabeloop SAS, Grenoble, France) [25], which is currently being tested as the future of T1D and insulin-treated T2D management [19]. CGM also has the potential to reduce healthcare costs [27].

Because devices like the FreeStyle Libre are now re-imbursed in some countries (including France) and have even received US Food and Drug Administration (FDA) approval, they will profoundly affect the way diabetes patients track their disease and the way healthcare professionals (HCPs) address key issues of diabetes management, given the increasing amount of data that must be taken into account. Also, in terms of research, there is now a window of opportunity for large-scale prospective studies with long-term follow-ups to use these devices to explore patterns of glycaemic variability, hypoglycaemia episodes and time spent within range in relation to QoL, diabetes distress and other psychological factors, and incidence of diabetes complications [28]. Such studies will soon offer an even better understanding of the role of glycaemia and blood-pressure variability and their determinants.

The open-source movement

As the community of people with diabetes is eager to access recent innovations as quickly and as affordably as possible [29] (see #WeAreNotWaiting on Twitter), it is of interest to observe open-source initiatives from communities such as the Open Artificial Pancreas System (OpenAPS) project [30]. In an effort to make safe and effective basic artificial pancreas system technology more widely available, thereby disrupting the usual lengthy marketing and authorization process for medical devices, this project has most notably designed tools that automatically adjust basal insulin pump delivery to keep blood glucose within range overnight and between meals, based on currently available insulin pumps and CGMs already in the marketplace. While these tools are not FDA-approved and not for sale, they are open-source designed, systems that people with T1D can choose to 'build' for themselves.

Thus, the paradigm shift comes from the fact that the OpenAPS reference design, toolset and implementation are all open-source and freely applicable to other open-source projects and research, and may also be included in proprietary products by the industry. Such initiatives should accelerate the pace of innovation in diabetes management.

Besides this open-source initiative for diabetes technology, there are similar initiatives involving the data generated by diabetes medical devices. The most charismatic initiative so far is the Tidepool project [31], a non-profit open-source effort that has developed a hub for diabetes data, where patients with diabetes can gather and visualize, in one place, all their data from commonly used medical devices (insulin pumps, CGMs, blood glucose monitors, mobile devices) and also add their contextual information in real time to help them manage their disease. Moreover, the Tidepool platform uses a health crowdsourcing approach, encouraging patients to donate their data to create large databases for research purposes and Big Data analyses.

Artificial intelligence and diabetes

AI has – and will continue to have – many applications in the field of diabetes. Already, AI has gained significant traction in recent years in the field of medical imaging [32]. Automated diagnosis of diabetic retinopathy (DR) and cardiovascular risk factor monitoring are now possible, thanks to deep learning algorithms based on large retinal fundus imaging datasets [33,34]. Other AI algorithms will soon be integrated into smart telemedicine devices and be increasingly used to provide personalized preventative programmes, as well as personalized diabetes management adapted to patients' lifestyles, treatments, genetic backgrounds and environments [35]. With constant improvement in models, closed-loop systems will also benefit from more powerful and accurate algorithms, thereby enabling a future artificial pancreas to consider more and more parameters to predict the correct amount of insulin to administer [36]. AI-based decisions will also be made by HCPs to choose the optimal line of treatment [37], based on deep or machine-learning algorithms trained on large medico-administrative or e-health record datasets [38].

The use of AI will allow the processing, in real time, of massive datasets into actionable information for both patients and clinicians [39], including the implementation of large-scale interventions personalized as per patients' characteristics and adapted, over time, to prevent events such as hypoglycaemia and diabetes complications. Nevertheless, so far and surprisingly enough, and despite the increasing offer of digital solutions, relatively little scientific and independent evidence is available to guide patients, their HCPs or even researchers on how to make the best use of all such generated data to improve our understanding of diabetes and its complications.

Digital tools and sensors allow transition from the occasional assessment of disease to prospective real time, continuous, high-throughput and no-burden remote monitoring of patients' symptoms, physiological data, behaviours, and social and environmental settings [6,7]. Furthermore, the causes of frequent hospitalizations related to chronic disease may be amenable to digital strategies that will eventually forego inpatient facilities [40]. Impressive progress in data science techniques, natural language processing (such as learning from unstructured texts and speech recognition) and AI also enables the processing of heterogeneous and massive datasets collected by digital tools to help manage care, monitor patients and predict their outcomes [41,42]. Indeed, digital medicine could allow large-scale dissemination of interventions for remote and continuous behavioural changes at low cost and initially personalized, but adapted over the course of treatment on the basis of context, timing and previous responses [6].

However, while the combination of digital technologies and AI has the potential to revolutionize healthcare for people with chronic diseases like T1D and T2D, it will also challenge current processes and organization of care, the nature and role of HCPs and their relationships with patients [43], information systems, the structure of healthcare facilities, funding of healthcare and the entire traditional chain of healthcare values [41]. Indeed, considerable effort is now required to exploit the full potential of these technologies and to overcome barriers to their widespread implementation, while nonetheless preserving the core values of the relationship between patients and their caregivers.

Social media and diabetes online communities

There is an active online diabetes community around the world [44,45]. These include a strong Twitter diabetes community that frequently shares feelings, everyday struggles and anxieties about the disease via specific hashtags such as #t1d (T1D) [44], #t2d (T2D) and #doc (diabetes online community) [45]. Patients with diabetes regularly share how they feel and how they behave because of their disease. Other dedicated social-media platforms, such as PatientsLikeMe and Carenity, also offer ideal environments for exchanges about diabetes and tips to improve diabetes management while also sharing the fears, anxiety and stress. These are digital spaces with no hierarchy for information sharing or the development of online communities [46].

The use of social media as part of diabetes interventions has been convincingly associated with HbA_{1c} reduction and potentially with benefits for health-related QoL, and diabetes empowerment and awareness [47]. These platforms also offer research scientists valuable information to better identify key determinants of good diabetes management and of tertiary prevention. Platforms such as Twitter are being increasingly used and has led to the publication of $>$ 1000 academic papers [48], albeit so far mostly for descriptive purposes such as cross-sectional associations with disorders like obesity [49] and for disease surveillance [50]. It has even been suggested that Twitter might also be used for analyzing disease-related symptoms and medication use [51,52]. In fact, psychological characteristics collected through social media have been associated with cardiovascular mortality at the community level [53].

Thus, in terms of research, combining unstructured textual data like Tweets with clinical data would be a novel approach towards what is now available in clinical settings [54], making this new form of research a promising arena, perched at the interface between computer science, epidemiology and medical research [50,55], in which to study signals for pharmacovigilance, patient-reported outcomes, psychological well-being, diabetes-related distress patterns and, more broadly, everyday diabetes management in a real-life setting.

Evolution of diabetes research

Digitization of the diabetes world has had a major impact on care, but will also have a considerable effect on diabetes research (Fig. 2). The field of diabetes e-epidemiology is growing rapidly, with new technologies collecting vast amounts of data while allowing access to powerful AI methods to analyze them. Traditional cohort studies are now more and more being replaced by e-cohorts – large populations followed online through e-questionnaires and monitored passively via connected devices and e-health records. This will profoundly change the paradigm of research recruitment and data collection, as patients will be

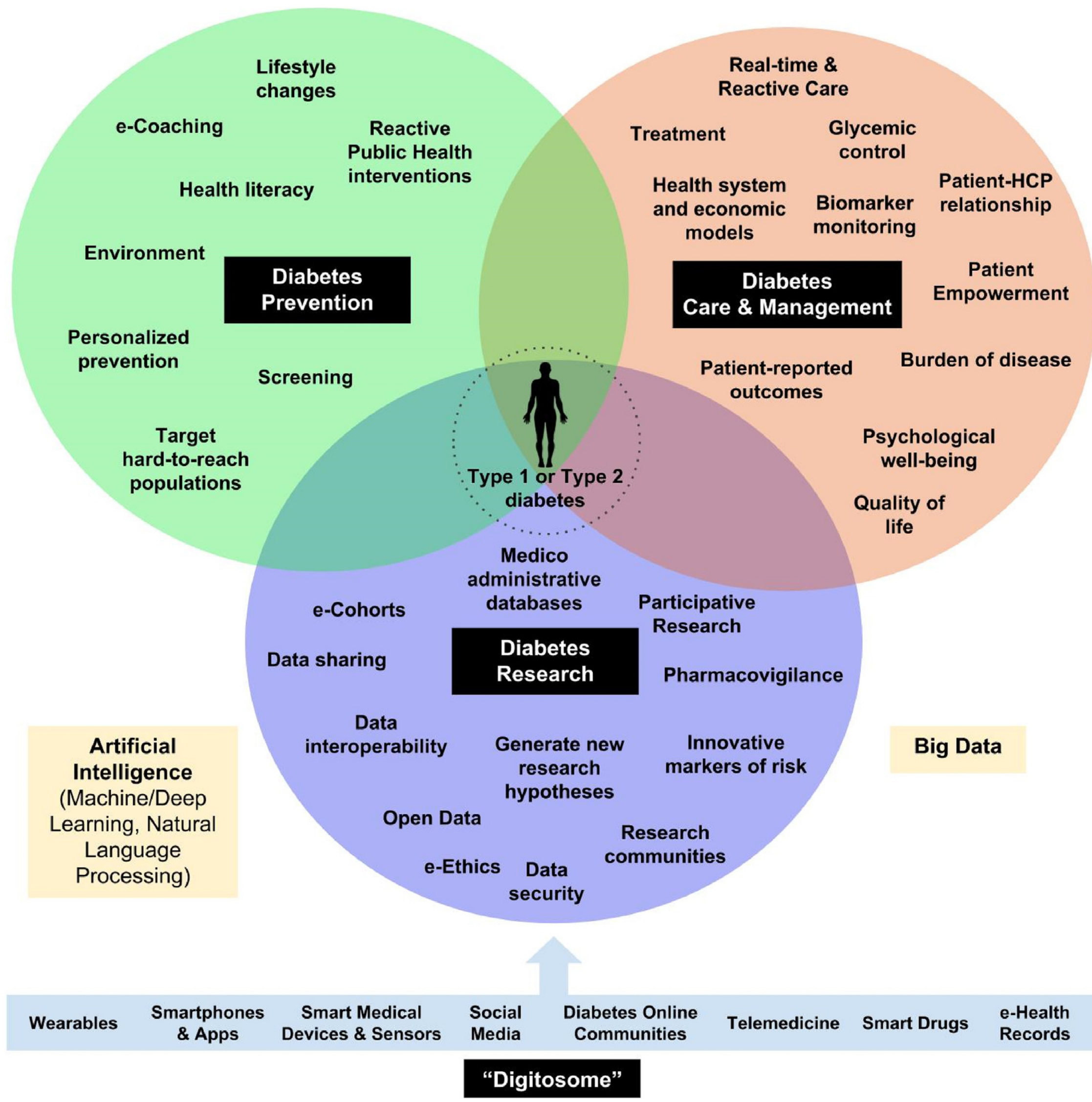

Fig. 2. The digitosome: new technologies, data and artificial intelligence at the service of diabetes prevention, management, care and research. See high resolution here: https://docs.google.com/drawings/d/1QjUVHoNRds9jGS-YwqoCagMyndxRjduHn2E5su0angk/edit?usp=sharing.

recruited once, but able to participate in multiple projects, and their data also collected only once, but used for multiple purposes [56].

These hybrid research materials, based on a variety of data sources [57], will ultimately help research scientists identify innovative risk markers of diabetes and diabetes-related complications, analyze new biological pathways, evaluate multiple morbidity more easily and nest clinical trials ('trials within cohorts', or TWICs) [58], along with providing more accurate participant selection. Privately funded e-cohorts, such as Project Baseline [59], have been specifically initiated to create new AI algorithms and to validate models. These new forms of research will, by design, place participants at the centre of the research process. Participants could even suggest research ideas directly to researchers through dedicated platforms [60], which might help investigators address key issues for people living with diabetes.

Future challenges

Defining new metrics for clinical practice

The identification of new digital biomarkers, based on data generated by CGMs/FGMs, activity trackers or other connected devices, is likely to profoundly change clinical practice by moving from an era in which controlling HbA_{1c} is the gold standard [61] to an era where an individualized approach towards HbA_{1c} monitoring can be combined with parameters derived from such devices, including time spent in range, glycaemic exposure, glycaemic variability, and hypo- and hyperglycaemia – with more to come soon. Ultimately, this will help clinicians and HCPs design personalized diabetes management [62]. Moreover, with more and more data available from personal connected devices and e-health records [63], AI methods will also help to devise more accurate risk prediction models for diabetes and diabetes-related complications that will, in turn, help to personalize treatment, care, surveillance and management strategies, thereby boosting our advance towards precision medicine in diabetes [64]. However, two conditions are necessary for such 'augmented diabetes clinical practice' to happen:

- the development of tools to routinely extract parameters and risk scores from raw data and visualize them in a descriptive manner, in parallel with;
- evidence-based guidelines provided by learned diabetes societies [65].

Challenges for patient–healthcare provider relationships

As it is estimated that 50–70% of routine follow-up clinical consultations could be replaced by remote monitoring, use of digital health records and virtual house calls [40] in combination with the huge amount of data continuously generated by patients themselves, making them 'experts' in their own health, it is evident that new technologies will also modify patient–HCP relationships. In addition, these new technologies are likely to have a major impact on the economic models currently used for HCP standard care.

In any case, patient empowerment evoked by digitization of care will certainly place patients living with diabetes at the centre of disease management and research. Digital technologies can therefore create tremendous opportunities to revisit patient–HCP relationships through empowering patients by giving them access to their own health data, thereby increasing their health literacy and understanding of their disease. Consequently, there is a need to train patients as much as caregivers on how to understand and take advantage of the digital transformation of healthcare. However, differential training of HCPs and patients on how to interpret data is a necessary condition for optimal use of data generated through digital means, thereby also implying a change in the way diabetes medicine is taught. Developing massive open online courses (MOOC) on the digital transformation of medicine for HCPs and patients with diabetes is one promising perspective [66]. Digital solutions can also increase the efficiency of the healthcare system from all perspectives: for instance, in the complex context of multiple morbidity where only 14% of T2D patients have no other comorbidities [67], it could improve patients' behaviours, avoid flare-ups and unscheduled hospitalizations, and prevent worsening of pre-existing conditions and/or the onset of new diabetes-related complications. This would also reduce the time spent in healthcare facilities and avoid unnecessary travel for patients. For medical staff, it would enable more flexible follow-ups whereas, for hospitals, the result would be more efficient use of resources. It has been estimated that, in the US alone, remote monitoring of people with diabetes could save up to 25% of the cost of their care [66,68].

Challenges for diabetes research

The development of data science methods and AI adapted for health data (development of methods to train new algorithms without breaching data privacy, transferability of algorithms in different settings) has led to the development of ecosystems of digital tools and sensors to remotely monitor patients, methods to co-construct, with patients, digital interventions for behavioural changes tailored to patient preferences and characteristics, but adapted over time, and methods for rigorous evaluation of the efficacy and efficiency of these new digital technologies. Nevertheless, thoughtful consideration of the philosophical and ethical issues underlying the use of digital tools and AI in diabetes (and chronic diseases more generally) is essential when dealing with various other related aspects, such as individually predicted prognoses, the 'Orwellian' nature of continuous remote monitoring and real-time alert systems, the balance between benefits and risk of data privacy exploitation, and the impact of digital medicine on patients, caregivers, care organizations and society in general. Indeed, patients' informed consent to participate in medical research, one of the fundamental rights of patients, will soon be radically transformed by new technologies involving block-chain tools [69,70].

Although digital solutions have a huge potential to modify the diabetes ecosystem, many barriers and challenges persist. However, the next stage in the production of diabetes knowledge will be reached once patients can be characterized by combining their clinical and epidemiological data with their genome and other – omics into exposomes and digitisomes, thus allowing the identification of innovative digital biomarkers correlating with established clinical outcomes. However, so far, there are no standard protocols for data exchanges and interoperability to do this. Limiting the risk of data or technological hacking and maintaining the trust of users for new technologies are also key issues in ensuring their long-term use and safety. Accelerating the open-data movement in diabetes by liberating huge amounts of de-identified datasets is also necessary to ensure breakthroughs in diabetes research, although yet another fundamental requirement is that the validity of the data collected for research purposes should prevail over their 'bigness' [71]. In addition, it is important to remember that the availability of new technology does not equate to acceptability by all. This means that ensuring adequate provision of evidence-based and informed education is now crucial, as is also co-designing services hand-in-hand with patients to maximize their utility. Similarly, there is a growing need for technical and psychological support of patients, which still needs to be addressed with the use of both conventional and new technologies. Doing so should create an opportunity for the expected benefits of new technologies to be realized [72].

Finally, the use of digital tools in diabetes should serve to reduce social inequities, while taking great care not to increase the already existing digital barriers to healthcare and treatment innovations by socially disadvantaged populations [73]. Indeed, there is a risk that not adequately considering access or the expertise needed for digital innovations may inadvertently widen the gap in healthcare socioeconomic and age-related inequalities [74]. In an effort to limit biases, discrimination against and underrepresentation of specific groups of populations by AI algorithms, it is essential to expand the diversity of participants in epidemiological and clinical studies [75]. This would allow tools like social media, online communities and smartphone apps to provide new opportunities for reaching the so-called hard-to-reach populations [76–78].

Conclusion

All forms of diabetes can be seen as e-diseases, as the world shifts from a place where patients are characterized by only a few recent measurements of fasting glucose levels and glycated haemoglobin to a place where patients, HCPs and research scientists are able to consider simultaneously thousands of data points of various key parameters. This will profoundly change the way in which diabetes is prevented and managed, and how people living with diabetes are characterized in medical research. However, given these digitally based data and technologies, there is also now an opportunity to design modern medical research paradigms, to promote open-data research to increase transparency and reproducibility, and to include diabetes patients and their online communities more effectively into all research efforts. Ultimately, new digital technologies, Big Data-driven analyses and AI applied to diabetes data will change the way diabetes and diabetes-related complications, and their prevention and management, are dealt with. They should complement, but not replace, what is usually done in traditional clinical settings. Indeed, they truly constitute a game changer that should be embraced by all, as they can provide solid research results transferable to patients, improve general health literacy, and offer tools to facilitate everyday decision-making processes for both HCPs and people living with diabetes.

Disclosure of interest

The authors declare that they have no competing interest.

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