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# Usability of Medical Devices for Patients With Diabetes Who Are Visually Impaired or Blind

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**Abstract**

The estimation is that every third to fourth patient with diabetes suffers from some degree of diabetic retinopathy. Medical products for insulin administration (such as insulin pens and pumps) or glucose monitoring not optimized to the needs of these patients' represent a high barrier for optimal diabetes therapy in daily practice. To date, the number of devices suitable for visually impaired and blind patients with diabetes is scarce. This manuscript outlines the specific needs of this patient group with regard to systems for insulin administration, blood glucose measurement, and continuous glucose monitoring. We see the clear need for a policy requirement for manufacturers to provide accessible/user friendly technical aids for visually impaired and blind patients with diabetes. This would represent an important step toward improving the situation for this impressively large patient group.

**Keywords**

visual impairment, blindness, blood glucose measurements, insulin pens, insulin pumps, barrier free

A whole range of medical products is available for diabetes therapy: diagnostic systems for blood glucose measurement (BGM) and continuous glucose monitoring (CGM) or therapeutic systems for insulin administration, such as pens and pumps. All of these systems have the following in common: the user must be able to adjust certain settings and carry out certain procedures to use them optimally. Therefore, patients with diabetes must have sufficient visual acuity and manual skills for their usage. Severe restrictions of such skills represent a serious barrier for usage of such systems. However, relatively small adjustments to the design/construction of these products would enable patients with visual impairment or those who are blind to perform their BGM without third-party assistance and self-administer appropriate insulin dose in a safe and efficient manner.

One would assume that modern medical products support patients with handicaps in their coping with their everyday lives, thus reducing barriers to use. However, it has to be pointed out that virtually no barrier-free insulin pen, insulin pump or BGM system is available. In the worst case this means affected patients cannot perform their daily diabetes care autonomously and are totally dependent on external assistance. This is not only associated with substantial additional costs to the health care system, it also leads to massive restrictions on the independence of the patients.

The aim of this review is to provide an overview and critical discussion of the different medical products available for visually impaired or blind people with diabetes and to provide suggestions for improvements of these systems to enable their usability. This is not a new topic, but surprisingly, there are a very limited number of publications on this subject so far.[1-11] Furthermore, proposals will be made for structural measures that could be taken to improve technical solutions for the care of this patient group and will argue for a implementation of the United Nations Convention on the Rights of Persons with Disabilities and the principles of the universal design.

## Visual Impairment and Blindness in Relation With Diabetes: Definition and Prevalence

The reasons for visual impairment are diabetic retinopathy (DR) and/or macular edema, as these are the most common

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microvascular complication seen in patients with diabetes. It is of interest to note that DR is not the cause of most of the visual impairment with diabetes; this is age-related macular degeneration. Cataract, glaucoma, and preexisting visual impairment also all contribute, along with other less-prevalent causes. DR usually develops gradually, but sudden vision loss can occur with vitreous hemorrhage or macula edema. But DR is not necessary for visual impairment to exist, and the existence of DR does not mean visual impairment is inevitable.

On the basis of a systematic literature review of population-based studies the international META-EYE Study Group was able to demonstrate that worldwide there are approximately 93 million people with DR, 17 million with proliferative DR, 21 million with diabetic macular edema and 28 million with vision-threatening DR. The overall prevalence found by the study group was 34.6% for any DR, 7.0% for proliferative DR, 6.8% (6.74%-6.89%) for diabetic macular edema and 10.2% for with vision-threatening DR.[12] Longer diabetes duration and poorer glycemic and blood pressure control are strongly associated with DR and emphasize the importance of modifiable risk factors for the development of DR.

However, an estimate of the prevalence of patients with visual impairment and blindness is associated with certain limitations, because worldwide there are different classification systems and data collection methods. For example, an evaluation in Germany of about 68,000 people with type 2 diabetes showed that only 0.8% of patients suffered from a macular edema that threatened visual acuity.[13]

This also holds true for the definition of blindness. Different countries have slightly different definitions of "low vision" (or "partial vision") and "blindness"; however, the WHO definition is widely accepted: 'Low vision' is defined as visual acuity of less than 6/18 but equal to or better than 3/60, or a corresponding visual field loss to less than 20°, in the better eye with the best possible correction. "Blindness" is defined as visual acuity of less than 3/60, or a corresponding visual field loss to less than 10°, in the better eye with the best possible correction. "Visual impairment" includes both low vision and blindness.[14]

## BGM Systems

The ability to carry out a valid BGM under all circumstances is an essential requirement for an efficient and autonomous treatment and also for the timely recognition of hypo- and hyperglycemia. This leads to specific challenges for visually impaired or blind patients (Table 1). In practice, there are a whole series of problems that are connected with this complex procedure. Even for patients with sufficient vision but limited motoric skills, serious issues can arise when trying to pick a small test strip from its box and insert it into the small slit of the blood glucose meter. Therefore, these patients generally like to use larger test strips. The correct placement of the blood drop on the test strip requires thorough training and is not equally possible with all BGM systems. Given the amount of effort necessary and the cost of the test strip, this procedure needs to give a high rate of success; that is, as far as possible every measurement made should lead to a valid device reading. In this respect it is important that the test strips are not too flexible—they should be stiff enough so that they can be guided, starting from the metacarpophalangeal joint, along the fingers to the hanging drop of blood (haptic feedback). Some devices start glucose measurement even if insufficient blood is taken, leading to incorrect readings.

**Table 1.** Blood Glucose Self-Monitoring—Special Requirements for Visually Impaired or Blind Patients.

- Easy gathering of all materials needed for the measurement
- These materials need to be placed so that they are quickly identifiable by touch when needed
- One must be able to pick up a test strip easily from the box
- The test strip needs to be inserted in the correct orientation into the corresponding slot on the meter
- A skin prick has to be applied so that a sufficiently large drop of blood is formed for the BGM
- The "hanging" drops of blood have to be applied at the right location on the test strip and in a sufficient amount so that the measurement can be started
- The patient should not contaminate themselves (eg, clothing) or the surrounding environment with blood
- Patients must be able to read the result (when they are only slightly visual impaired) or the result is indicated by acoustic signals (see below)
- The result needs to be interpreted so that the appropriate conclusions for acute adjustments in therapy can be drawn
- The measured values must be documented in a suitable form

Another major problem is being able to "read" the measurement results. For visually impaired patients BGM systems should have a sufficiently large display with good backlight; that is, there should be a good contrast of the number on the display, allowing good readability even under less than optimal lighting conditions or under strong light.

An alternative is the "announcement" of the measurement result by a series of tones. Many visually impaired and blind people find, once they have familiarized themselves with the system, that it is easier to recognize and interpret discrete tones rather than a voice output, especially when taking the environmental noise into consideration.

Verbal outputs help visually impaired and blind people to use tablets and smartphones. Through a screen reader, an easy to understand computer voice reads out the different elements that the user is currently touching. Some phone operating systems have an integrated screen reader (Windows Phone 8.1 [Narrator], Android [Talkback], iOS [voiceover]). This opens the way to create barrier-free applications. Elements such as menus, buttons, text entry boxes or images have a specific "placeholder" in the software for the optical display and the

acoustic output. The developers only need to ensure that both areas are correctly marked. As a consequence the interface element "button" will be labeled correctly for both the optical display and acoustic output according to its current function, for example, "Cancel" or "OK."

## BGM Systems Currently Available on the Market

To our knowledge, there is only a very limited selection of BGM systems currently available on the market for the visually impaired patients and the market is dominated by niche suppliers. A number of brand manufacturers claim to offer BGM systems suitable for use by the elderly; however, most manufacturers provide only a limited solution for this patient group. Some manufacturers have special websites from which information about diabetes as well as their products can be read aloud. Other manufacturers that produce devices with integrated voice output functions also provide further information on their systems on their own websites. However, only few innovative BGM systems for this peer group have entered the market in recent years. Information on the measurement accuracy of the systems available with voice output is hard to find, either on the manufacturers' websites or in the literature.

For patients with diabetes, BGM represents an essential task in everyday life. Therefore, in the future, all BGM systems should be designed for barrier-free accessibility and each manufacturer should have at least 1 system for the visually impaired/blind in their programs. These BGM systems should meet certain requirements (Table 2).

**Table 2.** Blood Glucose Monitoring Systems—Special Requirements for Visually Impaired or Blind Patients.

- Sufficiently large device with good handling and good haptics
- Sufficiently large display and good display quality (good contrast, antiglare display)
- Sufficiently large test strips with good tangibility
- A large port for the test strips or a suitable alternative (some devices have a drum with test strips, that is, the test strips do not have to be individually inserted into the BGM system)
- A sufficiently large and tactile area on the test strips for applying a drop of blood
- An audible alarm when the volume of blood is too small or an erroneous measurement is made
- Acoustically well audible output of the measurement result in the form of speech or tone sequences
- Acoustic output of the last saved readings
- Transfer and analysis of the measured data with a computer-aided documentation and analysis program together with an acoustic output
- Support the handling of the device by voice messages; for error messages additional instructions for problem solving should be provided
- Acoustic support of control measurements
- Acoustic warnings at too low/high readings
- Acoustic trend analysis of measured values

## Insulin Pens

Insulin pens provide support for patients when adjusting the dose and application of insulin, so that the patients can be certain that the correct dose of insulin is applied. To avoid any confusion, insulin pens for visually impaired/blind patients need to be clearly distinguishable in their tactile properties. For most insulin pens, the insulin dose can be regulated in increments of 1 to 2 units. For children or the elderly, it can be useful to be able to dose the insulin in increments of 0.5 units. A helpful characteristic for the visually impaired are insulin pens that after each unit adjustment a clear, loud and audible "click" can be heard. Also one should only be able to dose so many units as are available in the insulin cartridge. Reminder functions regarding the time and amount of insulin last delivered would be extremely beneficial. There are indeed insulin pens available that possess such a function, for example, the NovoPen 5 (Novo Nordisk, Bagsvaerd, Denmark), the HumaPen Memoir (Eli Lilly, Indianapolis, USA), or the pendiq insulin pen (pendiq, Moers, Germany). However, none of these pens have a special acoustic version, although an interface for an acoustic reminder for the next insulin injection already exists in the pendiq insulin pen device. In addition, changing the needle or the insulin cartridge should be easily performed and supported by acoustic instructions. Requirements for barrier-free insulin pens are listed in Table 3.

## Insulin Pumps

When handling insulin pumps it is important for visually impaired or blind patients that the pumps can guide the user through the various menus and so on with suitable tones. Unfortunately, the insulin pumps from Animas provide no sound at all, and for the range of different Medtronic insulin pumps (Medtronic, Minneapolis, USA) available, only the MiniMed 640G has settable audio options. The most suitable insulin pump for this group of users is the Accu-Chek Spirit Combo from Roche Diagnostics. This pump has an acoustic mode that makes it suitable for use by blind patients. However, its use is limited because the associated BGM system Accu-Chek Aviva Combo (Roche Diabetes Care, Mannheim, Germany) has no acoustic mode. Hence, the sophisticated treatment options that the combo system provides cannot be used. As the bolus calculator of the combo system is situated in the blood glucose meter and not in the pump, it also cannot be used. Both the Accu-Chek Insight and the Accu-Chek Spirit insulin pumps (Roche Diabetes Care, Mannheim, Germany) have different tones or pitches available in the acoustic mode and offer visually impaired users an advantage through the use of prefabricated insulin cartridges.

**Table 3.** Requirements for Barrier-Free Insulin Pens.

- Sufficient size for gripping
- The housing should have markings that make the use of insulin pen easy for blind or visually impaired patients and to help prevent confusion with other insulin pens that may contain other types of insulin
- Audible and tactile feedback to select the units of insulin
- Protection mechanism so that one cannot select more insulin units than are available in the cartridge
- If possible acoustic or tactile reminders of the time and the amount of the most recent insulin injection
- Easily readable display for the visually impaired

**Table 4.** Requirements for Barrier-Free Insulin Pumps.

- The housing has markings that make the pump simple to operate
- Acoustic signal to control the delivery of selected units of insulin
- Audible signal after completion of a correctly executed bolus delivery
- Acoustic differentiation of the alarms
- Readable, antiglare display for the visually impaired
- Programming the pump with the help of acoustic feedback or by remote control with voice output
- Support of the handling of the device (eg, changing of the infusion catheter or insulin cartridge) by voice messages; for error messages additional instructions for problem solving should be provided
- Easy to use acoustic user manual

To read the error messages at the very least with a computer, it is important to be able to transfer the data stored in the insulin pump. Although it is possible for visually impaired or blind people to perform insulin pump therapy, many of the important features are not available to them. Requirements for insulin pumps for a barrier-free handling for visually impaired or blind patients are listed in Table 4.

## CGM Systems and the Flash Glucose Monitoring System

Currently there is no CGM system on the market that is suitable for use by visually impaired or blind patients. However, a recent DexCom system (DexCom, San Diego, USA) can be connected with the iPhone which is able to provide audible information. Even the Flash Glucose Monitoring system (FreeStyle Libre from Abbott) (Abbott, Chicago, USA) which has certain characteristics that distinguishes it from other CGM systems, offers no acoustic reading of the measurement result, although a successful measurement is indicated by a tone. As the actual measurement is not laborious and is easily carried out, this system is in principle well suited for the group of patients referred to here, were it not for the lack of acoustic messaging.[15]

## Instruction Manuals

Visually impaired or blind patients have to have a good sense of humor, when they are faced with an instruction manual for a given medical product that is several hundreds of pages long. Although such voluminous manuals are needed for regulatory requirements, in practice the patient will read a few relevant pages only. In principle it should not be too cumbersome to translate such manuals into a speech mode and to provide them as "Audio Books."

## Apps

Smartphones support the users—also the patients groups described here—in handling of many daily life aspects. They also offer the user a variety of diabetes-related apps; however, there are only a few apps that are suitable for use by visually impaired or blind patients. Unfortunately, many apps do not meet the requirements for accessibility and therefore this group of patients cannot use it. For instance, the order of the tabs is illogical and owing to the lack of guidance the patient is unable to enter various inputs. Furthermore, the labeling of the buttons and additional elements (graphics/images) are missing—for the visually impaired all nontextual elements need to have a legend or labeling that can be reproduced by a screen reader.

It would be ideal if the medical devices needed for self-treatment, can transmit their data via Bluetooth to a smartphone, which in turn could read out the respective values. It should not be too difficult to program such apps for barrier-free accessibility. A current trend in the development of new products for diabetes treatment is the integration of mobile- and Internet-based solutions. Thus, from the BGM readings and other therapeutic data a clear picture of the glucose profile of a given patient over time can be obtained which provides the basis for an individually optimized diabetes treatment.

## Why Are Most Medical Products Not Being Designed to Be Barrier-Free?

From the point of view of the manufacturer, the development and approval of barrier-free medical products is associated with additional costs and risks of product liability; in particular this last point represents a problem for the manufacturers. As long as there is no legal obligation to supply barrier-free devices, nothing will change in the future on this front, in spite of the fact that 160 countries worldwide have ratified the United Nations Convention on the Rights of Persons with Disabilities. The countries which signed the convention committed to the following, stated in Article 9—Accessibility, "To enable persons with disabilities to live independently and participate fully in all aspects of life, States Parties shall

take appropriate measures to ensure to persons with disabilities access, on an equal basis with others, to the physical environment, to transportation, to information and communications, including information and communications technologies and systems, and to other facilities and services open or provided to the public, both in urban and in rural areas." In addition it is stated in Article 25—Health, "In particular, States Parties shall: a. Provide persons with disabilities with the same range, quality and standard of free or affordable health care and programmes as provided to other persons, including in the area of … population-based public health programmes; b. Provide those health services needed by persons with disabilities specifically because of their disabilities, including early identification and intervention as appropriate, and services designed to minimize and prevent further disabilities."[16]

Since this UN resolution has no third-party binding effect, there is no obligation for third parties, such as companies that produce diabetes products, to comply with this ruling. It is a matter for each respective state to ensure compliance of this convention. On behalf of those who are severely affected, urgent demands must be made to governments and/or the respective governmental agencies in these countries to ensure the provision of these important barrier-free aids and diabetes technologies.

As Williams and Schnarrenberger pointed out,[9] according the movement of "universal design"[17] all new technologies for people with diabetes should be designed barrier-free. Universal Design does not mean specific products for a specific group of people, but rather good design for all ages and conditions with the elements intuitive use, flexibility in use, error tolerance and low physical effort.

## Reducing the Incidence of Visual Impairment or Blindness Through Intensified Insulin Therapy

The importance of adjusting the insulin therapy through adequate insulin administration and glucose measurement is supported by the results of the Diabetes Control and Complications Trial (DCCT), which confirmed that there was a reduction in the incidence of retinopathy, by 76%, and retinopathy progression, by 52%.[18] In a recently published analysis of long-term data from the DCCT/EDIC (Epidemiology of Diabetes Interventions and Complications) trial, it was found that during the DCCT phase in 1983 to 1993, those participants who received an intensified insulin therapy (6.5 years on average), after an average of 27 years, had a one-third lower risk of death (HR: 0.67, 95% CI: 0.46 to 0.99, $P = .045$) relative to those who received a conventional standard therapy during this time.[19] Although since the end of the DCCT all patients now use an intensified conventional therapy, those that had received intensified therapy in the original trial have undergone 45% less vitrectomies and 48% less retina and cataract surgery (data taken up till 2014). The cost for all eye surgery in the control group was US$634 925, which is 32% higher than that of the treatment group (US$429 469).[20]

## Discussion

People with diabetes who are visually impaired, whether slightly or severely, or who are blind are not a minority group—in fact they represent a considerably large group of people. As it is estimated that every third or fourth person with diabetes suffers from retinopathy to a given degree, the demand for barrier-free systems for diabetes therapy is more than justified. In principle the technologies available today, such as CGM systems, the Flash Glucose Monitoring system or modern insulin pumps, enable these patients to live independently and participate fully in all aspects of life.

Economic considerations or fear of regulatory or legal problems should not be roadblocks for offering barrier-free medical products, or even worse, removing them from the market. It is the task of politicians and in this sense that of the regulatory authorities to ensure that in future the UN disability convention is properly implemented and all medical aids necessary for diabetes self-treatment are offered as barrier-free, by default. If manufacturers argue that there is not enough demand for such devices, specifically those relevant for the patient group discussed here, then the question arises, why is there special support from legislation for drugs (and their development) for relatively small groups of patients (orphan drugs; keep in mind that diabetes type 1 is a rare disease), but not for technological aids (orphan devices)? Since most of the devices mentioned here already have an acoustic mode, it should be possible, with reasonable efforts, to provide barrier-free devices for visually impaired or blind patients. Such developments make not only life with diabetes easier for such patients, it would also help to save costs in the health care system: patients who are unable to manage their diabetes therapy independently require considerably more external help and care, for which the nursing services are insufficient in the current structure. One solution is 24-hour assistance, financed by the patient, or they may require more inpatient health care resulting from the lack of opportunity for self-therapy. For the health care system, significantly higher costs are associated with patients who are no longer able to handle their diabetes therapy on their own.

In summary, we see substantial need for action in this matter. A first step could be a round table meeting of all interested parties to discuss the points raised and find technological solutions and mandatory standards that support visually impaired or blind patients in their daily struggle with diabetes therapy.

### Abbreviations

BGM, blood glucose measurement; CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; DCCT, Diabetes Control and Complications Trial; DR, diabetic

retinopathy; EDIC, Epidemiology of Diabetes Interventions and Complications.

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## References

1. Blubaugh MV, Uslan MM. Accessibility attributes of blood glucose meter and home blood pressure monitor displays for visually impaired persons. *J Diabetes Sci Technol*. 2012;6:246-251.
2. Burton DM, Enigk MG, Lilly JW. Blood glucose meters and accessibility to blind and visually impaired people. *J Diabetes Sci Technol*. 2012;6:242-245.
3. Burton DM, Uslan MM, Blubaugh MV, Clements CW III. Are current insulin pumps accessible to blind and visually impaired people? *J Diabetes Sci Technol*. 2009;3:613-618.
4. Marom L. Insulin pump access issues for visually impaired people with type 1 diabetes. *Diabetes Res Clin Pract*. 2010;89:e13-e15.
5. Uslan M, Blubaugh M. Analysis: including visually impaired participants in validation design studies of diabetes technology. *J Diabetes Sci Technol*. 2010;4:1236-1237.
6. Uslan MM, Burton DM, Clements CW. Blood glucose meters that are accessible to blind and visually impaired persons. *J Diabetes Sci Technol*. 2008;2:284-287.
7. Uslan MM, Burton DM, Wilson TE, Taylor S, Chertow BS, Terry JE. Accessibility of home blood pressure monitors for blind and visually impaired people. *J Diabetes Sci Technol*. 2007;1:218-227.
8. Uslan MM, Eghtesadi K, Burton D. Accessibility of blood glucose monitoring systems for blind and visually impaired people. *Diabetes Technol Ther*. 2003;5:439-448.
9. Williams AS, Schnarrenberger PA. A comparison of dosing accuracy: visually impaired and sighted people using insulin pens. *J Diabetes Sci Technol*. 2010;4:514-521.
10. Williams AS. Creating low vision and nonvisual instructions for diabetes technology: an empirically validated process. *J Diabetes Sci Technol*. 2012;6:252-259.
11. Windecker R, Heinemann L, Sawicki PT. Self-monitoring of blood glucose in blind diabetic patients. *Diabet Med*. 1997;14:703-706.
12. Yau JW, Rogers SL, Kawasaki R, et al. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care*. 2012;35:556-564.
13. Hammes HP, Kerner W, Hofer S, et al. Diabetic retinopathy in type 1 diabetes—a contemporary analysis of 8,784 patients. *Diabetologia*. 2011;54:1977-1984.
14. World Health Organization. *International Statistical Classification of Diseases, Injuries and Causes of Death*. 10th revision. Geneva, Switzerland: World Health Organization; 1993.
15. Heinemann L, Freckmann G. CGM versus FGM or: continuous glucose monitoring is not flash glucose monitoring. *J Diabetes Sci Technol*. 2015;9:947-950.
16. United Nations. Convention on the Rights of Persons with Disabilities. Available at: http://www.un.org/disabilities/convention/conventionfull.shtml.
17. Preiser WFE. Universal design: From policy to assessment research and practice. *Int J Architect Res*. 2008;2:78-93.
18. Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329:977-986.
19. Writing Group for the DCCT/EDIC Research Group. Association between 7 years of intensive treatment of type 1 diabetes and long-term mortality. *JAMA*. 2015;313:45-53.
20. DCCT/EDIC Research Group, Aiello LP, Sun W, et al. Intensive diabetes therapy and ocular surgery in type 1 diabetes. *N Engl J Med*. 2015;372:1722-1733.