"Do It Yourself" (DIY)—Automated Insulin Delivery (AID) Systems: Current Status From a German Point of View

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Abstract

A group of dedicated people with a high affinity for technology and good understanding of how to treat their type 1 diabetes have developed systems that enable automated insulin delivery (AID). These persons build these AID systems only for themselves (do it yourself [DIY]) and the quality of glucose control achieved with DIY AID systems is impressively good. This overview presents the current status of this development from a German point of view. A high degree of efforts is required to start and maintain this type of therapy and the user must always remain aware of what she/he is doing in everyday life. One main obstacle is liability, because the medicinal products used by persons with diabetes for DIY AID systems are not approved for this indication. They must be regarded as experimental systems. As long as persons with diabetes build and use these systems for themselves and not for other people, they act at their own risk. If a person with diabetes expresses interest in such a system or is already using it, the diabetologist should inform him about the improper use of the medical devices and about the associated risks. The physician should document this information accordingly.

Keywords

automated insulin delivery, insulin therapy, closed loop, artificial pancreas

Introduction

For decades, people with diabetes have dreamed of a cure for their metabolic disorder. Currently, at least one technical solution toward this goal is emerging. The subcutaneous insulin supply varies automatically according to the current demand; this demand is estimated by the constant monitoring of glucose concentration levels (continuous glucose monitoring [CGM]) in the interstitial fluid in the subcutaneous tissue. The achievement of this "holy grail" of diabetology through a system for automated insulin delivery (AID) has been a recurring topic over the past decades in lectures on the future of diabetes therapy. After more than 40 years of repeated announcements that AID systems would be available "soon," technical solutions are now approved by regulatory bodies in the United States and the European Union and are on the market, at least in the United States. Such AID systems are based on CGM, the availability of algorithms that use the glucose values to calculate the necessary insulin supply, and an insulin pump that is controlled by it (eg, Tauschmann et al[1] and Phillip et al[2]).

Several companies and research groups are active worldwide in developing AID systems as approved medical devices for diabetes therapy and in proving their safety and efficiency in clinical studies. The speed with which such innovative products are developed from the initial idea of an approved medical device until it is market-ready seems slow from the patient's point of view.[3] These developments and approval processes take years, sometimes decades. There are additional factors including the time required for the market launch as well as uncertainties regarding the reimbursement of costs. This is in stark contrast compared to the high speed at which development is progressing in other areas of technology (eg, in the computer industry or smartphones).

Background

In view of these protracted, complicated, and largely nontransparent processes, it is understandable that persons with type 1 diabetes in Germany are looking for other solutions. They follow new technological developments in, for example, the United States via social media with great interest and want to make immediate use of these devices and developments.[3,4] There is a group of patients who build AID systems themselves. There are various building instructions on the Internet that use commercially available real-time (rt)CGM systems and insulin pumps. Patients must implement algorithms on the computer or smartphone they are using and adapt them to their

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individual situation. However, the medical devices used by these patients are not approved for this purpose.

There are currently three do-it-yourself (DIY) AID systems[5-8] (https://openaps.org, https://diyps.org, https://androidaps.readthedocs.io/en/l10n_dev/DE/index.html):

1. OpenAPS: Insulin pump, CGM system, and a small computer running the algorithm. A smartphone can be used to monitor the system.
2. AndroidAPS: Here the algorithm runs on a smart phone with an Android operating system. The smartphone can receive data from the CGM system and then communicates with the insulin pump via Bluetooth.
3. Loop: Here, the algorithm runs on an Apple smartphone. The data from the CGM system can be received directly and an adapter is required for Bluetooth communication with the pump ("RileyLink").

Not all the DIY AID systems automatically deliver prandial insulin and, where this is the case, the user must initiate delivery of the insulin bolus. The user chooses the DIY AID system on the basis of which insulin pumps can be used together with that particular system—although the choice of pump could also be made on the basis of the preferred DIY AID system. Especially for (liability) legal reasons (see later), there are no (or at least no publicly known) commercial offers for DIY AID systems.

There are currently several thousand "Loopers" worldwide.[3,6] These patients exchange information via social media and a highly active community has formed.

All DIY AID systems place high demands on users:

- They must be very familiar with their diabetes therapy.
- They need to know exactly how to adapt the insulin dosage to variations in the glucose level.
- There is also a considerable amount of work involved in constantly updating the software and hardware used (see later).

DIY AID systems are therefore not suitable for patients who want to "give up" their diabetes, but for patients who are highly motivated and have an affinity for technology. Less tech-savvy individuals who want to use DIY AID systems might see them as a way of "forgetting about" their diabetes. In this regard, Android APS, by requiring the user to go through a series of gates before they can access the full system, provides a safeguard that the other DIY AID systems do provide to the same extent.

Technical Aspects

To use the rtCGM system, the insulin pump and the "computer" in a DIY AID system, data communication between the devices involved must be established. The glucose data are transferred from the rtCGM system to the computer and from there to the insulin pump for insulin infusion. The lack of communication standardization (= lack of interoperability) in the data exchange between the devices presents a considerable hurdle. So far, the manufacturers of the relevant medical devices have primarily ensured that their own devices can "talk" to each other. The Food and Drug Agency (FDA) establishes an "i" standard that promotes better *i*nteroperability between the CGM system and the computer and "ACE" (alternate controller enabled) standard for the insulin pump; interoperability problems will probably soon no longer be a hurdle.[9]

The algorithm used in each DIY AID system is responsible for processing the data and controlling the CGM system/insulin pump. The computer programs developed by the developers of the DIY AID systems to run the algorithms are not approved software (software is a medical product!). Since these algorithms automatically control the dosage of the insulin infusion (at least between meals), they require regulatory approval, that is, a CE mark in the European Union.

To prevent "hacking" of the medical devices used in the DIY AID systems, the manufacturers of the devices must ensure that no "unauthorized persons" can establish communication with their products. This is the case for modern generations of these products (especially insulin pumps), but not for older pumps. For this reason, until recently, DIY AID systems have mostly used old insulin pumps with "hack-able" interfaces.[4]

A cybersecurity problem can occur if the DIY AID systems themselves are hacked, that is, if the system is accessed from outside and its function is manipulated. A further security problem concerns data protection, that is, the question of whether the data transmitted externally by DIY AID systems is suitably encrypted before transmission.

Quality of Glucose Control

The quality of glucose control that users report to achieve with a DIY AID system is impressive. However, these results can be considered as individual reports but not as study-based evidence.[10] The achieved stability of the glucose profiles, with few fluctuations into low or high glucose ranges, is hardly achievable for many patients with the usual diabetes therapy. With DIY AID systems, this is achieved by permanently varying the insulin supply.

The quality and scientific reliability of the individual "anecdotal" reports is still limited. There are only a few systematic studies (randomized, controlled, clinical trials) to date, and some have recently been started in the United States and the European Union. These studies should also investigate how good the glucose control of the users would be if they did not use a DIY AID system and still paid so much attention to their diabetes.

Table 1. Components for DIY AID systems that are not available for commercially available AID systems.

- Pump dosing directly via a smartphone
- Interaction with the system via Siri, Google Assistant, and Alexa
- Unannounced meal compensation
- Personalized glucose targets
- Glucose prediction
- Autosensitivity/AutoTune (automatic analysis and adjustment of, eg, basal rates, carb ratio)
- Remote web app monitoring and adding carbohydrates
- Dynamic carb absorption tracking
- Integration of pharmacokinetic information of new prandial insulins into algorithms
- Automatic training target setting with Google Calendar and more

Algorithms of (DIY) AID Systems

Calculating the amount of insulin necessary to compensate for changes in glucose concentration on the basis of current and continuously available glucose data might appear trivial. In reality, the requirements for the algorithms are quite complex. For example, the glucose concentration in the interstitial fluid is measured in the subcutaneous tissue and not in the blood. Rapid fluctuations in the glucose concentration in one of the two compartments lead to corresponding fluctuations in the other compartment only after a time delay.

There are various calculation rules (algorithms) for calculating the necessary insulin dose in the literature. While the manufacturers of commercial AID systems do not publish the details of their algorithms because their development involves a lot of effort and costs, the developers of DIY AID systems do the opposite and publicly publish the algorithms used (via corresponding platforms for computer codes such as GitHub). The algorithms used in DIY AID systems are the joint work of many users, with some users (eg, Dana Lewis, Ben West, Scott Leibrand) leading the way. Because the computer code used is publicly available (open source), any user can make suggestions and corrections. There are defined release procedures for the patients responsible for the algorithms. This is to prevent negligent or intentional manipulation.

The collective approach chosen here enables a permanent further development of the algorithms, be it by error corrections or by adding new options that better cover the situation, for example, during and after physical activities (Table 1). A version history is documented so that changes are visible. The accumulated user knowledge stored here is considerable.

The developers of commercial AID systems cannot maintain such a permanent optimization of the algorithms, which are medical devices and would have to be tested for their security and at all major changes. These would require a re-approval process that would not only take several months, but would also involve costs and effort. Furthermore, the new software would need to be installed on the AID systems on the market, or there would need to be a new generation of these systems. The advantage of "official" software development, however, is that the procedures used are documented in detail and each step is checked multiple times.

Safety Aspects

The complexity of the algorithms in DIY AID systems is considerable and their development is progressing rapidly. On the one hand, this enables permanent optimization in relation to the needs of the patients; however, on the other hand, new risks can arise. The implemented changes only show, in everyday life, whether an improvement in glucose control has occurred or whether there has been a reduction in risks or not. If relevant risks occur, the question arises as to how they can be identified and documented in a comprehensible manner. Manufacturers of medical devices are obliged to record and communicate all reports of relevant problems with their products. Such procedures do not exist with DIY AID systems. So far, however, there has only been one report of two severe hypoglycemic events in a given user outside the United States that have occurred when using a DIY AID system. This led to a warning letter by the FDA.

Differences Within the European Union and Between the European Union and the United States

There are a number of active users of DIY AID systems not only in Europe, especially in Great Britain, but also in smaller countries such as Finland. In contrast, an American patient organization (Juvenile Diabetes Research Foundation [JDRF]) is a major driver of the DIY AID movement in the United States. In 2017, the JDRF initiated an "Open-Protocol Automated Insulin Delivery Systems Initiative" (grantcenter.jrdf.org) in the United States with the aim of achieving greater and more positive participation by representatives of major manufacturers and regulatory authorities. The manufacturers were asked to disclose the protocols for the interfaces of their medical devices (primarily the CGM systems and insulin pumps) so that the developers of the DIY AID systems could use them.

Cooperation between patient organizations, patients, the DIY AID community, manufacturers, and regulatory authorities is also intended to clarify specific legal problems. In the past, this type of cooperation—for example, with the NIGHTSCOUT movement—has resulted in manufacturers obtaining approval comparatively quickly for improved communication options for their rtCGM systems with other communication options (eg, smartphones).

Manufacturer

In general, not only does the intensive use of technical options in DIY AID systems represent an attractive business

expansion for the manufacturers of the medical devices used, they also learn a lot about the content of these activities.

The purpose of a medical device is clearly defined when it is approved, and the user may only use it for this purpose. If medical devices are combined into a new system, as is the case with DIY AID systems, this immediately and automatically leads to the expiry of the approval and the manufacturer is no longer being liable for it. The purpose of these specifications for manufacturers is to achieve the highest possible safety of their products for users. Patients and their physicians should be able to assume that a medical device can be used safely and effectively.

In reality, however, such requirements have undesirable side effects from the patient's point of view, for example, delayed implementation of innovative diabetes therapies. If the regulatory requirements were less rigid, new products might come onto the market faster and more cost-effectively. At the same time, the user could not be sure that the products would have been adequately tested for possible risks. If one looks at the experience of recent years with medical devices as a whole or with diabetes products, such requirements are both extremely sensible and indispensable.

It is important to find a suitable balance between the different aspects. At the same time, all those involved should remain open to new developments and—if necessary—regulatory systems should be able to adapt sufficiently quickly to changing needs. Regulatory requirements must not be a barrier to innovative approaches.

Physicians in Private Practice

Physicians are not subject to any particular testing obligation with regard to the medical devices they prescribe to their patients. They can be confident that, when used properly, they will provide reliable results. If a patient independently builds a new overall system with these devices, the physician can no longer rely on them. The more pronounced the consequences (risks) which result from the use of the data for the therapy are, the less the physician can rely on it.

Physicians That Work in Hospitals or Similar Institutions

For physicians who treat patients in their own practice, the legal situation is different from that of those employed in a hospital or similar institution. These physicians must follow the guidelines of their employer, who will in all likelihood exclude any reference to the use of an unauthorized medical device in order to avoid economic harm to the institution.

Liability Concerns Versus Medical Action

Assuming a physician would prescribe a drug to a patient that has not been approved for this purpose (or is not approved at all, ie, has not undergone a clinical development process), this would be a clear violation of the law. The physician would be liable for any damage suffered by the patient as a result. In this case, a medical trial is permissible. So what would it be like if doctors recommended a DIY AID system to their patients to improve their glucose control (they cannot even prescribe it)? Can, should, or must the doctor be guided by legal concerns? Or should the physician, in an effort to provide his/her patient with the best possible therapy, point out new therapy options, even if these are not legal or if she/he does not want to and cannot assume any liability for them? For example, if the patient has a lower risk of suffering severe hypoglycemia or achieves a significant improvement in glucose control as a result of such therapy options, these are relevant advantages from a medical point of view.

Patients With Diabetes

All patients with diabetes carry a certain basic risk due to their disease and the associated therapy. A person with type 1 diabetes risks his or her life every day with an inappropriate insulin dose. The accuracy of even the most careful human decisions is limited; hypoglycemia unexpectedly interrupts the daily routine of people with diabetes about twice a week and requires (life-saving) intervention. Against this background, automated insulin dosage does not represent an additional risk, but probably a reduction of it. However, proof of these positive assessments is still lacking. This also applies to commercial AID systems if this has not been sufficiently done in studies for their approval.

The question arises as to whether all patients are fully aware of the consequences of using a DIY AID system. They entrust their lives (or that of their child) to this system. The fact that no manufacturer assumes liability for such systems in the event of difficulties initially appears to be an abstract problem. However, if a patient has to be admitted to a hospital and the reason for this (eg, severe hypoglycemia) can be traced back to the use of a DIY AID system, the question may arise as to who pays for the treatment. On the other hand, it can be argued that users of DIY AID systems have better glucose control, which significantly reduces the risk of the occurrence of (cost-intensive) severe hypoglycemia, and more stable glucose control reduces the risk of diabetes-associated complications. Patients also report that using DIY AID systems reduces the need for physician contact. It is important to consider whether, from a purely economic point of view, the cost of the DIY AID system compensates for the (potential) costs of hospital treatment. In addition, there are savings if the user's ability to work is maintained longer and better. It is possible for patients to use DIY AID systems to work in professions that were previously inaccessible to them.

In addition to the cost of hardware, the considerable training required to safely and efficiently use modern technical systems for diabetes therapy must also be taken into account. Only if patients intrinsically understand why and how the

DIY AID system acts and reacts can safe long-term use be achieved. The users do not have to be computer experts, they do not have to understand and know all the details of the hardware and software used, but they should know how their individual diabetes and its therapy "works" and what happens if they change the parameters of their DIY AID system. It becomes legally problematic if they ask for help from other people, for example, the treating physician or diabetes consultant (see later).

For the patients (and their relatives), psychological aspects are of great importance: If they achieve a safer and more stable glucose control, this may be reflected in a better quality of life and improved undisturbed sleep.

Handling by a Third Person

If a third person (partner, friend, parent) "builds" or handles a DIY AID system for a person with diabetes, then this system is no longer "DIY," but becomes a medical device. This person then brings a medical device onto the market and is liable to prosecution or liability for this product. It must be clarified whether the use of the DIY AID system was the patient's decision or not and whether the patient has a complete overview of the associated risks. One controversial issue is the role of parents choosing to use a DIY AID system for their child with diabetes; the parent becomes liable to prosecution as the device is no longer DIY. Child safeguarding issues have to be taken into account.

Reimbursement

The costs of medical devices used in connection with diabetes therapy are usually borne by the payers (Statutory Health Insurance); since 2016, the costs of rtCGM systems have also been reimbursed by them in Germany. Since DIY AID systems are not approved medical devices, payers are not allowed to pay for them, even if they are usually unaware that an rtCGM system is being used as part of a DIY AID system.

Regulatory Authorities

The previous development and approval processes for medical devices have in many—but not in all—cases proven their usefulness. In a rapidly and dynamically changing environment, however, new developments must be adequately taken into account without neglecting safety aspects. This means: Even regulatory authorities must not act in a way that is unrealistic and remote from patients.

Evidence

To date, the approval of medical devices has also been based on the results of clinical studies, although these have not always been absolutely necessary (depending on the risk class). With adequate planning and execution, these provide reliable information on the safety and efficiency of the products. Thus, a positive benefit-risk ratio can be assumed with a certain probability. Since so far no results of such studies with DIY AID systems are available, no reliable statements are possible.

Studies have recently been initiated in the United States and the European Union to remedy this deficiency. A study with the appropriate title "OPEN" (Outcomes of Patient's Evidence with Novel, DIY AP tech) is supported by a grant from the European Horizon 2020 RISE Program. An international consortium of diabetologists and patients (Charité Berlin, Germany; Steno Diabetes Center, Denmark; Insight Data Analytics Centre Dublin, Ireland; IDF Europe, Belgium; and Diabetes Australia, Australia) is working to investigate in particular the patient-reported outcome of loopers.[11,12] The aim is to exchange knowledge and evaluate the clinical outcomes and quality of life of users of DIY AID systems. Together with an observational study conducted by the Helmsley Charitable Trust and the JDRF, this study will help to demonstrate the use and benefit of DIY AID systems through a systematic clinical study. There is another safety study that will be conducted in cooperation with the Children's and Youth Hospital Auf der Bult (T. Danne), the Charité Berlin and a coordinating center in Prague. The results of observational studies have already been presented as posters at the American Diabetes Congress 2018 in Orlando.[13] The results of a separate small clinical study have also been published.[14]

Legal Aspects

The board of directors of the German Diabetes Association (DDG) has commissioned a legal evaluation of DIY AID systems in medical, criminal, and civil law terms from a law firm in Berlin. As long as there are no judicial decisions or other legal assessments, the assessment dated July 30, 2018 (published on the DDG homepage) is in our opinion the best basis for statements on legal issues in this context (https://www.deutsche-diabetes-gesellschaft.de/fileadmin/Redakteur/Stellungnahmen/2018/Gutachten_D_B_Looper_%C3%BCberarbeitet__30.7.2018_.pdf). The DDG posed a number of questions to the firm for the evaluation (see p. 4 in the evaluation), for example, may a physician refer a patient to DIY AID systems or may a physician continue to treat a patient using a DIY AID system? The firm has answered such questions in a structured manner; the 23-page answer is divided into a short summary, a detailed description of the facts and a legal evaluation of the questions (Table 2). Some statements are not clearly formulated, at least from a medical point of view, for example, on the situation of parents who build a DIY AID system for their children with diabetes.

Summary

Since no changes in the legal requirements are to be expected for medical devices as a whole or because of one indication

Table 2. Core statements of the legal evaluation in the form of nonliteral quotations (see summary pp. 1 and 2).

- From the patient's point of view, the construction of a DIY AID system is not a criminal offense. Since, however, the intended purpose of the devices is violated, there is no liability on the part of the manufacturers of the medical devices used.
- Patients who build DIY AID systems and "sell" them to other patients are liable to prosecution under the Medical Devices Act (MPG). The placing on the market and commissioning of such a system are prohibited. The person who builds and sells the system is responsible under the Product Liability Act.
- Physicians do not have to refer patients with type 1 diabetes to DIY AID systems.
- If a patient expresses interest in such a system or is already using it, the physician must inform the patient of the improper use of a medical device and of the associated risks. The physician should document this information accordingly.

From the further remarks results:

- Physicians have a criminal and liability problem if they carry out active support measures (see p. 3) for DIY AID systems. They should not offer a platform for exchange about DIY AID systems or even training. This can be seen as an application of a medical device contrary to its intended purpose. The physician has a special position as the patient's confidant. A violation of the duty of care can lead to criminal and civil claims.
- According to the explanations above, the attending physician does not set up a medical device if she/he is merely available to advise the patient. The legal limits in the medical treatment of patients—in particular in the provision of information and advice as part of the doctor-patient consultation—must also be seen from a civil law perspective (see p. 21 and above all p. 23).
- The MPG makes an important distinction between personal use and passing on to other patients. In the latter case it concerns an offense against MPG §6 (see pp. 9 and 18 of the evaluation).
- If a physician trains patients to use DIY AID systems, she/he becomes the operator of a medical device (see pp. 12 and 16). This violation of the MPG can have liability consequences.
- If a patient builds a DIY AID system and passes it on to other patients, she/he violates the MPG (see p. 9) according to §6 para. 1 S.1 and is liable to prosecution according to §41 MPG.
- If the physician makes contact with "loopers" that offer self-made systems, the physician puts himself into a position of a possible punishment for placing medical devices on the market without CE marking (see p. 19).
- If doctors provide training and medical devices are used contrary to their intended purpose, they are not liable to prosecution under the MPG. Under certain conditions, however, criminal liability may be considered for negligent killing or negligent bodily injury (see p. 20).
- From the point of view of civil law, there are in particular liability issues if damage to health occurs when using the DIY AID system.
- There is no claim of a patient against the manufacturer of the used products. If the DIY AID system is passed on, the patient himself becomes liable.
- The physician is obliged to inform patients about the intended use of medical devices (= therapeutic information) (see pp. 20 and 21). This is otherwise a treatment error.
- The physician must point out the dangers that may arise when using a DIY AID system. The physician should clearly distance himself from the use of a DIY AID system and not encourage patients to use the system.

area alone in Europe/Germany, other solutions will be needed to prevent a growing group of patients in Germany (and their treating physicians) from using DIY AID systems and thus from getting into a difficult legal situation.

If the previous development and approval paths have been too complex and long lasting (this problem does not only apply to DIY AID systems), then the question arises: Will there be (disruptive) developments that simply ignore such structures, as has happened in recent years in completely different areas? Some of the big digital companies have sufficient financial resources and the self-confidence not to care about the official (well-established) ways and structures. In the field of diabetes, Abbott's intermittent scanning CGM (Freestyle Libre) system has shown very successfully how a large group of patients (more than 1 million users worldwide) can benefit from the advantages of a CGM system if they do not follow the usual structures for market introduction of a medical device and reimbursement.

It could be possible for AID systems to receive a preliminary approval and at the same time be closely monitored, for example, by an AID registry. The DDG Executive Board supports the establishment of such a register in the sense of a vigilance check. The costs for the maintenance of such a register would have to be clarified, and the cost bearers and manufacturers would also be required to do so.

The commitment of DIY AID system users to react quickly to requirements with their creativity, competence, and abilities (by using swarm intelligence and open cooperation) has led to a "medical device" which does not meet the regulatory and legal requirements, but in everyday life, covers the real needs of at least a certain group of patients well. It remains to be seen whether "We are not waiting!" only applies to the (sub)group of patients who use DIY AID systems or whether considerably more patients would join in the sense of "let's tackle it!"

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: LH works for a number of companies that develop novel diagnostic and therapeutic options; however, he has no conflict of interest when it comes to DIY AID systems. KL declares no conflict of interest.

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