Glucose Measurement and Control in Patients with Type 1 or Type 2 Diabetes

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ABBREVIATIONS

AGDT	Working Group for Diabetes & Technology
AGP	Ambulatory Glucose Profile
AGPD	Working Group for Paediatric Diabetology
AID	Automated Insulin Delivery
ATTD	Advanced Technologies and Treatments for Diabetes
CGM	Continuous Glucose Monitoring
CSII	Continuous subcutaneous Insulin Infusion (Insulin pump therapy)
CT	Conventional insulin therapy
G-BA	Federal Joint Committee
GOD	glucose oxidase
GDH	glucose hydrogenase
GMI	glucose management indicator
FDA	Food and Drug Administration
ICT	Intensified conventional insulin therapy
iscCGM	Intermittent-scanning CGM
ISF	Interstitial fluid
KV	Association of Statutory Health Insurance Physicians (Kassenärztliche Vereinigungen)
MARD	Mean Absolute Relative Difference
PARD	Precision Absolute Relative Deviation
rtCGM	Real-time CGM
SMBG	Self-measurement of capillary blood glucose concentration
SaP	sensor-augmented pump therapy
TaR	Time-above-Range
TbR	Time-below-Range
TiR	Time-in-Range
CV	Coefficient of variation

Overview

Regular glucose measurements are indispensable for monitoring the progress of diabetes therapy and are used either to make immediate decisions on the appropriate dosage of antidiabetic medication or on the intake of carbohydrates. The retrospective analysis of the metabolic situation using the HbA1c measurement serves mainly to assess the long-term risk for microvascular and macrovascular complications. New statistical parameters for evaluation, such as the time in target range (TiR) or the coefficient of variation (CV) from the software offers of the tissue glucose monitoring systems, can be used to further specify the quality of diabetes control.

The classic method for self-monitoring is capillary blood glucose measurement (SMBG). Over time, some blood glucose measurement systems have been able to achieve a measurement accuracy that comes close to that of laboratory systems. Blood glucose measurements display the current glucose level. Information on the trend from the past and in the imminent future is only possible with continuous glucose monitoring (CGM). Systems for CGM in interstitial tissue fluid (ISF) have been available since 1999: While measurements with SMBG systems under everyday conditions are performed on average 4–7 times daily in adults with type 1 diabetes, CGM systems provide a complete 24-hour overview and deliver measured values at 1–5 min intervals (depending on the system). The registered CGM profiles visualize the glucose trend, i. e., they display fluctuations in glucose concentrations. Although satisfactory glucose control is possible in many patients who perform sufficiently frequent SMBG measurements, CGM can promote participation in life and reduce psychological stress. This applies in particular to children with type 1 diabetes who are not yet able to identify physical symptoms, e. g. hypoglycaemia. The number of blood glucose measurements required daily is often more than 20 – which often places a high burden on both children and parents. This is especially the case for regular night-time measurements. CGM systems are also a technical innovation, as they enable the establishment of automated insulin delivery (AID) systems that match current glucose levels.

The current generations of real-time-CGM (rtCGM) systems have considerably improved measurement accuracy compared to systems of earlier generations. There is currently no standard procedure for determining the accuracy of CGM systems as there is for blood glucose monitoring systems. Irrespective of this, there may be deviations between the measured concentrations in the two compartments of blood and tissue glucose due to a physiological time lag, especially in the case of rapid increases and decreases in the glucose trend. A bias of the systems can also be caused by factory calibration, if different references are used, or by own calibration in case of faulty behaviour during blood glucose measurement or if inaccurate blood glucose measurement systems are used.

Long-term metabolic optimisation requires continuous use of CGM systems, although how patients use CGM systems in reality has not been well studied so far. However, initial studies suggest that without appropriate comprehensive and specialised CGM training and qualified supervision, the possibilities of CGM systems are insufficiently used and thus do not lead to any improvement in glucose control. In a US study, it was shown, especially among adolescents with type 1 diabetes, that there was an increase in the HbA1c value after these technologies were introduced, which may be due, among other things, to a lack of training in the USA. In Germany, the CGM-TRAIN study showed that the SPECTRUM training programme resulted in an increase in CGM knowledge among participants – both in theoretical knowledge and practical implementation. In our view, this is evidence that the provision of the technical options per se is not sufficient, but that patients and diabetes teams need to be adequately trained in the proper use of this diagnostic option. Furthermore, regular retrospective data analysis is necessary to adjust therapy in order to achieve a sustained improvement in glucose control. Manufacturers support this process with increasingly better software solutions for CGM data analyses. Such analyses can provide concrete indications for the adjustment of diabetes therapy. Overall, the patient should have an "active" view of the glucose values and "work" with them. Likewise, the doctor and diabetes team should regularly support the patient with a constructive and structured data analysis.

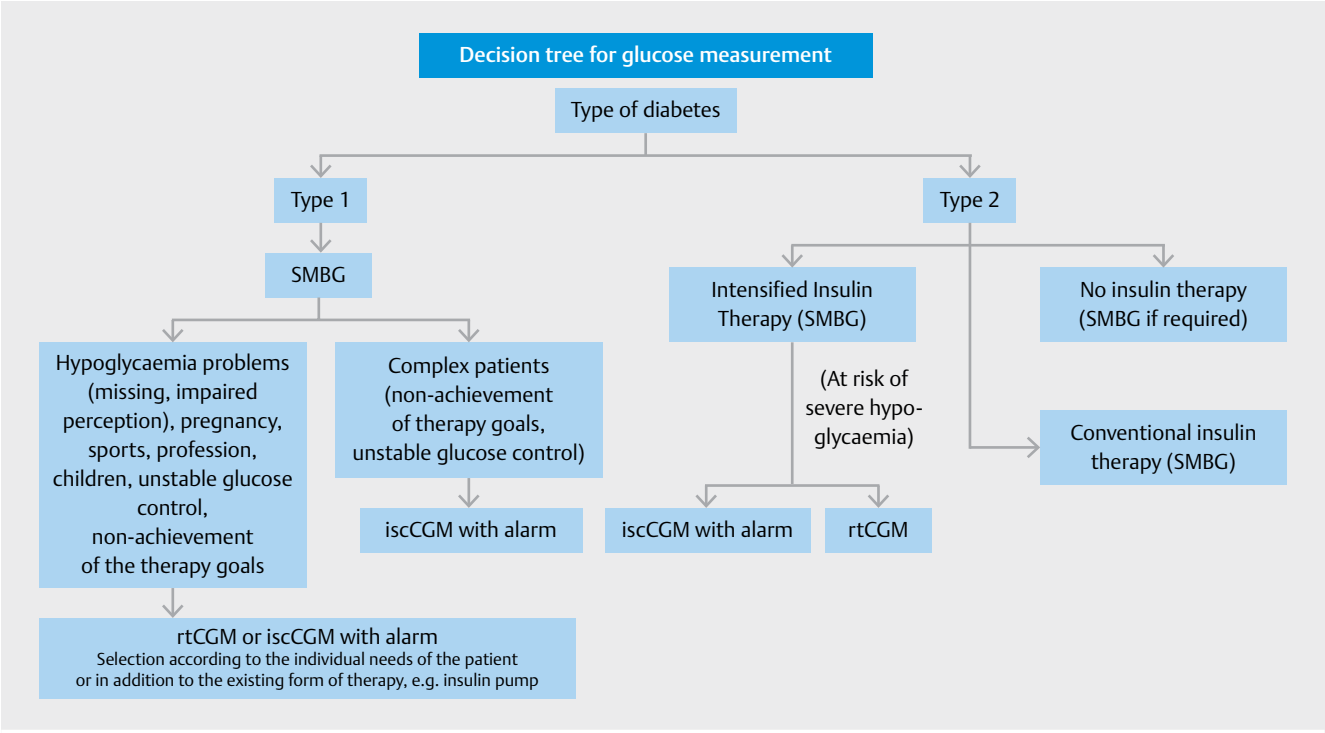
The CGM systems are usually based on what are called "needle sensors", which enable the measured glucose values to be displayed directly on special receiving and display devices (handhelds), insulin pumps or via an app on a smartphone (rtCGM). As an alternative to the needle sensors, an implantable long-term sensor for an rtCGM system (life cycle up to 6 months) is also available. Another widely-used variant of CGM systems is a needle sensor system in which the reader must be held close to the sensor to display/read out the measured values (intermittent-scanning CGM, iscCGM).

In the following, the various options for glucose measurement using a uniform structure are explained. The decision tree in (▶ **Fig. 1**) provides a quick overview of which glucose measurement system is best suited for which individual patient. The starting point is the patient coming to the practice or hospital. The diabetes team then needs to recognize the patient's diabetological needs and discuss the various options for glucose measurement with the patient. The patient, diabetologist and diabetes consultant should all jointly make the decision as to which option is best for the patient. The CGM system used should be changed if it does not properly meet the medical needs of the patient. Due to the long duration of health insurance prescriptions for any product, a product change may need some lead time or well-founded arguments.

The decision as to which system fits the patient best should be guided primarily by medical and social indications (e. g. hypoglycaemia, pregnancy, professional life and private life), not by economic aspects. SMBG is the first level that every patient should master and use. Only then should a conversion to rtCGM/iscCGM take place. The decision as to which of the two CGM options currently offered is suitable depends on the individual conditions of the patient. Intensive training in the selected form of diabetes therapy is a prerequisite for CGM use and is required for each CGM version. Not adhering to rtCGM or iscCGM should lead to ending the use of these systems.

The procedure may differ for children. Nowadays they often first receive an insulin pump and a CGM system quickly follows. In many cases, children under 2 years of age receive both directly. This patient group benefits greatly from the new technical options, e. g., that also enable remote monitoring and advice, e. g., at day-care or other activities, via the follower function.

Statements on the therapeutic use of the glucose monitoring values obtained by various patient groups are made in the respec-



▶ **Fig. 1** Decision tree for the various glucose measurement options. SMBG = self-measurement of capillary blood glucose concentration; CGM = continuous glucose monitoring; rtCGM = real-time CGM, iscCGM = intermittent-scanning CGM.

tive DDG (German Diabetes Society/Deutsche Diabetes Gesellschaft) practical recommendations.

These Practice Guidelines do not mention product names for SMBG systems, although there is a clear need for a positive list. Similarly, no information is provided on the technical details of specific products, as their further development is too rapid (see the manufacturers' homepages).

This Practice Guideline is not an evidence based S3 guideline and, accordingly, statements are not supported by literature quotations. The guidelines are based on the clinical and practical experience of the authors and the evidence derived from studies for the purpose of the achieving the best possible usability in everyday life. As well, no statements are made on the diabetes diagnosis and the use of glucose measurement systems to do so (see the corresponding practical recommendation).

The authors of this Practice Guideline are members of Working Group for Diabetes and Technology/AG Diabetes & Technologie e. V. (AGDT) and/or the Working Group for Paediatric Diabetology/Arbeitsgemeinschaft für Pädiatrische Diabetologie e. V., (AGPD), which are working groups under the umbrella of the DDG.

Self-measurement of capillary blood glucose concentration (SMBG)

Goals/indications

In order to achieve the therapy goals, e. g. an HbA1c value set with the treating physician, reduction of hypoglycaemia, improvement of the preprandial or postprandial BG values, properly-trained patients with diabetes mellitus regularly measure the glucose concentration in capillary blood samples (information on the correctly performing the measurement is found in ▶ **Tab. 1**). Blood glucose measurements are also used to detect acute metabolic disorders (hypoglycaemia or hyperglycaemia).

With different therapy approaches (oral therapy, bedtime insulin administration, conventional insulin therapy (CT), intensified insulin therapy (ICT), insulin pump therapy (CSII)) and different diabetes types (type 1, type 2 with and without insulin therapy, pancreatic diabetes mellitus, gestational diabetes and others), different times and frequencies for measuring blood glucose concentrations are common and objectively indicated (▶ **Tab. 2**). The glucose measurement results are used to adjust the insulin dose or other antidiabetic drugs, modify exercise to the current glucose situation or carbohydrate intake for an (imminent) hypoglycaemia.

There is a clear indication for SMBG in patients with type 1 or insulin-dependent type 2 diabetes. Measuring glucose not only involves proper patient training on how to precisely and correctly perform the glucose measurements, but it also necessary to have an understanding of how the measurement results are converted into therapeutic steps. The ability to perform SMBG correctly is essential even if a CGM system is used. Blood glucose test strips must therefore continue to be prescribed. Only then can patients check unexplained glucose values when needed or have an alternative to therapy control in case of technical problems with the CGM system. Furthermore, some CGM systems need to be calibrated.

▶ **Tab. 1** Practical procedure in capillary blood glucose measurement.

Preparation
Wash and dry hands before measuring, as food residues, skin cream or disinfectants can falsify the measurement. If this is not possible, wipe off the first drop of blood and use the second drop for the measurement.
After lancing the fingertip to obtain a drop of blood, the measurement should be performed quickly. Therefore, all material should be ready beforehand.
Lancing
Lance the side of the fingertip:
The fingertip is particularly sensitive and scarring damages the sense of touch.
Do not prick index finger or thumb.
Press the lancing device firmly into place. Start with the smallest penetration depth of the lancing device. Check which penetration depth results in a sufficiently large blood drop. Change the lancet of the lancing device for each measurement.
Lancets are disposable articles; they become dull due from puncture and damage the skin when reused.
Measurement
Know the special features of the respective SMBG system, e. g.:
How and where should the blood sample be applied to the test strip?
Can blood be added subsequently if the amount of blood was insufficient?
Which drugs can interfere with the measurement?
In which temperature range can measurements be made? (Important when outdoor temperatures are low or high.) Test strips are sensitive.
When measuring, do not touch or press down on the test strip, fold or bend it.
Always store test strips in closed tube/package and keep it dry and away from light.
Observe storage temperature (especially important in case of heat or frost).
Measurement results
Measurement results must be documented, values must be recorded in a diary or electronic documentation options must be used.
The patient and doctor can only discuss the quality of glucose control and possible therapeutic changes if the measured values are documented. Coordinate target values, measurement frequency and measurement times with the doctor.
Do not trust measured values blindly.
Despite correct execution of the measurement procedure, the measurement result may be incorrect! Patient symptoms are more important than a measurement value, in case of discrepancies repeat measurement.
SMBG systems
Due to further technical development and damage to the device caused by use, SMBG systems should be replaced every few years.
If several/different SMBG systems are used at the same time, note the differences in operation. Systematic differences between the systems may occur in the measurement results.

Frequency of measurements

Patients with type 1 diabetes and ICT with multiple insulin injections daily (ICT) or an insulin pump should measure blood glucose concentration at least 4 times daily (preprandial and before bedtime) and every 2–3 weeks during the night. In addition, measurements may be taken in special situations, e. g. to check the effects of meals, in suspected hypoglycaemia, sport, illness, holidays, etc. This results in an average need for at least 5 glucose test strips per day (▶ **Tab. 2**). **Patients with type 1 diabetes and hypoglycaemia perception disorder** form a special group. In addition to the measurement times already described, measurements are carried out before each car journey, during physical activity, during sport and during everyday work. This results in a quarterly requirement of at least 800 test strips. The need for test strips in children, especially toddlers, increases even further as children cannot reliably express themselves regarding the symptoms of hypoglycaemia or hyperglycaemia and are also more prone to much faster and more intense glucose fluctuations than adults with type 1 diabetes.

Patients with insulin-dependent type 2 diabetes with ICT should also determine preprandial and occasionally postprandial glucose levels and measure them before bedtime. The daily requirement is at least 4–5 test strips, which corresponds to at least 500 test strips per quarter. Patients with insulin-dependent type 2 diabetes and CT or bedtime therapy require at least 2 measurements per day; this results in a quarterly requirement of at least 200 test strips.

Patients with non-insulin-dependent type 2 diabetes undergoing therapy with insulinotropic oral antidiabetics (sulfonylureas, glinides) require test strips for detecting hypoglycaemia. Practical experience shows a requirement of at least 50 test strips per quarter. It makes medical sense to provide all patients with type 2 diabetes and oral antidiabetic therapy with at least 50 test strips per quarter in case of manifestation or for training purposes or if the therapy goals are not achieved.

Pregnant women with a pre-existing type 1 or type 2 diabetes perform preprandial and postprandial glucose measurements, resulting in a requirement of at least 7 test strips per day, i. e., at least 700 test strips per quarter. Women with gestational diabetes should always measure fasting blood glucose and postprandial glucose 2–3 times per week. In cases of insulin dependence, regular preprandial and postprandial glucose measurements are necessary which leads to a requirement of at least 7 test strips per day.

Measurement method

In the SMBG systems commonly used by patients, the enzyme used is either glucose oxidase (GOD) or glucose hydrogenase (GDH). The glucose oxidase method is susceptible to substance and drug interferences (e. g. ascorbic acid, paracetamol, blood oxygen content). As well, relevant interferences must be taken into account, especially in patients with multimorbidities (interferences caused by medications, uric acid, etc.). For patients with high or low haematocrit values, the respective SMBG system (▶ **Tab. 2**) should be checked (manual/test strip package insert) for compatibility to the patient.

Available systems

There are many different SMBG systems currently available from various suppliers. Overviews of the properties of these systems are primarily based on the information provided by the manufacturers, however, there are no official lists of the measurement quality of the various systems. Many modern SMBG systems have addi-

▶ **Tab. 2** Recommendations for the use of self-measurement of capillary blood glucose concentration (SMBG) in the various types of diabetes and forms of therapy.

Diabetes	Therapy	Measurement frequency	Measurement situation Preprandial: before the meal Postprandial: 1.5 h after meal	Measurement interval	Test strip requirement
Type 1	ICT	At least 4 × daily	Preprandial and possibly postprandial, before going to bed	On a daily basis	> 4 strips daily At least 500 strips per quarter
			At night (2:00 a.m. to 4:00 a.m.)	Every 2–3 weeks	
			In special situations (suspected hypoglycaemia, sport, illness, before driving, etc..)	When required	
Type 1 children and adolescents	ICT	At least 10 × daily	Preprandial, postprandial, before going to bed, at night	On a daily basis	> 10 strips daily At least 1000 strips per quarter
			In special situations (before/at/after sports	When required	
			During feverish infectious diseases, etc..)	Every 2–3 h	
Type 1	Insulin pump	At least 5 × daily	Preprandial and possibly postprandial	On a daily basis	> 5 strips daily At least 600 strips per quarter
			Before going to bed at night (2:00 a.m. to 4:00 a.m.)	Every 2–3 weeks	
			In special situations (suspected hypoglycaemia, sport, illness, before driving, technical mistake, etc..)	When required	
Type 1 children and adolescents	Insulin pump	At least 12 × daily	Preprandial, postprandial, before going to bed, at night	On a daily basis	> 12 strips daily At least 1200 strips per quarter
			In special situations (before, during or after sports)	When required	
			During infectious diseases, technical mistake, etc..)	Every 2–3 h	
Type 1 with hypoglycaemia perception disorder	ICT/ insulin pump	At least 8 × daily	Preprandial and postprandial, before going to bed	On a daily basis	> 8 strips daily At least 800 strips per quarter
			At night (2:00 a.m. to 4:00 a.m.)	Every 2 weeks	
			In special situations (suspected hypoglycaemia, sport, illness, before driving, technical mistake, etc..)	When required	
Type 2	ICT	At least 4 × daily	Preprandial and possibly postprandial, before going to bed	On a daily basis	> 4 strips daily At least 500 strips per quarter
			At night (2:00 a.m. to 4:00 a.m.)	Every 2–3 weeks	
			In special situations (suspected hypoglycaemia, sport, illness, before driving, etc..)	When required	
Type 2	CT	At least 2 × daily	Preprandial (before injection)	Daily	> 2 strips daily At least 250 strips per quarter
			At night (2:00 a.m. to 4:00 a.m.)	Every 2–3 weeks	
			In special situations (suspected hypoglycaemia, sport, illness, before driving, etc..)	When required	
Type 2	Bedtime insulin	At least 2 × daily	Preprandial fasting, before going to bed	On a daily basis	> 2 strips daily At least 200 strips per quarter
			At night (2:00 a.m. to 4:00 a.m.)	Every 2–3 weeks	
			In special situations (suspected hypoglycaemia, sport, illness, before driving, etc..)	When required	
Type 2 with hypoglycaemia risk	Insulinotropic oral antidiabetics (sulfonylureas, glinides)	At least 2 × per week	Preprandial fasting, before going to bed	1 × per week	> 1–2 strips daily At least 50 strips per quarter
			At night (2:00 a.m. to 4:00 a.m.)	Every 2–3 weeks	
			In special situations (suspected hypoglycaemia, sport, illness, before driving, etc..)	When required	
Type 2 without hypoglycaemic risk	Oral therapy		In special situations (manifestation, for training purposes, failure to achieve the therapy goals, etc..)	When required	At least 50 strips per quarter

▶ **Tab. 2** Recommendations for the use of self-measurement of capillary blood glucose concentration (SMBG) in the various types of diabetes and forms of therapy.

Diabetes	Therapy	Measurement frequency	Measurement situation Preprandial: before the meal Postprandial: 1.5 h after meal	Measurement interval	Test strip requirement
Type 1/type 2 Pregnancy	ICT/ insulin pump	At least 7 × daily	Preprandial and postprandial, before going to bed	On a daily basis	> 7 strips daily At least 700 strips per quarter
			At night (2:00 a.m. to 4:00 a.m.)	On a weekly basis	
			In special situations (suspected hypoglycaemia, sport, illness, before driving, technical mistake, etc..)	When required	
Gestational diabetes	Nutrition	At least 15 × per week	Fasting,	On a daily basis	At least 350 strips per quarter
			Preprandial and postprandial, before going to bed	3 × per week	
Gestational diabetes	Insulin	At least 7 × daily	Preprandial and postprandial, before going to bed	On a daily basis	> 7 strips daily At least 700 strips per quarter
			At night (2:00 a.m. to 4:00 a.m.)	Every 2 weeks	
			In special situations (suspected hypoglycaemia, sport, illness, before driving, technical mistake, etc.)	When required	

ICT = Intensified conventional insulin therapy; CT = conventional insulin therapy

tional functions, such as data storage and readout, marking of values as preprandial or postprandial, colour coding of displayed values for better assessment, a light at the test strip slot to facilitate handling, bolus calculators, calculation of an estimated HbA1c value or the possibility of transmitting data to an app/cloud (connectivity).

Specifications for measurement quality/standards

Like all medical devices, blood glucose monitoring systems have CE marking. CE marking is not a mark of quality; the SMBG systems available the market must, however, fulfil the ISO Standard 15 197: 2015. There is no systematic evaluation of the measurement quality of SMBG systems after their introduction to market. Over time, many independent evaluations have shown that some systems on the market exhibit inadequate measurement quality.

Costs/refund of expenses

Health insurance covers the costs for blood glucose monitoring systems (device and test strips) for patients with type 1 diabetes and patients with insulin-dependent type 2 diabetes. Patients with type 2 diabetes who do not undergo drug therapy or who take oral antidiabetics without a hypoglycaemic risk are only covered by statutory health insurance in special situations (unstable metabolic conditions, readjustment or change with an increased risk of hypoglycaemia).

The prescribing physician determines the number of test strips deemed appropriate for the given insulin-dependent patient. An exact indication is important. For example, a manifestation or pregnancy in a type 1 or type 2 diabetes patient has a significantly higher test strip consumption ranking than in CT does. In reality, the prescribability of blood glucose test strips is regulated by a Federal Joint Committee/Gemeinsamer Bundesausschuss (G-BA) decision and is laid down in the Pharmaceutical Directives/Arzneimittel Richtlinien Annex III (Overview of prescription restrictions and exclusions/Übersicht über Verordnungseinschränkungen und -ausschlüsse). The Association of Statutory Health Insurance Physicians/ Kassenärztliche Vereinigungen (KV) regulates the prescription of blood glucose meters and test strips. The health insurance companies and the KV signed a common guiding framework, agreements and contracts leading to "recommendations" as to which costs are covered for which type of diabetes and of therapy. These recommendations are, however, not binding. **For users of CGM systems, the number of blood glucose measurements can be reduced, but never completely dispensed with.**

Quality control (Internal and external/ interlaboratory comparisons)

Quality control for personal glucose measurement systems can be performed by the patient with a system-specific control solution; these are offered by manufacturers for their products. Ideally, the patient should carry out quality controls of the measurement quality of the SMBG system at home every time a new test strip package is opened and for the situations specified in the operating instructions.

According to the German Medical Association guidelines (RiliBÄK), systems used in laboratories, clinics, practices and in other institutions (retirement homes) where medical personnel measures glucose in patients must meet the requirements for internal quality control (control solution measurements) but not those for external quality control (interlaboratory comparisons). The internal quality control for SMBG systems in use must be carried out regularly in every practice. The implementation of external quality control by participating in interlaboratory comparisons can provide additional information on measurement quality.

Safety issues/side effects

An incorrect SMBG measurement results in the administration of an incorrect insulin dose, which can have immediate and significant consequences such as severe hypoglycaemia. Therefore, when

training patients, it is imperative to focus on the prerequisites for correct glucose measurement using SMBG systems (▶ **Fig. 2**).

For the patient, lancing a fingertip to obtaining a blood drop for SMBG can be a painful procedure. Despite the modern lancing devices available today, lancing is still felt and repeatedly lancing the same sites can lead to considerable scarring of the fingertips and reduced sensitivity in the future. Younger children, who do not yet understand the necessity of these measures, may experience considerable psychological stress and disturbance of the parent-child relationship. Nonetheless, even for adult patients, the pain that is self-inflicted several times a day can be a psychological burden.

Practical implementation of the measurement

During the measurement, it is important to consider the factors that are important for a correct measurement (▶ **Fig. 2**) (see Guidelines for Blood Glucose Self-Monitoring/Leitfaden zur Blutzuckerselbstkontrolle: https://www.vdbd.de/fileadmin/portal/redaktion/Publikationen/190516_VDBD_Leitfaden_Glukose_Selbst.pdf).

Use with different patient groups

The SMBG "market" is usually only divided into patients with type 1 or type 2 diabetes and women with gestational diabetes. In reality, however, there are a number of subgroups, especially when it comes to SMBG: there are hardly any monitoring systems on the market that are suitable for patients with impaired vision or for the blind (devices with speech output or acoustic instructions for use). The same applies to elderly patients with limited manual dexterity. They need devices with simple operation and a clearly legible display.

Training/psychological aspects

The preparatory steps for SMBG, in particular obtaining a capillary blood drop, as well as correctly performing the actual measurement require sufficient theoretical and practical training. Ideally, this should be done using the SMBG system that the patient will later use. A one-off introduction is often not enough, i. e., the various steps to be taken should be repeatedly trained, discussed and closely supervised.

Since performing SMBG in public (school, workplace, restaurant, etc.) makes it visible that the person has diabetes, they often do not perform a measurement in such situations. This can entail significant risks as acute glucose derailments are then not detected. The patients' understandable desire for discretion makes other glucose monitoring options (CGM, see below) attractive. However, not all patients want to permanently wear a technical device on their body or be disturbed by alarms.

Comment

The performance of SMBG monitoring systems has improved in recent decades to such an extent that considerable further improvements are no longer to be expected in the foreseeable future. SMBG systems still have the largest market share of glucose monitoring systems in the field of diabetes technology – in part, due to the lower costs compared to rtCGM/iscCGM systems.

One important option for further development of SMBG systems is their interoperability, i. e., improved automatic availability of measurement results for evaluating data in programs or apps. The merging of glucose values including data from the insulin dose (by using smart pens), carbohydrates consumed (by an automated analysis of the carbohydrate content of meals) or exercise (by using data from fitness wristbands) enables an additional calculation of such data sources for calculating the optimal insulin dose.

Real-time CGM (rtCGM)

Goals/indications

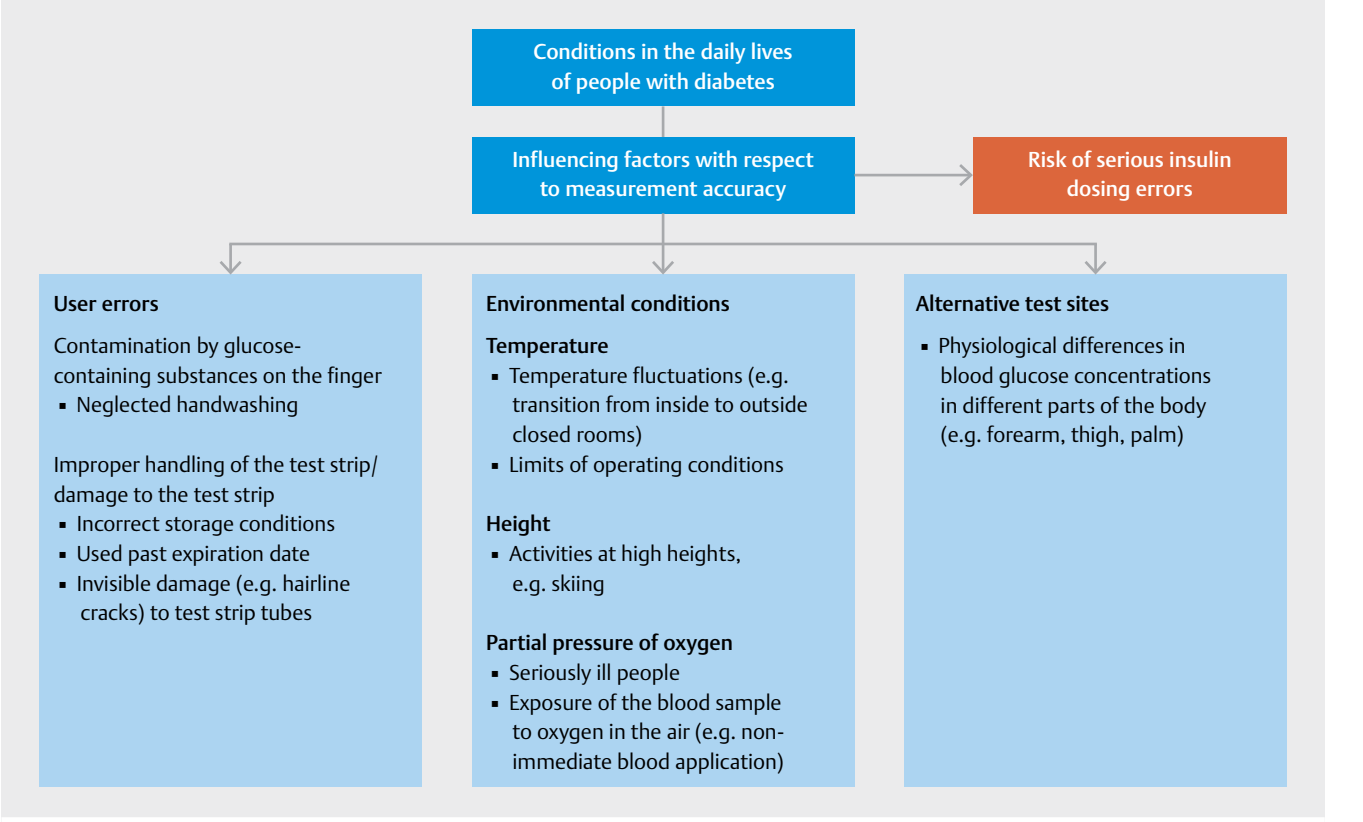
When using rtCGM systems, therapy goals can be better achieved by increasing the quality and quantity of information (continuous display of the current glucose value, trend display and alarms when pre-set limit values are reached as well as predictive alarms, systematic data analysis (▶ **Tab. 3–5)**. The continuous use of rtCGM systems can enable motivated users to increase the amount of time within the target range (time in range, TiR) and achieve their therapy goals of reducing the HbA1c value and duration and the occurrence of (severe) hypoglycaemia. In addition to assessing current glucose control, the information on glucose trend also helps in assessing the impact of therapeutic interventions on food intake, physical activity or other influencing factors. In order for patients to adequately use the quantity and quality of the information provided and to be able to translate it into therapeutic interventions, which is a complex task, they must receive theoretical and practical training in addition to technical instruction on the respective rtCGM system. For this purpose, there is the SPECTRUM training programme in Germany; the effectiveness of its use was proven by the CGM-TRAIN study published in 2020.

Indications for using rtCGM apply for the following patient groups (▶ **Fig. 1**):

- Type 1 diabetes
- Type 2 diabetes with ICT
- Insulin-dependent diabetes with frequent hypoglycaemia or hypoglycaemia disorder
- Pregnancy with pre-existing insulin-dependent diabetes
- In other individual cases

In consultation between patient and physician, an individual decision must be made as to whether rtCGM use is medically necessary and sensible (▶ **Figs. 1 and 3**). A test phase can be helpful for the patient and the diabetes team to weigh the individual benefit.

rtCGM systems can be used either as stand-alone devices, e. g. for patients with ICT, or in combination with an insulin pump. In sensor-augmented pump therapy (SaP) or an AID system, the rtCGM system is in direct communication with the pump. rtCGM is a central factor in both SaP and AID systems. In SaP, some pumps automatically stop the basal insulin infusion if the sensor glucose values fall rapidly (predictive low glucose suspend). In hybrid AID systems, the basal insulin delivery is adapted according to the current glucose values with the help of an algorithm. At low glucose levels, the insulin infusion rate is reduced or stopped completely; at hyperglycaemic glucose levels, it is increased. In hybrid AID systems, insulin is still administered manually by the patient at mealtimes. Commercially-available AID systems automatically regulate



▶ **Fig. 2** Factors that have an influence on the self-measurement of capillary blood glucose concentration result.

basal insulin delivery to a target value. Currently, and in the near future, various AID systems can be expected in which both the algorithms and the parameters to be set differ. Systems that automatically deliver correction boluses in addition to basal insulin delivery (AH-AID, advanced hybrid-AID) are also already available.

Almost all rtCGM systems also allow the measured values to be transferred to a cloud. From there, the data can be forwarded to family members or the diabetes team if the patient so desires (connectivity).

In addition to rtCGM systems where a needle sensor is inserted under the skin, a long-term rtCGM system is available in which the sensor is inserted under the skin with minimal surgical intervention. Through a transmitter on the skin, which can be removed at any time, the glucose concentration in the ISF is determined and transmitted to a receiver. This is the only rtCGM system where vibration alarms of the transmitter are available directly on the body in addition to the usual alarms triggered by the smartphone/receiver. The sensor is removed by a certified physician after its functional period of up to 180 days.

In our opinion, the majority of patients who require a more intensive diabetes therapy should first use an rtCGM/iscCGM system and subsequently add an insulin pump. Studies demonstrate the benefit of rtCGM in patients who perform ICT with multiple daily injections. With regard to an improvement in HbA1c levels and a reduction in the risk of hypoglycaemia in children under 8 years of age with type 1 diabetes, a start should be made with an rtCGM system and with an insulin pump as early as the manifestation of diabetes. With SaP therapy, TiR is usually improved further than

▶ **Tab. 3** Factors that have an influence on the continuous glucose monitoring (CGM) measurement result.

Application-related factors:
- Placement of the sensor in individually unfavourable locations (e. g., too little/too much fatty tissue, mechanically stressed sites, unforeseeable factors)
- Sensor insertion site not approved/tested (depending on sensor system: upper arm, abdomen, thigh, buttocks) with individually varying good blood circulation, increased mobility of the sensor in subcutaneous fatty tissue
- Calibration error (if necessary): calibration with CGM values instead of blood glucose values, calibration during rapid rise, rapid fall or hypoglycaemia, no calibration when this would be appropriate and possible, calibration with unclean fingers
- Repeated calibration with incorrectly low values leads to differences between GMI (lower) and laboratory HbA1c (higher) and vice versa
- Pressure on the sensor site due to belt, waistband, sleeping position (falsely low values during pressure application)
- Mechanical instability of the patch, sensor patch partially or completely detached
- Sweat or water (shower, etc.) penetrates the sensor site (false low values)
- Inflammation of the skin at the insertion site of the sensor

Technical and environmental factors:
- Defective sensor (e. g., transport or storage of sensors outside the recommended temperature range, error in production/related to batch).
- Reproducibly limited measurement accuracy with certain users when using a certain sensor system (not predictable, individual biocompatibility?)
- Chemical interfering substances, depending on the sensor system (see operating instructions, e. g., vitamin C, paracetamol)
- Too high “underpatch” in the case of patch allergy (several millimetres, off-label!), which places part of the sensor in the fatty tissue and part in the patch

▶ **Tab. 4** Parameters for characterizing continuous glucose monitoring (CGM) data (retrospective analysis).

Consensus Advanced Technologies and Treatments for Diabetes (ATTD): all parameters should be available to assess CGM data		
Time-in-range/Time-in-target-range (TIR)		**70–180 mg/dl**
		3.9–10 mmol/l
Time-below-range (TBR)/Time-below-target-range	Level 1	54–69 mg/l
		3.0–3.8 mmol/l
	Level 2	< 54 mg/dl
		< 3.0 mmol/l
Time-above-range	Level 1	181–250 mg/dl
		10.1–13.9 mmol/l
	Level 2	> 250 mg/dl
		> 13.9 mmol/l
Glycaemic variability		Coefficient of variation/standard deviation
Mean glucose value		–
Glucose management indicator		–
CGM visualization		Ambulatory glucose profile (AGP)
Episodes of hyper- and hypoglycaemia		At least 15 min duration
Recommendation on the amount of data that should be available for evaluation		At least 70 % of CGM data from 14 days

▶ **Tab. 5** Guideline values for target values of continuous glucose monitoring (CGM)-derived parameters in adults with type 1 or type 2 diabetes.

Consensus Advanced Technologies and Treatments for Diabetes (ATTD) 2019		
Parameters	**Characterisation**	**Guideline values for target values**
Time-in-range/Time-in-target-Range (TIR)	70–180 mg/dl	> 70 %;
	3.9–10.0 mmol/l	> 16 h 48 min
Time-below-range (TBR)/Time-below-target-range	< 70 mg/dl	< 4 %;
	< 3.9 mmol/l	< 1 h
	< 54 mg/dl	< 1 %;
	< 3.0 mmol/l	< 15 min
Time-above-range	> 180 mg/dl	< 25 %;
	> 10.0 mmol/l	< 6 h
	> 250 mg/dl	< 5 %;
	> 13.9 mmol/l	< 1 h 12 min
Glycaemic variability	Coefficient of variation/standard deviation	≤ 36 %

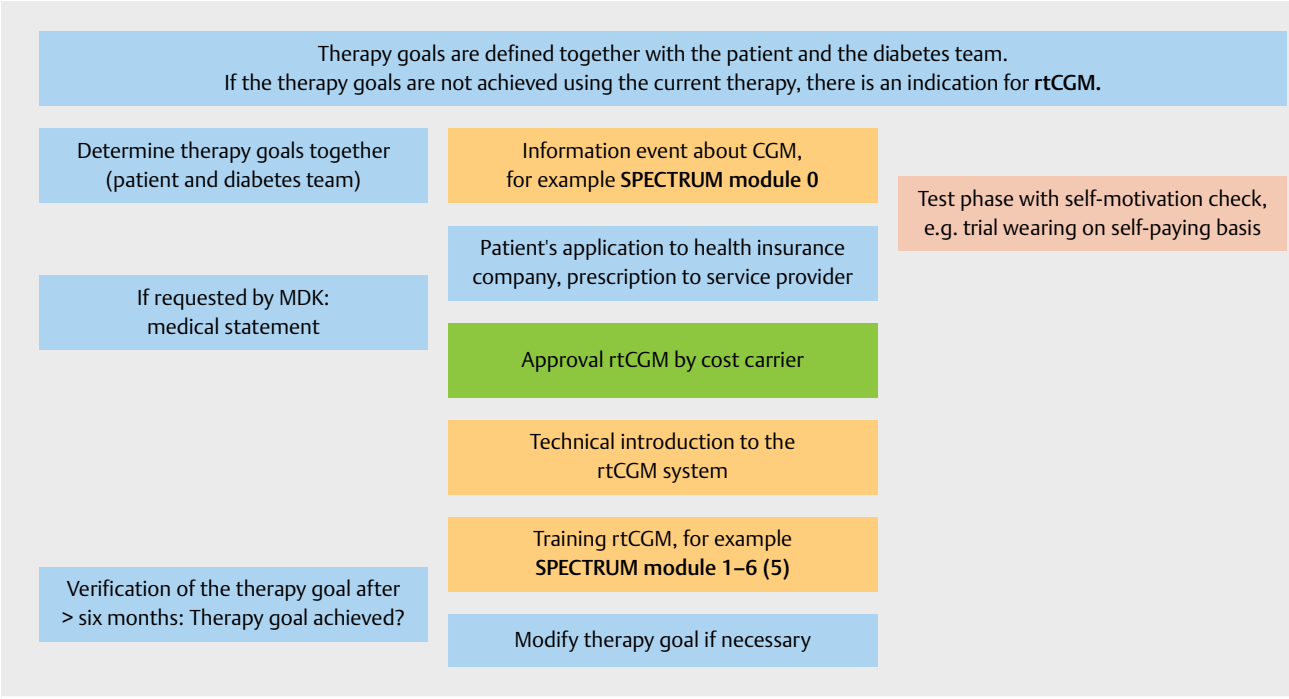
under CSII without a CGM system. This applies equally to children and adults.

Measurement method

In the transcutaneous needle sensors of the rtCGM systems currently available on the German market, glucose is measured using an enzymatic method (GOD, see SMBG) in the ISF in subcutaneous fatty tissue (▶ **Tab. 6**). The transcutaneous rtCGM systems have a life cycle of up to 14 days after which the glucose sensor should then be replaced according to the manufacturer's instructions. The sensors normally transmit an average value obtained every 5 min to the corresponding receiving device. As with blood glucose monitoring systems, medication can result in interferences (**e. g. paracetamol and vitamin C, see device operating instructions**) and all factors that have an influence on the measurement result must be taken into account (▶ **Tab. 2**). With the implantable long-term rtCGM systems, the glucose measurement is fluorescence-based which can lead to short-term measurement interruptions, especially at the beginning during bright sunlight.

Available systems

The rtCGM systems available up to several years ago were not directly intended to be used for a therapy decision (insulin dose adjustment); an adjustment of the insulin dose should therefore be based on the measurement result of an SMBG measurement and not on the CGM data (adjunctive usage). In practice, however, many patients have relied on the accuracy of the rtCGM data and used them to make treatment decisions. Therapy decision/insulin dose adjustment is now permitted on the basis of the CGM measurement result (non-adjunctive usage) with the most frequently-used rtCGM systems. With the latest generation of rtCGM systems, there is no need for calibration (as with the iscCGM system, see below). However, calibration is optional, i. e., the measurement supplied by this rtCGM system can be related to the blood glucose value. In some patients, the accuracy of the measurement seems to be im-



▶ **Fig. 3** Practical procedure for starting real-time continuous glucose monitoring (rtCGM) (blue: doctor/patient; yellow: training/introduction of technology; green: costs approved or self-funded) MDK = Medizinischer Dienst der Krankenversicherung (Health Insurance Medical Service).

proved by one calibration per day, especially if this is done in the first days after the sensor is inserted. It should be noted that various factors influence the quality of rtCGM measurements (as well as for iscCGM systems). Such patient factors include the patient's BMI, the specific body site where the glucose sensor is inserted, the ambient temperature and the external pressure on the sensor (e. g. during sleep). There is also always a theoretical risk, confirmed by practical experience, that certain differences in quality or measurement accuracy may occur between batches and individual sensors from one manufacturer. Therefore, it is generally recommended to perform daily comparative BG measurements, especially in the first 2 days after restarting a sensor. This is especially true when using AID systems to check them, because not only is a CGM curve recorded, but the insulin delivery is controlled.

The performance of rtCGM systems is usually evaluated in clinical trials funded by the manufacturers. Head-to-head studies, in which patients wear more than one rtCGM system at the same time (up to 3 different systems, each with 2 devices from the same company), provide important information on the analytical performance of the rtCGM systems in direct comparison.

Specifications for measurement quality/standards

For the approval of rtCGM systems, there are no established standards for evaluating measurement accuracy such as the ISO norm for SMBG monitoring systems. If and when this could take place cannot be foreseen. Recently, the U.S. Food and Drug Administration (FDA) published guidelines on how it believes the measurement quality of rtCGM systems should be characterized (iCGM). So far, only few systems meet these requirements. The IFCC has established a working group to look at standards for CGM (https://www.ifcc.org/ifcc-scientific-division/sd-working-groups/wg-cgm/).

By defining the “Mean Absolute Relative Difference” (MARD), an attempt is made to describe the measurement quality of an rtCGM system. To determine the MARD value, the difference between individual measured blood glucose values and simultaneously-determined rtCGM values is calculated. This value determined in clinical studies is significantly influenced by the study protocol used and the selection of the patients examined. The MARD value should therefore only be used as a guide. Another parameter which deals with the measurement quality of an rtCGM system is the “Precision Absolute Relative Deviation” (PARD), calculated simultaneously for the same patient from the direct comparison (see above) of an rtCGM system with a second sensor from the same system.

However, due to the high inter-individual variability with regard to measurement accuracy, study data are of limited help in everyday clinical practice. What is of interest here is rather whether a particular sensor system is sufficiently accurate for a particular user. The individual, personal measurement accuracy depends on technical and application-related factors (see ▶ **Tab. 3**). So far, there is no established standard for assessing measurement accuracy at the patient level. An approach to estimate CGM accuracy can be found under this link (download worksheet under https://www.kirchheimshop.de/out/media/Thurm_Gehr_Pumpenfibel_Onlineanhang.pdf or QR-Code). This method has not yet been scientifically proven.

Costs/refund of expenses

Based on a positive assessment of benefit by IQWiG, the G-BA published a decision in 2016 providing for cost coverage of rtCGM if the patient submitting the application fulfils defined criteria (as is the case for therapeutic devices). The prescription for an rtCGM

▶ **Tab. 6** Information on current rtCGM and Intermittent-scanning CGM (iscCGM) system(s); the systems are in constant development.

CGM model (dated 7.2021)	Associated sensor	Approval age group	Life cycle per sensor	Connectivity smartphone/ wearable	Connectivity insulin pump	Calibration	Initialisation phase	Recommended insertion site	Glucose display	Glucose range	Replacement for blood glucose measurements
Abbott Freestyle Libre 2/3 (with high/low alarm)	Sensor FreeStyle Libre 2/3	From 4 years	Up to 14 days	Yes, Android and iOS App, Follower App	No	Factory calibrated	1 h	Upper arm	After scan (Libre 2), every minute (Libre 3)	40–500 mg/dl (2.2–27.7 mmol/l)	Yes, with adherence to company specifications
Dexcom G6 CGM System	Dexcom G6 Sensor	From 2 years Pregnant women (with t:slimX2 from 6 years)	Up to 10 days	Yes, Android, iOS, App, Smartwatch/ Apple Watch	DexcomG6: Connectivity YES to Tandem TSlim X2: predictive low glucose suspend (Basal IQ); automated basal rate and correction (Control IQ)	Factory calibrated; calibration optional	2 h	Abdomen, upper buttocks (children and adolescents 2–17 years)	Every 5 min	40–400 mg/dl (2.2–22.2 mmol/l)	Yes, with adherence to company specifications
Medtronic Guardian Connect[1]	Medtronic Guardian Sensor 3	Without age limit	Up to 7 days	Yes, iOS, App; Follower App	No	2 h after insertion, 6 h after first calibration, then every 12 h	2 h	Abdomen; upper buttocks; (upper arm)	Every 5 min	40–400 mg/dl (2.2–22.2 mmol/l)	No
Medtronic 640 G/670 G/770 G Insulin Pump[1,2]	Medtronic Guardian Sensor 3	Without age limit (640 G); as of 7 years (670 G/770 G)	Up to 7 days	No (640 G/670 G); Yes (770 G)	Yes, Smart-Guard (predictive low glucose suspend; automated basal rate)						No
Medtronic 780 G	Medtronic Guardian Sensor 4	From 7 years	Up to 7 days	Yes, Android and iOS App, Caregiver, Follower-App / Apple Watch (only Alarm)	Yes-SmartGuard-predictive low glucose suspend; automated basal rate, automated correction bolus	no calibration	2 h	buttocks and back of upper arm (children and adolescents 7-17 years) abdomen and back of upper arm (18 years and older)	every 5 minute	50–400 mg/dl (2.8–22.2 mmol/l)	Yes, with adherence to company specifications
Medtrum A6 touch care	Medtrum A6 touch care CGM	From 2 years	Up to 7 days	Yes, Android, IOS, Apple Watch.	Yes (predictive low glucose suspend)	Every 12 h	2 h	Upper arm, abdomen, buttocks	Every 2 min	40–450 mg/dl (2.2-25 mmol/l)	No
Menarini GlucoMen Day CGM	GlucoMen Day CGM Sensor	From 6 years	14 days	Yes, Android, IOS	No	Every 24 hours	45 min	Abdomen	Every minute	40–400 mg/dl (2.2–22.2 mmol/l)	Yes

▲ **Tab. 6** Information on current rtCGM and Intermittent-scanning CGM (iscCGM) system(s); the systems are in constant development.

CGM model (dated 7.2021)	Associated sensor	Approval age group	Life cycle per sensor	Connectivity smartphone/ wearable	Connectivity insulin pump	Calibration	Initialisation phase	Recommended insertion site	Glucose display	Glucose range	Replacement for blood glucose measurements
Sensesonics Eversense CGM System	Eversense Sensor	From 18 years	Up to 180 days	Yes, Android, iOS, App Apple Watch	No	24 h after insertion, 4 times within 6–36 hours, then every 10–14 h	24 h	Upper arm (implanted)	Every 5 min	40–400 mg/dl (2.2–22.2 mmol/l)	No

Company portals: www.dexcom.com; www.freestylelibre.de; www.medtronic-community.de; www.medtronic.com/de-de/fachkreise/diabetes.html; www.medtronic.com/de-de/diabetes/home.html; www.medtrum.com; www.eversense.de; www.menarinidiagnostics.com. [1]Paracetamol can lead to incorrectly high CGM values with some sensors – depending on the level of the dose acting in the body. The information provided by the manufacturers must therefore be carefully checked. The companies that have listed this interaction in their technical information are marked here. [2]The Ascensia Contour Next Link 2.4 blood glucose meter, which can be connected to the MiniMed Medtronic 640G and used for calibration, bolus and correction insulin calculation, has a measuring range of 20–600 mg/dl (2.2-33.3 mmol/l). CGM glucose levels of the Guardian 3 sensor can be displayed on the insulin pump between 40 and 400 mg/dl (2.2–22.2 mmol).

system can only be made by a specialist doctor such as: doctor of internal medicine, endocrinology and diabetology or a doctor of internal medicine specialised in general medicine/paediatrics/juvenile medicine with the recognition “Diabetologe DDG” (German Diabetes Society Diabetologist) or with comparable qualifications recognised by the respective regional medical association or doctors specialised in paediatrics and juvenile medicine with the paediatric endocrinology and diabetology recognition.

In reality, the implementation of the G-BA decision varies greatly in the various KVs, despite the now available standardized guideline of the Health Insurance Medical Service/Medizinische Dienst der Krankenversicherung (MDK). The written application should be based on the MDK guideline and it might be helpful to use the rtCGM application proposal of the DDG/AGDT (available online on the DDG and AGDT homepages). In addition to this application form, the MDK requests glucose protocols and, depending on the MDKs, both digital and handwritten formats are accepted. The content of the protocols also varies between the different MDKs. It makes sense for patients to draw up a letter describing their individual prerequisites, daily requirements and motivation for using an rtCGM system.

In practice, the problem is that when a new CGM system comes onto the market, some manufacturers offer a type of ‘exchange programme’, while others do not. This can involve a justified change, e. g., to a new generation of sensor-supported pumps or to CGM systems with new functions. If company X comes onto the market with a new pump linked to a CGM system and the patient still has a similar CGM system and performs ICT, experience shows that the change is difficult because the MDK initially wants the patient to try out pump X alone with the “old” CGM system. If the HbA1c value then decreases, the claim to a CGM system for the pump is voided; consequently, the patients actively prevent this – otherwise it would become necessary to write another letter of assessment explaining this paradox.

The time required by the diabetes team for the application, the medical instruction on the rtCGM systems and the training is not reflected by the cost carriers (health insurance companies). The EBM number in use since April 2017 is to be understood as a medical instruction number. Individual or group training courses are regulated differently throughout Germany depending on the federal state, KV district and cost carrier. Some health insurance companies do offer additional support. The AOK Baden-Württemberg, for example, rewards the training for rtCGM (SPECTRUM) and for iscCGM (flash) under certain conditions. General cost coverage for CGM training programmes is required.

Quality control (internal and external/ interlaboratory tests)

There are no quality controls for rtCGM systems. The SMBG measurements performed regularly for calibrating the rtCGM systems and further SMBG measurements are the only possibility for drawing conclusions about measurement quality. Carefully performing blood glucose measurements for calibration at times of low glucose fluctuations and correctly entering these values are prerequisites for obtaining reliable glucose measurements from rtCGM systems.

▶ **Tab. 7** Tips for interpreting the indications on the display of the continuous glucose monitoring (CGM) device. In the interpretation, the last 2–3 h of the trend curve must be taken into account. The meaning of the trend arrows varies from manufacturer to manufacturer.

	Abbott Libre 2	Dexcom G6	Medtronic Link 3	Medtrum A6	Sensonics Eversense
→	< 1 mg/dl/min	< 1 mg/dl/min		present	< 1 mg/dl/min
	< 0.06 mmol/l/min	< 0.06 mmol/l/min			< 0.06 mmol/l/min
↗↘	1–2 mg/dl/min 0.06–0.11 mmol/l/min	1–2 mg/dl/min 0.06–0.11 mmol/l/min		present	1–2 mg/dl/min 0.06–0.11 mmol/l/min
↑ ↓	> 2 mg/dl/min	> 2 mg/dl/min	1–2 mg/dl/min	present	> 2 mg/dl/min
	> 0.11 mmol/l/min	> 0.11 mmol/l/min	0.06–0.11 mmol/l/min		> 0.11 mmol/l/min
↑↑ ↓↓		> 3 mg/dl/min	> 2 mg/dl/min	present	
		> 0.2 mmol/l/min	> 0.11 mmol/l/min		
↑↑↑ ↓↓↓			> 3 mg/dl/min		
			> 0.2 mmol/l/min		

Even if factory-calibrated sensors are used, control measurements should be carried out in order to detect individual "bad" sensors (batches) and to avert dangers caused by this (e. g., severe hypoglycaemia after insulin administration with incorrectly high sensor values). There are no established recommendations on the frequency of control measurements. More frequent control measurements seem reasonable at the beginning of a sensor session, every 1–2 days thereafter and additionally in the situations recommended by the respective manufacturer (discrepancy between symptoms and displayed value, etc.).

Safety issues/side effects

There are a number of safety aspects to be considered when using this diagnostic option:

- What happens when the rtCGM measurement results are used to make therapy decisions?
- What is the quality used to detect low glucose levels, i e. how well is hypoglycaemia detected in everyday life?
- What are the clinical consequences of miscalculations due to incorrectly performing SMBG?
- What incorrect measurements (= low glucose values) occur, e. g. when the patient lies on the sensor at night?
- Does the patient hear the alarms? Do they take place in time to be able to react adequately?
- As described in the rtCGM system operating instructions, SMBG measurements must be carried out when implausible results are obtained!

If patients adjust their insulin therapy based on the measurement results of an rtCGM system, not all rtCGM systems have been approved for this purpose in Germany so far; however, it is practised by many patients due to the predominantly good measurement quality of the sensors. The measurement quality of rtCGM systems in the hypoglycaemic range is not satisfactory, therefore SMBG should be performed for symptoms indicative of hypoglycaemia (with conflicting rtCGM glucose values). SMBG measurement is also recommended if the rtCGM system indicates hypoglycaemia without symptoms of hypoglycaemia. In the case of rapid tissue glucose changes (induced e. g. by food intake or sport), there may be physiological and technical differences between the glucose concentrations in blood and ISF. These differences are not measurement errors, they stem from the fact that glucose is measured in two different compartments. The clinical experience of some diabetologists indicates that with such extreme differences, the alignment of therapy adjustments to rtCGM readings is safer than the alignment to SMBG readings alone.

rtCGM systems displays the glucose trend from the near past into the close future using trend arrows (▶ **Tab. 7**). It should be noted that the direction of the trend arrows can change rapidly, especially postprandially. Many users of rtCGM systems do not only orientate their therapy adjustment on the current glucose value, but also on the current trend arrow. Some German experts have created easy-to-use recommendations for different patient groups and published them in the form of scorecards. Together with qualified training, these scorecards can help patients react in a considered and appropriate way to fluctuations in their glucose level and the indication of their rtCGM.

Wearing glucose sensors on the skin with a plaster for several days and repeated use of the same skin site can lead to skin reactions in these areas. The reactions range from mild skin irritations to the development of contact allergies against components (especially acrylates) in the adhesives and/or the housing of the transmitters, which represent a considerable impairment and can make further use of a CGM system impossible. For these patients the implanted long-term rtCGM with daily changeable silicone plaster is a therapy option.

A questionnaire for recording skin reactions is available online at the following link: https://www.idt-ulm.de/images/Befundbogen_fr_Hautreaktionen_IfDT_englisch.pdf

Conditions to be observed in practice

In all rtCGM systems, algorithms are integrated which convert the measured current flow or the fluorescence signals of the sensor into glucose values based on blood glucose calibration values, reduce the noise of the electronic measurement signal and eliminate implausible values. The algorithms of the companies are different (e. g. different time delays to blood glucose, different calibration methods, differences depending on the SMBG system used for calibration); little is known about how they work. This point should be considered by the patient when changing the rtCGM system. The handling and concept of the systems can also differ considerably. For this reason, the patient should receive proper instruction after a system change in order to understand the changes in the calibra-

tion process, the data evaluation with the new software and to react correctly.

Use with different patient groups

The G-BA decision sets out clear guidelines on the patient groups eligible for cost reimbursement of rtCGM systems, namely for insulin-dependent diabetes with ICT or CSII. In view of the number of people with type 2 diabetes (the scope of the costs) and the heterogeneity of this patient group, the decision on whether it makes sense for individual patients to use rtCGM can be quite varied.

Additions to the list of indications for the use of rtCGM in special patient groups:

- In patients who perform ICT with multiple injections daily or with an insulin pump
- For patients with specific, individual problems (type 1 or type 2)
- Temporarily for therapy review in patients taking oral antidiabetics that may induce hypoglycaemia
- During pregnancy
- In patients with pronounced secondary diseases, e. g. a painful peripheral polyneuropathy
- For training purposes
- To compensate for a handicap caused by diabetes at work

The only implanted long-term rtCGM system to date offers additional vibration alarms on the body and a plaster which is well-tolerated in patient and occupational groups with specific indications as compared to the transcutaneous rtCGM systems.

Training/psychological aspects

rtCGM is a very potent, but also cost-intensive diagnostic and therapeutic tool. A prerequisite for optimal use, especially with regard to the modification of therapy, is that patients and medical staff are comprehensively trained. It is not considered sufficient for patients to be solely instructed by the manufacturers in device-specific aspects. The AGDT and AGPD have developed the manufacturer-independent rtCGM training program SPECTRUM. The time required to train patients in the diabetes practices is considerable and the patients themselves must receive qualified training. The training units can be taught individually or together, depending on the patient's needs; they can be taught to groups or individuals in both outpatient and inpatient settings.

For patients, the permanent availability of information on the glucose trend in their own bodies can be both a blessing and a curse. On the positive side, rtCGM warns of acute events and helps optimise glucose control. Patients who make intensive use of the information and advice provided by the rtCGM systems report a significant increase in safety, freedom and quality of life; this applies in particular to children and their families. Many parents can sleep through the night for the first time in years without having to get up several times at night to carry out an SMBG measurement. Furthermore, the reduction in lancing for SMBG measurements, especially in children, is a significant psychological relief.

On the other hand, the rtCGM system constantly reminds the patient of diabetes. Frequent alarms (e. g. when alarm limits have not been sensibly programmed) can disturb and unsettle patients and their relatives immensely, especially if they are false positives. Some patients feel bothered by constantly wearing a technical system in everyday life and their body awareness is impaired. As a result, these patients do not wear the rtCGM system continuously, but only situatively. Other patients are not in agreement with their readings being passed on to family members or members of the diabetes team. They see it as an invasion of their privacy with negative feedback and consequences.

A prerequisite for successful rtCGM use is comprehensive training that not only presents technical aspects but also trains data analysis and therapy adjustment. This training can only be successfully provided by qualified diabetes counsellors with extensive practical experience in the use of all rtCGM systems. In addition, the required software should also be available in the doctor's office and used during consultation with the patient.

Comment

Continuous glucose monitoring is rapidly gaining importance in the context of modern diabetes therapy due to the advantages of the permanent availability of glucose data, prevention of hypoglycaemia and reduction glucose fluctuations.

One requirement of the G-BA decision is that data security must be safeguarded when using an rtCGM system, i. e., the measured data (even if uploaded to a cloud) should not be accessible and traceable for third parties. It is therefore important to inform patients of the legal situation in this respect.

Manufacturers regularly bring new generations of their rtCGM systems onto the market – with improvements in measurement quality, more simplified handling, improvements in interoperability and connectivity. If such models (or a combination of insulin pump and rtCGM) offer the patient a relevant therapeutic advantage, it should be possible to apply for a change via an expert assessment before the expiry of the one-year flat-rate care charge (rtCGM) or four-year flat-rate care charge (insulin pump). There are a number of innovative measurement principles in preclinical and clinical development that will rectify some of the drawbacks of the rtCGM systems available to date, as well as offer new options and be more cost-effective to manufacture.

The constant availability of glucose values in rtCGM systems makes it perspectively possible to supply bolus computers with significantly more data than was previously possible with SMBG values; however, there are still no approved systems on the market. Alternatively, the rtCGM values can be transferred to apps on smartphones in the future and their algorithms can make suggestions for the insulin dose.

Intermittent scanning CGM (iscCGM)

Goals/indications

The use of iscCGM uses trend displays of the currently scanned glucose value and the presentation of retrospective CGM data to help achieve therapy goals by avoiding acute complications. The measurement technology of the iscCGM systems (see below) is based on a technology similar to that of rtCGM systems with the difference that the glucose values are not continuously displayed but rather must be actively "scanned" by the user. The costs of this option are lower than those of rtCGM systems. Similar to SMBG, the success of the follow-up depended on the patient being active.

Nonetheless, the procedure of scanning versus obtaining blood requires only minimal effort. With the second generation of devices on the market, it has become possible to turn on threshold limit alarms (hypoglycaemia alarm, hyperglycaemia alarm). However, this method does not directly reflect the currently-measured value, the value this is only available after an active scan. The AGDT has prepared an updated statement on replacing blood glucose measurements by measurements using rtCGM or iscCGM systems (https://www.deutsche-diabetes-gesellschaft.de/fileadmin/Redakteur/Stellungnahmen/2019/Stellungnahme_der_AGDT_2019_5_28_clean.pdf). Recently, the National Association of Statutory Health Insurance Funds (Spitzenverband der Gesetzlichen Krankenversicherung GKV) has decided that these second-generation devices are an rtCGM system as per the G-BA decision, and that they will be included in the catalogue of therapeutic devices and aids, and can therefore be prescribed. In terms of cost allocation, there is then no longer any differentiation between rtCGM and iscCGM.

However, there are differences between rtCGM systems and iscCGM systems because regular automatic transmission and display of the values to a receiver does not take place with iscCGM. An iscCGM cannot be calibrated either. Furthermore, it is possible to switch off the alarm functions and the selection of different alarm functions is limited to threshold alarms. In order to be able to provide the individual patient with the best option for a CGM system, we still consider a medical differentiation between rtCGM and iscCGM systems to be useful.

Measurement method

From a measurement point of view, iscCGM is a transcutaneous CGM method based on electrochemical needle sensor technology with low drift of the measurement signal. The manufacture of these sensors can be standardised in such a way that calibration of the glucose measurement during manufacture is possible and no further calibration by the patient is required. Therefore, patients can largely do without SMBG, unless, e. g., hypoglycaemia symptoms do not match the values and the glucose trend displayed, or very high glucose values or strong glucose fluctuations are present and a blood glucose measurement is necessary as per the operating instructions. Due to the factory calibration, calibration errors by the patient are not possible with iscCGM.

Available systems

To transfer the data for iscCGM systems, the reader or a smartphone with the corresponding app must be actively brought by the user to the inserted glucose sensor. A maximum of the continuously monitored glucose values (every 15 min) of the last 8 h and the current value are transmitted and displayed on the device as the current glucose value, a trend arrow and a glucose profile. If the device measures too low or too high glucose values, it emits an alarm; the limit values are adjustable. However, an active scan must first be performed to display the current glucose value and the type of alarm. Irrespective of the alarm function, data must still be retrieved every 8 h by scan so that no data gaps occur. There is no automatic transmission and recording of all measured values to/from the receiver.

Many patients use an app on their smartphone to read out or “scan” the data.

In addition to the still-available second generation of the manufacturer's iscCGM system, an rtCGM system is coming onto the market (▶ **Tab. 6**). This continuously displays the glucose values and trend arrows on a smartphone app; a scanning process is no longer necessary for this. The sensor characteristics and threshold alarms (high and low alarms, no trend alarms) correspond to the iscCGM system. The life cycle of the sensor is 14 days.

Specifications for measurement quality/standards

Just as for rtCGM systems, there are no established standards for assessing the measurement quality of iscCGM systems. Studies have provided information on the MARD value of this system. Of greater interest in individual cases, however, is the individual measurement accuracy (see ▶ **Tab. 3**).

Costs/refund of expenses

At present, Institute for Quality and Efficiency in Health Care (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen, IQWiG) has not performed an assessment of benefit for iscCGM. Despite this legal situation, the iscCGM system has been included in the index of health insurance aid numbers. Some health insurance companies no longer reimburse the cost of test strips for SMBG if an iscCGM has been approved; others try to replace approved rtCGM systems with an iscCGM system.

Quality control by the user (internal and external/ interlaboratory tests)

There are no quality controls for the iscCGM systems. The SMBG measurements for calibration, which need to be carried out regularly, are no longer necessary, so that no conclusions can be drawn about the measurement quality of these systems in everyday life. However, the manufacturer expressly describes the necessity of additional SMBG measurements in certain situations in the respective operating instructions. In addition, from clinical experience, plausibility measurements are recommended after the start of a sensor session and at a lower frequency in the further course of the sensor session, analogous to the situation with rtCGM (see above).

Safety issues/side effects

As with rtCGM, there are safety aspects to be considered when using iscCGM (see above). In this system too, patients should perform SMBG measurements according to the specifications in the operating instructions (e. g. in the case of hypoglycaemia symptoms, especially in low but also in very high glucose ranges), regardless of what the iscCGM system indicates.

Wearing glucose sensors on the skin for 14 days and the fact that the same skin site is often used can lead to skin reactions in these areas. The reactions to substances in the plaster and/or plastic sensor housing range from mild skin irritations to the development of contact allergies in some patients. The allergic reaction is not only a considerable impairment, it can make the further use of this system impossible and can lead to accompanying reactions to the plasters when using other technical systems (e. g. an insulin pump). As a result of the fact that a defined acrylate, which is known to trigger allergic reactions, is no longer contained in the plastic housing of the system, the frequency of skin reactions has been significantly reduced.

Conditions to be observed in practice

The iscCGM system data can be read and analysed with a company-specific software. In everyday life it should be noted that sensor artefacts (these are long hypoglycaemic episodes displayed which have not actually occurred) can occur as a result of lying on the sensor while sleeping; this also applies to rtCGM systems with needle sensors. Such measurement artefacts must be effectively communicated to the user in the technical briefing and training for safe operation of a CGM system. For this purpose, the recognition of a defective sensor by systematic BG control measurements should also be taught, if necessary.

Use with different patient groups

iscCGM can be used in patients who perform ICT or CSII without pronounced hypoglycaemia perception disorder and with the wish to have the glucose values displayed on a separate reader and not on a smartphone app. The use of iscCGM should also be considered in cases of less complex therapy schemes (▶ **Fig. 1**). Thus, the use of iscCGM can also be intermittent, i. e., adapted to requirements, in oral therapy with hypoglycaemia risk, during therapy changes or while participating in a training course. The results of a clinical study are available for patients with type 1 and type 2 diabetes who are undergoing intensified insulin therapy.

Training/psychological aspects

For the first generation without alarms there is a training program (flash) which was evaluated in a clinical study. The development was financed by the manufacturer of the system and is tailored to this product. Some differences, especially the lack of alarms in the first generation iscCGM system, result in the training course covering different topics than the rtCGM training program. Some patients find it beneficial not to be constantly disturbed by alarms, especially during the night. The self-determined, occasional retrieval of glucose values and the omission of calibration measurements are also deemed positive. The second generation of iscCGM devices allows the activation of a high and a low alarm and, after an alarm message by a scan, displays the current measured value. The high and low alarms are distinguished by acoustically different alarm tones. These options require additional training similar to rtCGM systems.

Comment

There is no general reimbursement or EBM number for training and consultation on iscCGM systems. For the diabetes team, this means that the care effort in most KV areas is not rewarded.

Parameters derived from CGM

Goals

Today, the basis for counselling during long-term outpatient treatment for type 1 diabetes is primarily the CGM data and the therapy data stored in parallel, i. e., insulin doses, nutrition, physical activity and the like. For the evaluation of CGM data, each manufacturer offers its own software; furthermore, there are manufacturer-independent, cloud-based or locally-installed software solutions. For clinical counselling, it is crucial that data from insulin pumps, insulin pens and rtCGM systems can be displayed together in one software, if possible, so that insulin doses and their effects can be graphically combined.

The handling of the programmes, i. e., the active reading of data, is partly complex and requires an introduction. However, the data of insulin pumps, pens and stand-alone CGM systems can also be displayed via an app on a smartphone and transferred directly to the manufacturer's software. This means that the devices need to be actively read out less often.

Current software solutions usually offer a clear initial evaluation of the CGM data with the help of the “Ambulatory Glucose Profile” (AGP) and other special trend views, which shows the distribution of the values in colour as a “wave” over 24 hours, in which the mean values or medians are highlighted as a line. With the manufacturer-specific CGM software, CGM-derived parameters such as mean glucose, glucose management indicator (GMI), glycaemic variability (GV) or time or proportion % in, above or below target range (TiR, TaR, TbR) can be calculated. The TiR provides information about the proportion of glucose values that were in the target range during a continuous recording. This characterises the current quality of glucose control.

Recommendations for the target values of various established CGM parameters were defined in an international consensus in 2019 (▶ **Tab. 4,5**). The American Diabetes Association has adopted these target values for the 2020 clinical practice guidelines.

One of the recommendations is to establish the evaluation with the help of the AGP (▶ **Fig. 4**). In addition to the AGP evaluation, the glucose management indicator (GMI) represents a new, important parameter. The GMI is based on an optimised calculation formula and has replaced the eHbA1c value (originally estimated HbA1c or eHbA1c) as the HbA1c analogue.

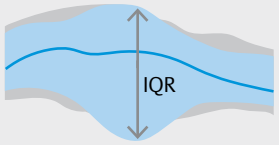
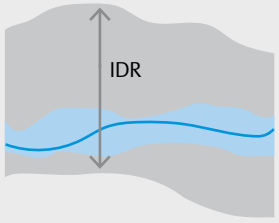
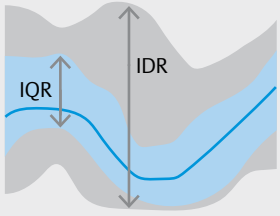
Differences between GMI and HbA1c values measured in the laboratory are possible for various technical, biological and probably also genetic reasons. The GMI is based on the glucose in the intracellular space of the fatty tissue, in which current changes in blood glucose are only reflected with a delay. The measurement of the HbA1c or calculation of the GMI takes place in two completely different compartments of the body. The GMI can be influenced by the quality of the measuring system and an incorrectly low calibration, whereas the HbA1c value can be influenced by a variety of diseases, which, among other things, affect the life span of the erythrocytes. The GMI is usually calculated over a self-defined period of 2–4 weeks, i. e., a relatively short period of time, and thus reflects recent changes in therapy or diet, whereas the HbA1c value represents a significantly longer period of 8–12 weeks (life span of the erythrocytes).

This can lead to different values, but can also be used to positively highlight successes of the therapy of the last 2–4 weeks due to the GMI.

Conditions to be observed in practice

Both time above, time below, time in target range and CV as a measure of the spread of glucose values can provide important information on fluctuations in glucose concentration, GMI can be used as an approximation to HbA1c value. However, some points need to be considered

The quality of the calibration (with blood glucose values or with sensor values), the measurement quality of the sensor and soft-

Ambulatory glucose profile	Assessment	Possible sources
	▪ Low variability in IDR and IQR ▪ Low glucose variability ▪ Comparable with glucose variability of a person with a health metabolism	
	▪ Low variability in IDR ▪ High variability in IQR ▪ Modification of therapy required	Resulting from the therapy*: ▪ Insulin dose ▪ Incorrect carb unit/bread unit factor ▪ Incorrect correction factor ▪ Constantly changing times/day patterns
	▪ Low variability in IQR ▪ High variability in IDR ▪ Modification required	Resulting from behaviour*: ▪ Meals not covered ▪ Unsuitable interval between injecting and eating ▪ Irregular mealtimes: occasional, varying times/day patterns ▪ Exercise ▪ Alcohol ▪ Incorrect carb unit/bread unit factor
	▪ High variability in IDR and IQR ▪ Modification of therapy required	Resulting from therapy and behaviour*: ▪ Insulin dose ▪ Incorrect carb unit/bread unit factor ▪ Incorrect correction factor ▪ Meals not covered ▪ Unsuitable interval between injecting and eating ▪ Irregular mealtimes ▪ Exercise ▪ Alcohol

▶ **Fig. 4** Examples of interquartile and interdecile glucose variability and possible causes of these glucose fluctuations. * The assessment of the AGP is restricted by an "irregular" daily routine. IQR: interquartile range (interquartile range, 25th-75th percentiles), IDR: interdecile range (interdecile range, 10th-90th percentiles).

ware settings of the respective CGM system used have an influence on the CGM-derived parameters. These can therefore vary significantly depending on the system. In principle, the use of rtCGM/isCGM systems also provides an overview of the quality of glucose control over time. Thus, a mean glucose value over time can be calculated, which correlates with the HbA1c value. The importance of the HbA1c value remains high despite the availability of CGM data. Currently, the HbA1c value is the only relevant surrogate parameter associated with subsequent complications. New parameters obtained by appropriate evaluation of the data provided by CGM systems, such as "time-in-range" (TiR) or "time-below-range" (TbR), facilitate the assessment of the quality of glucose control (▶ **Tab. 4,5**). For example, the TiR/TbR show fluctuations in the glucose concentration better than the HbA1c value, but the information on the parameters in the software of the different manufacturers also depends on the system.

Comment

In our opinion, parameters such as TiR/TaR/TbR and the GMI are a valuable complement to the HbA1c value, but not a substitute (https://www.deutsche-diabetes-gesellschaft.de/fileadmin/Redakteur/Stellungnahmen/2019/20190509_KLD_Stel lungnahme_Time_in_Range_2019_final.pdf).

HbA1c

Goals/indications

The long-term quality of glucose control has a direct influence on the risk of developing diabetes-associated secondary diseases. The HbA1c measurement allows an assessment of the prevailing glucose control over time. The HbA1c value is mainly determined by the blood glucose values of the last 2–3 months and has been used in diabetology as a quality indicator for glucose control for many years. However, the HbA1c value does not allow an adequate statement about glucose variability. The attending physician should agree on an HbA1c therapy target with the patient, based on the

▶ **Tab. 8** Causes for incorrect HbA1c values.

Physiological causes			
	Falsely low	**Falsely high**	**Opportunities**
Erythrocyte formation	Increased	Slows down due to lack of available iron	▪ Determination of an "HbF-adjusted" HbA1c ▪ Reticulocytes + Ferritin ▪ Urea ▪ Hb electrophoresis ▪ For Hb variants, determine HbA1c using an immunological method. ▪ Fructosamine
	Very high	Iron deficiency anaemia	
	Pregnancy	Infectious anaemia	
	Bleeding, blood loss	Tumour-induced anaemia	
	Blood transfusion		
	Erythropoietin administration		
	Iron supplementation		
Erythrocyte breakdown:	Too soon	Too late	
	Haemolytic anaemia	Splenectomy	
	Chronic renal insufficiency	Aplastic anaemia	
	Cirrhosis of the liver		
	Folic acid deficiency?		
	Hemoglobinopathies: ▪ HbS ▪ HbC ▪ HbD	Hemoglobinopathies: ▪ HbH ▪ HbF (Thalassemia)	
	Spherocytosis		
Laboratory technical causes	**False high – ONLY for HPLC-HbA1c measurements through carbamylation**	**False high – ONLY for immunological HbA1c measurements**	**Possibilities for objectification:**
	Terminal renal insufficiency, uraemia, creatinine > 5 mg/dl	Betalactam antibiotics	Newer HPLC columns are no longer influenced by carbamylation, ask laboratory. Laboratory method other than HPLC required: Immunological technique, enzymatic technique (written note on the laboratory request form)
	Alcoholism (acetaldehyde)	Contraceptive pill	
	Aspirin (from 500 mg/d over weeks)	Hydroxyethyl starch (HES) solutions	
Other causes			
	Falsely low	**Falsely high**	
	Nutritional (alcohol, fat)	Pharmaceuticals: Immunosuppressants Protease inhibitors	
		Genetically-induced hyperglycation in certain ethnic groups	
		Age	
		Organ transplantation	
		Hypertriglyceridemia	
	Hereditary causes	Hereditary causes	
HPLC = High-performance liquid chromatography			

patient's individual situation. Especially if a patient does not perform SMBG, HbA1c measurement at quarterly intervals is necessary to get an overview of the quality of glucose control. If some form of self-monitoring is performed by the patient, the HbA1c value should always be assessed in combination with the results of the self-monitoring. Since considerable intra- and interindividual deviations between the measured HbA1c value and simultaneously-determined SMBG values can occur in individual patients, which are based, e. g., on diseases or other factors, the HbA1c value alone should never be considered (▶ **Tab. 8**). In practice, the measurement of other glycated proteins (e. g., fructosamine) is of secondary importance.

▶ **Tab. 9** Conversion table: HbA1c values measured according to International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) in mmol/mol or National Glycohemoglobin Standardization Program (NGSP) in %. Conversion from % to mmol/mol: HbA1c (mmol/mol) = (HbA1c (%) – 2.15) × 10.929. Conversion from mmol/mol to %: HbA1c (%) = (HbA1c (mmol/mol) × 0.0915 + 2.15.

IFCC HbA1c (mmol/mol)	NGSP HbA1c (%)
31	5.0
37	5.5
42	6.0
48	6.5
53	7.0
58	7.5
64	8.0
69	8.5
75	9.0
80	9.5
86	10.0
91	10.5
97	11.0
102	11.5
108	12.0

Measurement method

There are a number of different methodological approaches to measuring HbA1c; in practice, a few have become established and are frequently used.

Available systems

There are various systems on the market; they can be differentiated according to measuring principles and laboratory systems, POCT (Point of Care) systems and small desktop devices that can also be used by patients.

There are HbA1c measuring systems that have been designed for use by practices and clinics, but also for use by patients at home. The size of the measuring device (comparable to a blood glucose meter) and the simple sample collection through a capillary blood sample, make it easy for patients to use. There are "professional" sets and small pack units that are primarily advertised for use in the home environment. When used, for example, in a video consultation, an HbA1c value measured by the patient in the blood can indicate the quality of glucose control as a supplement to the parameters derived from the CGM measurement. However, all HbA1c measurement systems require proper instruction in correct sample collection and sample preparation (preanalytics) as well as evaluation of the results. Small errors in sample preparation (temperature of the system) or a too small or too large blood sample in the measuring capillary falsify the results. Each HbA1c measurement system has a specific standard range that can lead to a deviating result from the measured value as obtained with the laboratory device in the outpatient clinic or practice. Such discrepancies can unsettle patients who compare different HbA1c readings - the HbA1c value calculated by the CGM system software and the GMI recently calculated by the software - and find differences. The instructions for use of the devices should include a standard range, information on precision and accuracy, interference testing of common interfering substances as well as limitations of the method, e. g., applicability for diagnostic purposes or in children or pregnant women. In principle, an HbA1c value measured at home or between outpatient appointments is associated with added value, as long as the patients find this information helpful and can use it to manage their therapy.

In the case of physiological causes or influencing factors, the measurement is correct, but the HbA1c value does not correctly reflect the metabolic situation. The laboratory causes are interference variables that influence the HbA1c value measurement.

Specifications for measurement quality/standards

In recent decades, the measurement quality of the HbA1c value measurement has been significantly improved by a number of measures, in particular by the creation of suitable reference material. The values with the international reference method (IFCC standardisation) are given in mmol/mol Hb. Conversion into percent and vice versa is possible with the help of equations (▶ **Tab. 9**). However, there are still considerable differences in measurement results between laboratories using identical blood samples; even intralaboratory differences can be substantial. In the case of systems designed for self-measurement by patients, it is important to note that the measurement quality is not subject to control, as is otherwise the case in laboratories.

Costs/refund of expenses

The costs for the HbA1c value measurements are borne by the cost carriers for all patients with diabetes.

Quality control (internal and external/ interlaboratory tests)

According to the specifications of the Rili-BÄK (www.bundesaerztekammer.de/rilibaek2019) for HbA1c, the operators of corresponding devices must participate in an internal and external quality control. Unit-use POCT systems are excluded from external quality control; if HbA1c is used for diabetes diagnosis, interlaboratory comparisons are required. Up until now, the guideline for the pass limit for external quality control (interlaboratory comparisons) was ± 18 %. At the end of 2019, this figure will be reduced to 8 % (with a transition period of 2 years). The requirements for internal quality control were reduced from 10 % to 5 % and later to 3 %. Furthermore, commutable (exchangeable) control material (whole blood) is now used in the interlaboratory comparisons, which improves quality control considerably. Overall, this measure contributes to a significant improvement in the measurement quality of this parameter, which is important for diabetology.

Safety issues/side effects

When using different HbA1c measuring methods, differences are observed that are relevant for therapy: Various systems can display HbA1c measured values differing by 0.5 % for the same blood sample. If a patient has a relatively low therapeutic target, such differences may increase the risk of hypoglycaemia. The erythrocyte life span has a considerable influence on HbA1c diseases that change the erythrocyte life span and correspondingly influence the HbA1c value (▶ **Tab. 8**). For example, due to the significantly shortened erythrocyte life span, pronounced haemolytic anaemia can lead to low HbA1c values which are independent of the mean glucose values.

Practical implementation of the measurement

Information on the practical implementation and interpretation of the measurement results is provided in the Diabetes Diagnosis Clinical Practice Guideline.

An HbA1c value (eHbA1c) can be calculated from fasting glucose values measured over a certain period of time and individual 7-point blood glucose profiles. Using CGM data, a glucose management index (GMI) can be calculated in addition to HbA1c that reflects the predominant quality of glucose control from such data over a period of time. At the request of the American health authorities, another term is used to avoid suggesting that this parameter corresponds to the HbA1c value.

Conditions to be observed in practice

The use of POCT devices for HbA1c value measurement allows the current measured HbA1c value to be discussed directly with the patient. There is also no need to send a blood collection vial to a laboratory. However, the measurement quality of all POCT systems is not sufficient.

Use with different patient groups

The HbA1c value measurement provides the desired information on long-term glucose control in almost all diabetes types. In older patients it should be noted that the HbA1c value increases physiologically (see Diabetes Diagnosis Clinical Practice Guideline).

Training/psychological aspects

In diabetes training, the concept of the HbA1c value should be explained to the participants so that they understand the importance of target values and work towards achieving their target values. However, thanks to the availability of CGM data, the focus can be placed on the reduction of glucose fluctuations as a medium-term therapeutic goal. If individual patients are deeply afraid of severe hypoglycaemia, they will tend to aim for rather high HbA1c values. The opposite is true for patients whose goal it is to avoid diabetes-associated sequelae ("low-flying patients") because of extreme, often unrealistic fear.

Comment

The HbA1c value has proven itself as a parameter for the longer-term quality of metabolic control. The HbA1c value is established as a surrogate parameter for the incidence and progression probability of microvascular complications. This established parameter should not be abandoned without good reason simply because new CGM-derived parameters such as TiR are available. The HbA1c value continues to play an essential role in regular metabolic monitoring.

Summary and outlook

The glucose measurement and control options presented have revolutionized diabetes therapy over the past 40 years, providing patients with an unprecedented degree of flexibility and safety in dealing with their disease. This development has accelerated significantly over the last two decades, and the market launch of AID systems will represent another quantum leap in diabetes therapy.

All methods for glucose monitoring are subject to rapid change and further development. Therefore, the statements formulated here should be continuously updated through current literature reviews and observance of the manufacturers' homepages. There is a need for an independent institute to evaluate the performance of the measurement systems on the market, especially after their market launch. This is also due to the weaknesses of the previous CE marking system.

Unfortunately, there is no European authority which is primarily concerned with medical devices (as is the case with medicine); this is covered by the EU Commission. The German authorities (BfArM) also have relatively few practical options, since medical devices are a country issue.

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Conflict of Interest

SS received lecturing fees from Abbott, Ascensia, Astra Zeneca, Berlin-Chemie, Dexcom, Lilly, Menarini, Medtronic, MSD, Novo Nordisk, Roche, Sanofi, Ypsomed Advisory Adboards: Abbott, Dexcom, Diabeloop, Lilly, Medtronic, Roche.

DD is on advisory boards of the following companies and have received speaking fees from Abbott, Ascensia, Menarini, Roche, Profusa, Senseonics.

BG: Lecture Fees and / or advisory boards of Dexcom, Diabeloop, Medtronic, Roche, Vitalaire.

KL reports being a consultant for Abbott, Medtronic, Sanofi-Aventis, and having received lecture fees from Astra Zeneca, BDI, BioMarin, Chiesi, Insulet, Lilly Deutschland, Medtronic, Menarini Berlin Chemie, MSD SHARP & DOHME, neubourg skin care, NovoNordisk, Roche Diabetes Care, Sanofi-Aventis, with no potential conflicts of interest relevant to this article.

SVS is on advisory boards of the following companies: Abbott, Dexcom, Insulet, Lilly, Medtronic and Novo Nordisk and has received speaking fees from Abbott, Berlin-Chemie, Dexcom, Hexal, Infectopharm, Lilly, Medtronic, Merck, Novo Nordisk and Sanofi.

AT was scientific director of Medtronic Germany, manufacturer and distributor of insulin pumps and CGM systems (till april 2020). He is on advisory boards of the following companies: Evivamed, Dexcom. He've got speaking fees from Berlin-Chemie, Dexcom, Novo Nordisk and Sanofi.

RZ is on advisory boards of the following companies: Abbott, Lilly, Novo and Roche and has received speaking fees from Abbott, Dexcom, Lilly, Menarini, Novo and Roche.

GF is general manager and medical director of the Insitute for Diabetes Technology (Institut für Diabetes-Technologie Forschungs- und Entwicklungsgesellschaft mbH an der Universität Ulm, Ulm, Germany), which carries out clinical studies e.g. with medical devices for diabetes therapy on its own initiative and on behalf of various companies.

GF/IDT have received speakers' honoraria or consulting fees from Abbott, Ascensia, Berlin Chemie, Beurer, BOYDsense, CRF Health, Dexcom, i-SENS, Lilly, Metronom, MySugr, Novo Nordisk, Pharmasens, Roche, Sanofi, Sensile, Terumo, Ypsomed.