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Review

Technological innovation of Continuous Glucose Monitoring (CGM) as a tool for commercial aviation pilots with insulin-treated diabetes and stakeholders/regulators: A new chance to improve the directives?

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ABSTRACT

Civil aviation pilots who develop insulin-treated diabetes and want to renew a Commercial Pilot License (CPL) represent a medical, social and regulatory problem. This depends on justified concerns about hypoglycemia, the most threatening event for people who carry out jobs requiring a high level of concentration and reliability. This negatively affects social and working aspects of pilots' lives, who have a high profile and a high-cost professional qualification. It could be possible now to revise this attitude thanks to the availability of Continuous Glucose Monitoring (CGM) devices. CGM clearly showed to prevent hypoglycemic events in insulin-treated diabetic patients by allowing strict monitoring and trend prediction of glucose levels. By systematizing available data on such devices and present regulations in CPL issuance worldwide, our review can be used as handy tool for a fruitful discussion among the scientific community, national and international civil aviation regulators, stakeholders and pilots, aimed at evaluating the evidence-based opportunity to revise CPL issuance criteria for insulin-treated diabetic pilots.

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For the above-mentioned reasons, there are, among the regulatory administrations of Civil Aviation around the globe, several different approaches and limitations set for the subjects with insulin-treated diabetes who want to obtain, or renew, a CPL.

Contents

1. Introduction

Civil aviation pilots who develop insulin-treated diabetes, and subjects already affected by this condition who want to obtain a Commercial Pilot License (CPL), represent a medical, social, and regulatory problem. The aeromedical certification, necessary to enable commercial flight crew, private pilots, air traffic controllers, cabin crew, and parachutists to flight operations, is not issued applying the same criteria worldwide when it comes to this aspect. As can be reasonably imagined, this document is released only to subjects meeting all medical requirements. The latter, however, are differently regulated by individual civil aviation administrations, particularly regarding diabetic subjects. For instance, whereas the International Civil Aviation Organization (ICAO) does not allow who is treated with insulin to fly commercial aircrafts [1], Transport Canada (TC) and the U.S. Federal Aviation Administration (FAA) authorize it subject to the issuing of a special medical certification of insulin-treated diabetic applicants for first-, second- and third-class license under strict requirements [2,3]. In Europe (EASA – European Aviation Safety Agency), the license is denied not only to the applicants with insulin-treated diabetes but also to already certified pilots asking for renewal and who have developed such condition in between certifications. This behavior has extensive impact on the social and working life of these subjects who, in turn, have (or are attempting to obtain) a high profile and expensive professional qualification. To review the characteristics of each of the three classes of medical certification, see Table 1.

On the other hand, it is also evident how preventing hypoglycemia, the most dangerous acute insulin treatment complication, is essential for both pilots and passengers, and could only be possible through tight blood glucose monitoring [4]. However, it is also crucial for the pilot to maintain entirely concentrated on steering tasks through the entire flight duration. The frequent use of a spot glucometer, which some countries support, represents a source of distraction that has never been quantified. Nowadays, this issue can be addressed with more efficacy: more modern systems for the evaluation of glucose concentration in biological fluids, like the Continuous Glucose Monitoring (CGM) devices, have been available since several years by now. When in place, such instruments do not need any active procedure and give an immediate reading of the glucose levels just giving a quick glance to the display. Moreover, they proved effective in improving glycemic control and HbA1c levels, as well as in reducing the number and severity of hypoglycemic episodes [5–11].

For these reasons, it seems to be of high interest to conduct a thorough examination of all aspects related to the certification of diabetic subjects for flight operations.

Due to the relevant medical, socio-economic, and commercial aspects involved, AIMAS (Italian Association of Aerospace Medicine) set up a technical committee dealing with this issue under the guidance of a Europe-wide Italian expert in the field. AIMAS invited a diabetes-related patient association strongly involved in sport flying and two Scientific Societies, all of which affiliated to the IDF (International Diabetes Federation) – i.e. ANIAD (Italian National Association of Athletes with Diabetes), AMD (Medical Association of Diabetes experts) and SID (Italian Society of Diabetology), respectively - to join the committee together with the Aeromedical Section of ENAC (Italian National Civil Aviation Authority) as the Governmental Agency deputed to specific national flight regulations. Each of these committee members appointed one representative endowed with unique expertise in the field

Table 1 – An example of Medical certification classification, as issued by FAA [3].

Medical Certificate	Class I	Class II	Class III
Type of License	Airline Transport	Commercial	Private, Student, Recreational
Description	Pilots who exercise airline transport pilot (ATP) privileges; (flying scheduled airliners and other pilots whose employers require this level of certification).	Pilots who fly commercially (operations such as crop dusting, delivering canceled checks, or carrying passengers or cargo for hire).	Student pilots, recreational pilots, and private pilots who fly for pleasure or personal business (not for hire).
Duration	6 months if ≥ 40 yrs age 12 months if < 40 yrs	12 months	2 years if ≥ 40 years 5 years if < 40 at exam
Distant Vision	20/20 in each eye, with or without correction		20/40 in each eye with or without correction
Intermediate Vision 32 in.-panel	50 years and older 20/40 with or without correction	50 years and older 20/40 with or without correction	N/A
Near Vision 16 in.	20/40 in each eye, with or without correction		
Color Vision	Colors necessary for safe performance of airman duties		
Hearing	Conversational voice at 6 feet with both ears, or audiometry		
Blood Pressure	No standard. If medication required, will need cardiovascular workup. Current guideline maximum is 155/95.		
EKG (Electrocardiogram)	At age 35, and yearly after 40	N/A	N/A
ENT (otolaryngology)	No disease causing vertigo or disturbance of speech or equilibrium		

to discuss details in depth. In order to efficiently discuss the different aspects of this complex issue, the committee members decided to review the literature and prepare an updated document concerning newly available devices expected to grant the best possible glucose control and prevention of hypoglycemic events in insulin-treated subjects. This document is aimed at representing both a suitable starting point for further discussion within the group and a useful update, eventually stimulating the scientific community to start thinking about the need to revise and harmonize the criteria currently used to issuing flight certification to pilots and flight crew members affected by diabetes.

We approached this undertaking by reviewing present worldwide regulations, the known issues, the newly available devices able to resolve such issues, and the available data in the literature supporting the use of the above devices. Our review aims at providing a useful tool for commercial aviation pilots, regulators, and stakeholders to re-evaluate problems encountered by insulin-treated subjects in obtaining or renewing a commercial piloting license at present and identify workable, evidence-based solutions.

2. Methods

We made a systematic review of the literature on most relevant electronic databases (MEDLINE, SCOPUS, EMBASE, PubMed, World of Science) by entering the following BOOLEAN research string with MESH terms: ((“Aircraft“[Mesh] OR “Aviation”[Mesh]) AND ((“Blood Glucose“[Mesh] AND “drug effects”[Mesh]) OR “Blood Glucose Self-Monitoring“ [Mesh] OR “Diabetes Mellitus” [Mesh] OR (“diabetes Mellitus“[Mesh] AND “complications”[Mesh]) OR (“Glycated Hemoglobin A“[Mesh] AND “Drug effects” [Mesh]) OR “Hypoglycemia“ [Mesh] OR (“Hypoglycemia”[Mesh] AND “complications“ [Mesh]) OR (“Hypoglycemic Agents” [Mesh] AND “therapeutic use“[Mesh]) OR (“Insulin” [Mesh] AND “therapeutic use“ [Mesh])) AND (“Humans”[Mesh]). Also, we used the following keywords in a free research modality: pilots AND aircraft AND diabetes; diabetes AND continuous glucose monitoring. A total of 72 papers, published between 1946 and 2020 popped out. Thus, we excluded all papers dealing with case reports and case series, as well as those written in languages other than English, or unavailable as full text or failing to match topics relevant to the aim declared above. Finally, we took into consideration 66 papers for the present writing. Moreover, we reviewed and cited the public documentation available on the regulation of the medical certifications necessary for obtaining or renewing the pilot license of the major civil aviation administration authorities worldwide and the technical documentation and user manuals for CGM devices.

3. Diabetes and glucose monitoring

The onset of insulin-dependent diabetes mellitus in flightcrew members, especially in civil aviation pilots, represents a significant problem, involving not only the pilot himself but also the stakeholders and regulators who have to decide whether to ground a pilot or not. The primary concern regard-

ing the certification of a pilot with diabetes mellitus is the requirement he may develop for a switch to insulin therapy. Regarding that, insulin therapy might be responsible notoriously for various complications, the most worrisome for a worker on a job requiring a high level of attention, such as piloting an aircraft, being represented by hypoglycemia. Symptomatic hypoglycemia affects not only the quality of life and the health status of the diabetic patient experiencing it, but also vigilance, resulting in possible accidents in the workplace [4,12–17]. Hypoglycemia has been recently classified into the following three categories: (i) level 1 corresponding to a glucose concentration ranging from $\geq$ 54 mg/dL to < 70 mg/dL, which can alert the patient to take the appropriate actions; (ii) level 2 hypoglycemia occurring at glucose levels lower than 54 mg/dL, which asks for immediate actions from the subject to prevent any signs of neurologic impairment related to central nervous system glucose deprivation (i.e., neuroglycopenia), and (iii) level 3 hypoglycemia, defined as an altered mental and/or physical status requiring the assistance of another person for recovery, occurring at any blood glucose level lower than 70 mg/dL [18]. Again, one of the methods to avoid the onset of hypoglycemia is careful and frequent monitoring of blood glucose concentrations [4]. Although, for pilots, this would apply to the entire flight duration, no published data are available so far about the extent of distraction caused by the use of a glucometer for Self-Measuring Blood Glucose (SMBG) levels during engaging tasks. Despite requiring quite simple operations, capillary glucose measurement involves both hand utilization for at least 90 s to perform the following: (i) taking out the instrument and test strips; (ii) turning on the instrument; (iii) inserting the strip; (iv) taking the finger-pricking device and loading it with a lancet; (v) pricking the finger; (vi) getting a drop of blood; (vii) letting the strip absorb it; and finally (viii) waiting for 5 to 20 s (depending on the type of instrument) to get the reading.

4. Present regulations issues

Regulations concerning flight certification of people with diabetes who want to obtain or renew their licenses are widely variable worldwide. The latter cases apply typically to people diagnosed with type 2 diabetes mellitus during their private or commercial pilot life and unexpectedly requiring insulin during the inter-renewal period. Whereas several national and international aviation administrations do not deem the medical certification as necessary to obtain the license or renewal, others, particularly in the last few years, have become more permissive. As a result, the lack of harmonization among nations, in turn, represents a significant issue as aircraft piloting, especially concerning commercial flights, is typically an international job. As a consequence of such a dissociated attitude, it may be hypothetically possible that someone who is allowed to pilot in the departure country would not be allowed in the arrival country. Table 2 reports the most important aviation administrations' regulations on the matter. In brief, some nations revised their protocols, others keeping full limitations, and others which accepted some progress mostly based on recommendations from their national scientific societies. Indeed, the latter, by opposing a "blanket ban" against flight certification for people with diabetes, suggest individual attendant assessments [19]. This is the case of the American Diabetes Association, whose recommendations led in the US to the issuance by FAA of a third-class certificate for diabetic subjects on insulin treatment, but only for private and recreational flights (like student pilots, flight instructors or sport pilots) [19]. An exception to those stringent rules is represented by the protocol adopted in the United Kingdom and, subsequently, in Ireland [20,21].

UK Civil Aviation Authority (UK CAA) allows the issuance of class 1 certificates for CPL to people on insulin (or sulfonylureas/glinides) who are deemed to be at low risk of hypoglycemia and follow a stringent protocol for glucose monitoring and treatment adjustments. This protocol, directly overseen by UK-CAA medical department, includes specific glycemic ranges: green ("safe for flying": 90–270 mg/dL), amber ("requiring attention" for hypoglycemia: 72–90 mg/dL or hyperglycemia: 270–360 mg/dL) which require also corrective actions, and red ("urgency": <=72 mg/dL or >=360 mg/dL) requiring priority actions. Also, a strict schedule of SMBG monitoring before, during, and after the flight, and semestral clinical surveillance by CAA medical staff are necessary [20,22]. CGMs and insulin pumps are permitted as adjuncts, but SMBG and injection insulin supplies are needed at hand. Recently, an observational study on the first applicants issued with this protocol has been carried out and published. Interestingly, the paper did not report any particular safety issue, thus supporting the efficacy of the protocol. In particular, over the 22,078 flying hours registered, among the 49 pilots issued with class 1 and class 2 certificates by applying the abovementioned protocol, only 0.12% of the time a red range was reported, without any pilot incapacitation occurrence[23].

5. The CGM devices explained and the available literature

As a possible response to the relevant concerns raised by the civil aviation regulators more modern and effective devices monitoring glucose levels in body fluids than those used for SMBG are available since several years by now. These are mostly represented by the Continuous Glucose Monitoring (CGM) devices. These instruments do not need all the manual procedures described for SMBG and, in turn, provide an immediate reading of the glucose levels just by giving a quick glance to the reading device display, or by performing a fast scan of it on the sensor applied to the skin. This technology provides continued monitoring of glucose levels for several days, whenever wanted, without any fingerprick.

So far a considerable amount of evidence has been acquired on the superiority of CGM over SMBG concerning the improvement of metabolic control [6–9,24–31]. Moreover, patients perceived improved compliance to constant self-monitoring, higher treatment satisfaction, and better quality of life more often when on CGM than on SMBG. Also, CGM has a clear advantage in terms of costs, thanks to the significant reduction of hypoglycemic events and consequent med-

Table 2 – Aviation safety regulations for diabetic persons among the most important aviation authorities from which a specific protocol has been issued.

Organization	Geographical area	Rules	Permission to fly to insulin treated pilots
ICAO – International Civil Aviation Organization	United Nations	Applicants with insulin-treated diabetes mellitus shall be assessed as unfit.	no
EASA – European Aviation Safety Agency	Europe	Metabolic and Endocrine Systems (c) Diabetes mellitus: (1) Applicants with diabetes mellitus requiring insulin shall be assessed as unfit. (2) Applicants with diabetes mellitus not requiring insulin shall be assessed as unfit unless it can be demonstrated that blood sugar control has been achieved.	no
Civil Aviation Authority (UK CAA)*	United Kingdom	Insulin treated (or sulfonylureas/glinides) applicants for commercial pilot licenses can obtain class 1 medical certificates if they are deemed to be at low risk of hypoglycemic events and follow a specific protocol for glucose monitoring and treatment adjustments.	Yes
Irish Aviation Authority (IAA)*	Ireland	Same as UK CAA	Yes
Austrian Civil Aviation Authority (A CAA)*	Austria	Same as UK CAA	Yes
FAA – Federal Aviation Administration	United States	Consideration will be given only to those individuals who have been clinically stable on their current treatment regimen for a period of 6-months or more. The FAA has an established policy that permits the special issuance medical certification to some insulin treated applicants. Individuals certificated under this policy will be required to provide medical documentation regarding their history of treatment, accidents, and current medical status. If certificated, they will be required to adhere to monitoring requirements and are prohibited from operating aircraft outside the United States.	yes (with special issuances, only third class certification, not for Commercial Pilot License)
CASA – Civil Aviation Safety Authority	Australia	Diabetes treated with insulin does not meet the medical standards. However, Class 2 applicants may be considered using the following two stage approach to medical certification: 1. Initial certification with a safety pilot if they are able to comply with the CASA Insulin Requiring Diabetes Protocol, for a minimum of 15 flights (details of types of flights and durations will be tailored by CASA to meet individual requirements). 2. To have the safety pilot requirement removed, the applicant must carry out the specified in-flight requirements and provide the on-ground and in-flight data to CASA for assessment and consideration.	Yes (with special issuances)
Transport Canada (TC)	Canada	In accordance with current TC policy, applicants with Insulin Treated Diabetes Mellitus may be assessed for medical certificates as follows: Those who already hold a professional pilot license (ATPL, Commercial Pilot License) may be considered for a Category 1 medical certificate, restricted to flying with an accompanying pilot, as well as for a Category 3 or 4 medical certificate.	Yes (with restrictions)

*EASA requirements apply in this country. A specific approved protocol for insulin-treated pilots, developed under specific provision, is in place in accordance to EASA rules.

ical/hospital interventions [32]. Finally, based on a recent systematic *meta*-analysis of RCTs conducted on CGM devices in type 2 and type 1 diabetes mellitus, all CGM devices improved HbA1c, time spent in euglycemia, and reduced time spent both "above-range" and "below range" (namely in hypoglycemia) (see Table 3)[31].

We underline that CGM can be achieved by using several devices and applying procedures each of them having its own features, which entail the acquisition of specific skills different from those needed to perform SMBG. However, the most relevant aspect of its application in the field of air operations could be its ability to forecast the evolution of glycemic levels after the last measurement, according to trend curves of the previously measured values, and, in turn, to suggest suitable actions to prevent hypoglycemia or excessive hyperglycemia [8,24–26,29–31]. [8,24–26,29–31]. Concerning this latter aspect, it has to be pointed out that also hyperglycemia represents a potential risk for the aviation operations: in fact, it can cause vision abnormalities and cognitive impairment.

5.1. *The devices*

Several CGM devices have been developed over time, with the last iterations being the most advanced and reliable. Indeed, it must be noticed that technological research in this field is evolving very rapidly. In this way, deliberately, this section of the paper does not describe every single newly developed device comprehensively but, instead, wants to give a general picture of the most common device typologies, to provide an insight on the "pros" and "cons" of the most common types of CGM, without any intention of recommendation. Moreover, the reader must also be aware that no such devices are presently certified for altitudes above 5500 mt and in hypobaric conditions, rapid decompression, or other extreme in-flight events. Therefore, it will take extensive testing and certification work before having rtCGM and FGM devices routinely used in aviation.

All CGM devices need a sensor with a micro-needle that fits the skin or gets implanted subcutaneously through a small skin incision. This thin sensor continuously measures the glucose levels in the subcutis and sends data to a display device via a wireless connection. These sensors measure glycemia in the interstitial subcutaneous fluid (ISF) continuously, thus avoiding the inconvenience of making repeated finger-pricks and contemporarily providing an amount of data not even imaginable with SMBG [33]. As far as the type of monitoring is concerned, we can distinguish two systems: the real-time CGM (rtCGM) and intermittently viewed CGM (iCGM), also called flash glucose monitoring (FGM). Both systems perform a continuous real-time measure of glucose levels but, whereas FGM provides the glycemic level every time the user scans the sensor with the reader (which can be a dedicated device or a smartphone), rtCGM passively (and continuously) transmits it, without any user intervention. The software developed for both devices is equipped with alarms (with sound or vibration) if a hyperglycemic or hypoglycemic trend is detected. The older models of FGM did not have such types of alarms.

Real-time CGM devices: At the time of the writing, the most popular rtCGM devices use transcutaneous sensors [34–36], and another one uses an implantable subcutaneous sensor [37].

FGM devices: The most popular FGM device has been recently approved in his 2.0 revision [38] which, in respect to the previous model, introduced the ability to set-up customizable alarms for glycemic events. A further 3.0 revision has become available in some countries just at the time of finalization of the present paper.

Both rtCGM and FGM devices measure glucose levels in the interstitial fluids (ISF) instead of SMBG, that directly measure glycemia. ISF and blood are different compartments with different characteristics and dynamics [39], for these reasons there is a little latency between the blood and the ISF about glucose measurements, because the glucose levels take some time to reach a balance between blood and ISF, which can be about 5–10 min [40,41]. This peculiarity can cause possible consequences on the sampling accuracy, that are similar between rtCGM and FGM. However, they are minimal in the case of hypoglycemia, which clinically still warrants a correct level of measurement reliability [42–44].

The differences between the two systems: The operational time of the sensors (the time after which the sensor needs replacement) is of 5–10 days for the rtCGM, 14 days for FGM devices which use transcutaneous sensors, and of 180 days for the one which use the subcutaneous implantable sensor [37,45,46]. The most relevant difference between the two systems is that rtCGM devices need to be calibrated by an SMBG measurement at least twice daily, whereas FGM is automatically calibrated.

The last iteration of one rtCGM device eliminated this procedure (is pre-calibrated). Moreover, some of the devices (i.e., all FGM devices and some rtCGM) operate at a sensibly lower electric potential and transmit on Bluetooth® or Bluetooth Low Energy® (BLE®), which, therefore, may have fewer problems of interference with the aircraft instrumentation [47]. The main technical characteristics of the most common CGM devices are reported in Table 4.

The importance for aviation operations: The most relevant aspect of both systems for flight operations is the correct information on the glycemic trend, comparable to an artificial horizon, similar to that used by the pilot to monitor the flight level. When the continuously registered values are stable, a horizontal arrow appears, whereas the arrow faces up or down if the glycemic values are expected to rise or decrease, independently of instantaneous values being still in the normal range. In other words, the software of these devices is capable of activating an alarm when the glucose levels are still in the normal range, but an imminent increase or reduction is expected. Thanks to particular algorithms, this alert is also able to make an immediate suggestion on the preventive actions to take to maintain blood sugar in a safe range, i.e., food or sweetened beverages consumption or, on the contrary, administration of extra doses of insulin (Fig. 1).

The application of whatever CGM technology represents an absolute improvement to meet the needs of flight safety and to extend the so-called "time in range" of glucose levels as much as possible not only for pilots but also for all crew members on insulin. It can represent a natural extension of the already active protocol in the UK and Ireland [48]. A paper from the Association of British Clinical Diabetologists just

Table 3 – Fifteen RCTs comparing SBGM with different types of CGM with reference to various primary outcomes. Every single study showed CGM superiority over SBGM in diabetes control under various settings and as for different outcomes (hypoglycemia events included). Modified from Maiorino et al. [31].

First author, year (reference no.), characteristics of subjects	Dia-betes type	Study design	Study duration (weeks)	N inter vention/ control	Intervention/sensor comparator	Insulin regimen	Primary outcome
JDRF, 2008 [7] <25 years old 15–24 years old 8–14 years old	T1	P, O	26	52/46 57/53 56/58	rtCGM/Dexcom SEVEN or MiniMed Paradigm REAL- Time or FreeStyle Navigator/SBGM	CSII, MDI	Change in HbA1c level at 26 weeks
O'Connell, 2009 [50], adult and pediatric	T1	P, O	12	31/31	SAP/MiniMed Paradigm REAL-Time/CSII	CSII	Difference in the proportion of TIR (70–180 mg/dL)
Battelino, 2011 [51], adult and pediatric	T1	P, O	26	62/58	rtCGM/FreeStyle/Navigator/SBGM	CSII, MDI	Time spent in hypoglycemia (63 mg/dL) during the26 weeks
Battelino, 2012 [9], adult and pediatric	T1	CO, O	24	77/76	rtCGM/Guardian REAL- Time/CGM sensor off	CSII	Difference in HbA1c levels between the sensor on and sensor off arms after 6 months of follow-up
Little, 2014 [52], adult	T1	P, O	24	42/41	rtCGM/CE-marked/rtCGM (Medtronic)/SBGM	CSII, MDI	Difference in hypoglycemia awareness at 24 weeks
Bolinder, 2016 [25], adult	T1	P, O	24	119/120	iCGM/Freestyle Libre/SBGM	CSII, MDI	Time spent in state of hypoglycemia (,70 mg/dL)
van Beers, 2016 [10], adult	T1	CO, O	16	26/26	rtCGM/Enlite/SBGM	CSII, MDI	Mean difference in percentage of time spent in state of normoglycemia
Beck, 2017 [8], adult and pediatric	T1	P, O	24	105/53	rtCGM/Dexcom G4 Platinum CGM System/SBGM	MDI	Difference in change in HbA1c levels from baseline to 24 weeks
Beck, 2017 [53], adult	T2	P, O	24	79/79	rtCGM/Dexcom G4 Platinum CGM System/SBGM	MDI	HbA1c reduction at 24 weeks
Feig, 2017 [54] Women planning pregnancy Pregnant women	T1	P, O	24 36	53/57 108/107	rtCGM/Guardian REAL- Time or MiniMed MiniLink/SBGM	CSII, MDI,	Difference in change in HbA1c ,
Haak, 2017 [26], adult	T2	P, O	24	149/75	iCGM/FreeStyle Libre/SBGM	CSII, MDI	Difference in HbA1c at 6 months
Ruedy, 2017 [55], adult	T1, T2	CO, O	24	63/53	rtCGM/Dexcom G4 Platinum/SBGM	MDI	Change of HbA1c from baseline to 24 weeks
Heinemann, 2018 [56], adult	T1	P, O	24	75/74	rtCGM/Dexcom G5 Mobile/SBGM	MDI	No. of hypoglycemic events measured by rtCGM during the follow-up phase compared with baseline
Oskarsson, 2018 [57], adult	T1	P, O	24	82/81	iCGM/FreeStyle Libre/SBGM	MDI	Change in time spent in a state of hypoglycemia (<70 mg/dL) from baseline
Bosi, 2019 [58], adult	T1	P, O	24	76/77	SAP/MiniMed 640G with SmartGuard/CSII plus SBMG	CSII	Mean no. of sensor hypoglycemic events: sensor glucose values ≤55 mg/dL (3.1 mmol/L) for > 20 min

(T1: type 1 diabetes mellitus, T2 type 2 diabetes mellitus, P: parallel; O: open label; CO: crossover; CSII: continuous subcutaneous insulin infusion; MDI: Multiple daily injections; TIR: time in range; SAP: sensor-augmented pump; rtCGM: real time Continuous Gylcemic Monitoring; iCGM: intermittent scanned Glycemic Monitoring).

Table 4 – Main features of commercially available CGM devices.

Monitoring type:	rtCGM	FGM
Devices	five main types (two of which from the same producer)	Two main types (same producer)
Detection fluid	Interstitial	Interstitial
Calibration	Twice daily by SMBG (automatic only in one)	Automatic
Sensor substitution interval	5–10 days; (180 days for only one)	14 days
Sensor placement	Transcutaneous (except one requiring subcutaneous intradermal implantation)	Transcutaneous
Access to glycemia data	Continuous (detectable by pushing a button on the display device)	Intermittent every time the display device (or smartphone) is passed over the sensor (scan)
Interference with acetaminophen	Only two of five devices	No
Calculation of the insulin dose without using SMBG	Yes for only two of five devices	Yes
Alarms for hyper-/hypo-glycemia	Yes	Yes in the newly available model
Trend lines	Yes	Yes
Operating conditions	Electrical potential	Low electrical potential
Data Transmission	Over standard Bluetooth	Over BLE (Bluetooth low energy)

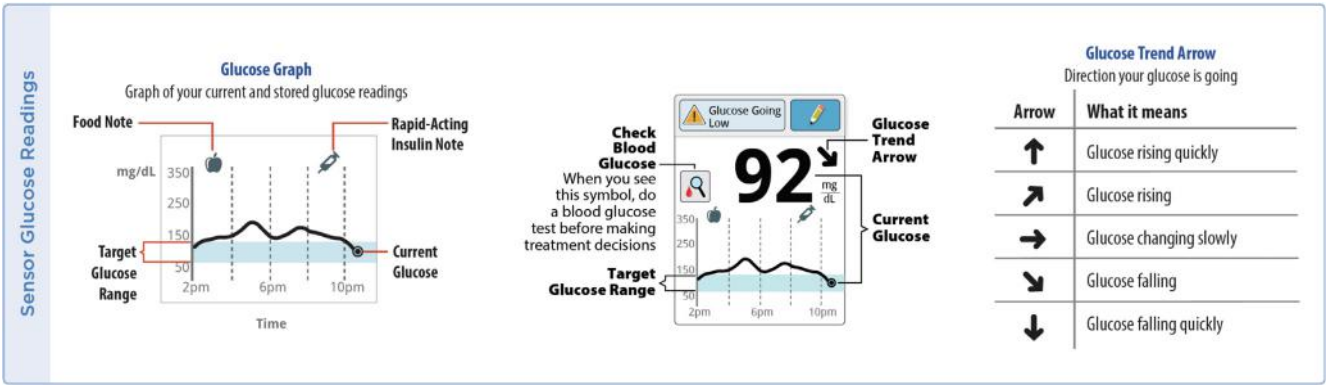

Fig. 1 – An example of the glucose reading graph and trend arrows representation and interpretation, here reported from https://provider.myfreestyle.com/pdf/FreeStyle-Libre-In-Service-Guide.pdf.

issued on Diabetes Care at the time of preparation of the present review gives further support to our hypothesis by showing that the use of Abbott Freestyle Libre flash glucose monitoring device was associated with significantly improved glycemic control and hypoglycemia awareness and a reduction in hospital admissions [49].

Known limitations: However, it has to be pointed out that CGM management requires a specific training for the comprehension of its usage and the interpretation of the data provided, especially for the determination of the actions to be taken in response to the trend lines announcing a hyper- or hypo-glycemia. It is imaginable that an external validation (maybe even a certificate) should be necessary to prove the proficiency in the correct use of the devices. Moreover, one could also envisage specific simulator training to recognize hypoglycemic/hyperglycemic conditions. It would also be necessary to carefully evaluate the correct functioning of the devices in various flight conditions, together with the assessment of no interference with the flight instrumentation. As already reported, SMBG or CGM systems are not presently certified for altitudes above 5500 mt (there are only data on obsolete devices no longer in use), and in hypobaric conditions, rapid decompression or other extreme in-flight events [22]. These and other open issues, such as privacy regulation (i.e., the communication of CGM data to software platforms that are external to the aircraft and, therefore, traceable by third parties), require careful consideration before submitting operative and innovative proposals to the civil aviation regulatory organs. In Appendix A, we provided a set of questions to be submitted to a "consensus panel" of experts, with the final aim of producing an "evidence-based" document on the matter. In Appendix B, we added two individual NHS-specific issues to be dealt with too.

6. Conclusions

After going thoroughly through the scientific literature available in the field, the technical committee set up by AIMAS and involving two Scientific Societies and one highly competent patient association affiliated to the IDF together with the Italian Civil Aviation Authority, achieved consensus on documented superiority of CGM and FGM systems on finger-prick based self-monitoring of blood glucose (SMBG) in terms of improved glucose control, lower HbA1c levels, reduced time spent in hypo- or hyper-glycemia and longer customized time in range (TIR) bedsides higher degrees of treatment adherence and patient satisfaction, as well as better quality of life and lower hypoglycemia-related hospitalization rate costs.

Based on the above, the technical committee agrees that such technology advances might improve working efficiency in insulin-treated flight personnel. Therefore, it expects the remote access subcutaneous glucose monitoring systems must be taken into due consideration by national and international regulatory authorities to revise and harmonize present flight certification criteria for pilots on insulin.

In conclusion, being this a complex field, which involves several professional figures, we believe that the abovementioned evidences could advocate the wish to create a technical table which could host an expert panel, composed by representatives of the Scientific Societies of the diabetology field, the stakeholders (i.e. airline companies), the civil aviation regulatory organs and the patients. This table should trace a roadmap aiming at addressing all the aspects linked to the future CGM systems use so as to allow or facilitate the issuance of medical certifications to the civil aviation pilots and cabin crew members on insulin treatment, possibly with an international agreement.

Compliance to ethical guidelines

The text does not contain its own experimental data, but represents a synthesis of what has been published by other authors.

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Declaration of Competing Interest

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Appendix A

An example of "working proposal" of questions to submit to a "consensus table" of experts to implement a PICO (Problem, Intervention, Comparison, Outcome) approach aimed at producing a PICO-GRADE document of evidences on the matter.

1. which HbA1c levels should a pilot attain to reduce hypoglycemia to a minimum?
2. which glucose levels should a pilot attain to fly safe?
3. which glucose levels should a pilot start with to reduce hypoglycemia to a minimum?
4. which and how many in-flight glucose measurements are required for a pilot with diabetes?
5. which advantages might CGM systems grant a pilot on insulin during flight?
6. might CGM system trend arrows substantially contribute to the efficient prevention of hypoglycemic / hyperglycemic events?
7. are CGM systems safe?
8. are CGM systems safe in-flight too?
9. does CGM allow to spare time, help attention and contribute to safety better than SMBG?
10. is it difficult to learn CGM management?
11. can an insulin-treated pilot fly safely?
12. should this be the case, what clinical requirements, what biochemical parameters, and what educational and self-care skills should he / she have?

Appendix B

As for Italian regulations concerning insulin-treated flight personnel, also the following issues should be dealt with:

1. should CGM systems be reimbursed to insulin-treated people by the Italian NHS?
2. who should certify a pilot as being able to utilize a CGM system appropriately?

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