Medical Certification of Persons with Insulin-treated Diabetes in the Aviation Industry

Australian Diabetes Society Position Statement

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Australian Diabetes Society

Authorship

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Executive Summary

1. The certification and operational rules for pilots with diabetes vary across the globe. These guidelines are strict and are guided by principles of risk of medical incapacitation.
2. Ensuring aviation safety is a paramount for public safety, but this should be balanced with the freedom and fair assessment of persons with diabetes in the workplace.
3. There is a need to update regulatory guidelines to account for advancements in diabetes treatment and technologies that assist in reducing incapacitation risk and to enable persons with diabetes to demonstrate safety to fly.
4. Review of Civil Aviation Safety Authority's current diabetes certification policy is recommended.
5. The principles of this review could be used to guide protocols in other safety-sensitive workplaces (such as defence personnel, police force, heavy rigid long-distance truck drivers).

Abbreviations:

ADS – Australian Diabetes Society

BGL – Blood glucose level

CAA – Civil Aviation Authority (UK)

CAM – Civil Aviation Medicine (Canada)

CASA – Civil Aviation Safety Authority

CASR – Civil Aviation Safety Regulations

CGM – continuous glucose monitoring

CPG – Clinical Practice Guidelines

CSII – continuous subcutaneous insulin infusion

DAME – Designated Aviation Medical Examiner

FAA – Federal Aviation Administration (US)

FDA – Food and Drug Administration

HCL – hybrid closed loop (insulin pump)

MDI – multiple daily injections

PGLS – predictive low-glucose suspend (insulin pump)

TGA – Therapeutic Goods Administration

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1 Preface

In 2019, the Australian Diabetes Society (ADS) commissioned a working group to draft a position statement on the medical certification of persons with insulin-treated diabetes in safety-sensitive industries. The working party consisted of two endocrinologists with an interest in type 1 diabetes, and a certified Designated Aviation Medical Examiner (DAME) who is also a pilot and an advocate for persons with diabetes.

To prepare this statement, a literature search was performed summarising the current evidence for incapacitation risk in insulin-treated persons with diabetes in the context of modern treatments and technologies. Guidelines from other aviation safety bodies across the globe and the available evidence for the safety of these protocols were also summarised. The position statement was then presented to the ADS council for approval in 2020. Feedback was also provided by representatives from the Australian Air Force, Transport Canada and the Civil Aviation Safety Authority (CASA).

This is the first ADS supported position statement to address medical certification of diabetes in the workplace. The main focus of this document is the aviation industry, but these guidelines may be adapted to other industries such as the defence force, police force and heavy vehicle drivers as required, although different levels of risk may apply in industries other than the aviation industry. We focus on insulin-treated persons with diabetes (both type 1 and type 2).

Readers should note that this document is intended only to provide updated specialist recommendations to guide regulatory bodies and assist authorities to identify persons with insulin-treated diabetes utilising currently available diabetes technologies and with no greater incapacitation risk than other pilots. The focus is specifically directed at management of blood glucose and excludes diabetes related complications.

This document should not be confused with the official standards for certification published by CASA.

2 Introduction

2.1 Aviation and medical certification

There are strict medical approval processes for individuals seeking aviation licensing. Guidelines consider the overall risk of a medical condition to safety and take into account the likelihood of a clinical event (causing incapacitation), likelihood of a detrimental aviation outcome (involving aircrew and/or the general public), and the acceptability of risk before and after risk-mitigation strategies.

There are several classes of medical certificates including:

- Class 1 – for professional pilots (holders of air transport pilot, commercial pilot, flight engineer or flight navigator licence)
- Class 2 – for private pilots (holders of student pilot or private pilot licence) and commercial pilots with operational restrictions (commercial aircraft pilot not carrying passengers and in aircraft weighing less than 8,618kg, commercial balloon pilot)
- Basic Class 2 – for private pilots (limited to piston engine powered aircraft, day visual flight rules, carrying up to five non-fare paying passengers)
- Class 3 – for air traffic controllers

The class of medical certification determines the degree of acceptable risk. For class 1 licence holders, experts have proposed an individual incapacitation risk of 1% per year for multi-crew operations and solo private operations.[1] These guiding principles are accepted by the aviation community.

2.2 Diabetes and medical certification

Aviation medical examinations are performed by DAMEs, who are guided by Clinical Practice Guidelines (CPGs) relating to specific medical conditions. There are four CPGs for diabetes, separated by type of diabetes and treatment strategy (and therefore risk of hypoglycaemia).[2–5]

High risk of hypoglycaemia	Type 1 Diabetes – insulin dependent
	Type 2 Diabetes – insulin requiring
	Type 2 Diabetes – non-insulin treated
Low risk of hypoglycaemia	Type 2 Diabetes – non-insulin treated

These guidelines acknowledge that within an aviation context, diabetes poses several challenges:

- Diabetes can affect aviation:
  - Overt incapacitation: cardiovascular or cerebrovascular event
  - Subtle incapacitation: visual impairment (fields, low contrast sensitivity, colour), impair motor and sensory function, impair autonomic function (including hypoglycaemia awareness)
- Diabetes treatment can affect aviation:
  - Loss of consciousness (or impaired judgment) due to hypoglycaemia
  - Impaired cognitive function from hyperglycaemia
- Aviation itself can:
  - impact blood glucose levels (from difficulty accessing blood glucose monitoring and treatment at usual times, irregular meal and sleep times and sedentary occupation).

Of each the above challenges, impairment from hyper- or hypoglycaemia is the main acute threat to flight safety (further discussed in section 3.1). Protocols for pre-flight, inflight and certification include guidelines to ensure that blood glucose related risks are appropriately mitigated.

2.3 Current Australian licencing restrictions for persons with diabetes

The guidelines for aeromedical certification of pilots with diabetes have been refined over time. Historically, a diagnosis of diabetes led to permanent disqualification from flying mostly due to concerns regarding incapacitation from hypoglycaemia or cardiac event. Across the globe, policies have shifted over time, resulting in an increasing number of persons with diabetes receiving certification to fly under stringent conditions (further detailed in section 3.2).

CASA policies have also changed over time to grant medical certificates for pilots with diabetes. Those managed with diet, oral or non-insulin injectables (GLP1 agonists) can be certified with a Class 1, 2 or 3 licences on the condition of demonstration of stable blood glucose levels on home blood glucose monitoring, and the absence of complications.

Currently, licensing rules mandate that persons with insulin-treated diabetes (type 1 and 2) are unfit to hold Class 1 or Class 3 medical certificates. However, applicants may be considered for a Class 2 medical certificate (allowing private and operationally restricted commercial flight) if they satisfy CASA's initial certification rules (table 1). If initial certification is achieved, these pilots must be accompanied by a safety pilot for a minimum 15 flights and may then apply to extend privileges to fly solo assessed by CASA on a case-by-case basis.

Table 1. Current Australian criteria for initial assessment for Class 2 medical certificate (for insulin-treated diabetes); table adapted from existing CASA guidelines.

Exclusion criteria	▪ Severe hypoglycaemia: 2+ episodes in 5 years and/or any in the past 1 year ▪ Presence of 1. Autonomic neuropathy 2. Significant cardiovascular disease (note significant not specified) 3. Retinopathy (note: grades of retinopathy not specified) 4. Renal disease (note: no definition of renal disease provided)
Medical factors considered by CASA (all assessed on a case-by-case basis)	Glycaemic factors ▪ HbA1c 6.5-8.0% ▪ No more than 5% readings < 4.0mmol/L (frequency of testing >4 times per day) ▪ 80% readings 5-15mmol/L Other factors ▪ Excessive hypo- or hyperglycaemia ▪ Hypoglycaemic unawareness ▪ Poor treatment compliance
Information to be supplied	1. HbA1c: 2 readings (6.5-8.0%) more than 3 months apart 2. Endocrinologist report 3. Ophthalmologist report 4. Cardiac risk assessment 5. Confirmation of diabetes education

Table 2 and 3 describe the current CASA guidelines for inflight glucose monitoring and management, and ongoing certification rules. In general, certification can be granted so long as there is demonstration of stable blood glucose levels, no evidence of complications, absence of severe hypoglycaemia and satisfactory specialist medical reports. We note that these guidelines lack specific definitions, including a definition for 'severe hypoglycaemia'. These guidelines also use ill-defined language such as 'loss of control' of diabetes.

These guidelines have undergone review in 2009 (following a CASA convened workshop of experts[6]), 2012 and 2017. Our revised recommendations are detailed in section 4 of this document.

Table 2. Current Australian guidelines for ongoing certification for Class 2 medical certificate (in insulin-treated diabetes); table adapted from existing CASA guidelines.

Monitoring	Inflight and on-ground logbooks (2 glucose meters, that can be downloaded to provide in-range statistics, blood glucose level [BGL] monitoring >4 times per day)
Events requiring immediate report	1. Severe hypoglycaemia 2. Accidents resulting in injury (regardless if due to hypoglycaemia) 3. "Loss of control" of diabetes 4. Change in diabetes treatment 5. New significant complications
Annual report	1. Collation of 3 monthly specialist assessment 2. Annual eye report 3. Cardiac risk assessment

Table 3. Australian pre- and in-flight guidelines for glucose monitoring and management; table adapted from current CASA guidelines.

Timing of glucose measurement	BGL (mmol/L)	Action
Pre-flight monitoring: 30 minutes prior to flight (* and no insulin within 90 minutes of flight)	>15 5-15 <5	Cancel flight Proceed with flight Ingest 15g carbohydrate, and recheck in 30 minutes
In-flight monitoring: First 30 minutes into flight, then hourly and within 30 minutes of anticipated landing	>15 5-15 <5	Land, do not resume flight control until 5-15mmol/L No action required Ingest 30g, land and do not resume flight until 5-15mmol/L
In the event of competing operational demands during flight	Unable to measure	Ingest 15g, and check BGL in 1 hour (if cannot check at this time, ingest 30g and land to check BGL)
Glucose meter	Carry 2 devices Must have memory function	

2.4 Insulin pump use in-flight

We note that in Australia, insulin pump use was allowed until 2012 when a published research paper raised concerns that changes in atmospheric pressure caused unintended insulin delivery.[7] Insulin pump users were advised to transition to insulin injections for the duration of flight. The 2017 guidelines do not directly discuss insulin pump use aside from the following:

'Flight should not commence within 90 minutes of the administration of insulin (either short or long acting types), unless an insulin pump is used.'

In practice, all insulin pump users are advised "to suspend or disconnect for the duration of the flight" with limited evidence to support this recommendation (see section 3.3.2). The use of continuous glucose monitoring systems (CGMS) is not addressed in detail by current guidelines.

3 Literature Review

3.1 The relationship between blood glucose and incapacitation risk

Individuals with insulin-treated diabetes are susceptible to hyper- or hypoglycaemia. The central nervous system relies on glucose to function optimally and acute hypoglycaemia may affect cognitive domains including attention, memory and mood.[8] In persons with diabetes, out-of-range glucose levels are the main risk to acute cognitive impairment inflight but the risk of impairment varies according to the degree of blood glucose derangement. More out-of-range glucose levels confer greater risks of cognitive impairment compared to mild derangements. Recognising this, international working groups have formulated definitions for hypoglycaemia and hyperglycaemia according to categories (table 4).

Table 4. Consensus definitions for hyper- and hypoglycaemia (adapted from Agiostratidou et al.[9])

	Definition
Hyperglycaemia	Level 1: glucose >10mmol/L and ≤13.9mmol/L Level 2: glucose >13.9mmol/L
Hypoglycaemia	Level 1: glucose <3.9 but ≥3.0mmol/L Level 2: glucose <3.0mmol/L Level 3: a severe event characterised by altered mental and/or physical status requiring assistance regardless of blood glucose level

The specified level 1 hypoglycaemia glucose range was selected according to the usual physiological threshold for neurohormonal responses to a falling glucose in persons without diabetes. The level 2 hypoglycaemia glucose range selected as the typical threshold for the development of neuroglycopaenic symptoms, and risk of cognitive dysfunction. The level 3 definition maintains a functional rather than biochemical definition, since it denotes severe cognitive impairment and the threshold for this may differ between individuals.

These thresholds correlate with clinical studies designed to test cognitive performance during acute glucose extremes. Cognitive function tests in children with type 1 diabetes confirmed decrements in mental efficiency at glucose thresholds that mirror the above definitions. Compared to performance at euglycaemia, mental arithmetic was significantly longer at glucose levels <3.0mmol/L and >22.0mmol/L. Reaction time was also significantly longer at glucose levels <3.0mmol/L.[10] Cognitive function during hypoglycaemia has also been tested in adults with type 1 diabetes using driving simulators and insulin infusions to achieve controlled hypoglycaemia (3 ranges tested: 4.0-3.4, 3.3-2.8 and <2.8mmol/L). Driving performance was disrupted within all hypoglycaemia ranges.[11] Studies examining the relationship between hyperglycaemia and cognitive performance in type 1 and type 2 diabetes also demonstrate that acute hyperglycaemia (glucose > 15mmol/L) is associated with mild slowing during cognitive performance tests, but that effects were highly individual.[12] These findings support the importance of maintaining blood glucose levels within target ranges to optimise cognitive performance. These defined levels for hyper- and hypoglycaemia are also likely clinically and functionally meaningful.

3.2 Certification of insulin-treated pilots: a global context

Insulin-treated pilots have been able to apply for class 1 medical certification in the UK (CAA) and Canada (CAM) since 2012 and in the USA (FAA) from November 2019. Each respective regulatory body abides by protocols that are unique to each country. These protocols share an emphasis on the assessment of pilots on an individual basis according to stringent criteria (table 5).

Table 5. A comparison of international guidelines for medical certification of insulin-treated pilots *, **

Class	Australia	UK	US	Canada
Commercial (Aus Class 1)	Unfit	Acceptable with co-pilot (since 2012)	Acceptable (since 2019)	Acceptable pending risk stratification (since 2012)
Private/ Recreational (Aus Class 2)	Co-pilot for 15 flights, then review for solo	Acceptable with safety pilot and dual controls	Solo if pass medical assessment (since 1996)	Acceptable pending risk stratification
Air traffic control (Aus Class 3)	Unfit	Unfit	Acceptable	Acceptable
Insulin injections	Accepted	Accepted	Accepted	Accepted
Insulin pumps	Not accepted (and not addressed in protocol)	Accepted	Accepted	Accepted
Date of last review	May 2017	November 2018	November 2019	March 2015

* in this table, type 1 and insulin-treated type 2 diabetes protocols are considered together.
** class definitions differ by country, but for the purpose of this table have been adapted to commercial, private/recreational and air traffic control categories.

There are now audit data available to assess the performance of these protocols to assist in decision making and future protocol designs. Audits of UK commercial licence and US recreational licence protocols for insulin-treated diabetes are presented here.

3.2.1 Audit of UK CAA protocol for insulin-treated commercial pilots

In 2010, with the assistance of an expert committee, the UK CAA developed a protocol that allowed insulin-treated pilots to achieve class 1 medical certification. Licences were issued from 2012. Prospective data were collected between 2012 to 2019 from 49 pilots who received certification. Initial data and extended data were published in 2017 and 2020.[13,14]

In summary, 49 pilots with insulin-treated diabetes received class 1 certification during the described period (96% were men, median age 44 years, 84% type 1 diabetes, median diabetes duration 10.9 years).[14] The pilots recorded 38 621 blood glucose measurements in the pre- and in-flight period, from 9181 flights over 22 078 flight hours. These data were analysed according to the CAA defined glucose categories grouped by urgency of action required. The protocol defines a traffic light model: no action required (green range: glucose 5-15mmol/L), corrective action required (amber range: glucose >4 and <5mmol/L OR BGL >15 and <20mmol/L), or priority action required (red range: glucose <4 or >20mmol/L). The audit revealed that 97.69% of glucose levels were within range (5-15mmol/L), 1.42% were in the low amber range (>4 and <5mmol/L), 0.75% in the high amber range (>15 and <20mmol/L), and 0.14% were in the red range (<4 or >20mmol/L). There were no episodes of pilot incapacitation. There were 14 low red range values recorded whilst in flight, representing 0.07% of all inflight measurements. The lowest recorded inflight reading was 3.1mmol/L and all episodes were self-treated. None required assistance.

Notably, this protocol allows for CGM to be used as an aid, but not a substitute for finger prick glucose monitoring since at the time the original protocol was created, the accuracy of CGM had not been validated at high altitudes. However, many pilots used CGM devices in addition to finger prick glucose monitoring. An observational study comparing inflight finger prick glucose monitoring with CGM is underway (ClinicalTrials.gov NCT04225455, DEXFLY study, note study currently suspended January 2023).

This evaluation demonstrates that UK pilots adherent to this protocol can safely perform operational duties. The frequency of low glucose readings was within acceptable industry limits (ie <1%) and there was no overt incapacitation from low glucose events. Glucose events >15mmol/L were infrequent and also not associated with incapacitation. These data represent a middle-aged cohort with relatively short duration diabetes and likely diagnosis after previous class 1 certification. Its applicability to persons with longer duration diabetes and diagnosed prior to initial certification is unknown.

3.2.2 Audit of US recreational licences

Dr Warren Silberman (US FAA) reported on 9 years of experience with class 3 licensing. This was presented at the Divers Alert Network Diabetes and Recreational Diving Workshop in 2005.[15] At the time of review, there were 425 pilots with insulin-treated diabetes who were issued a US third-class licence (recreation/private). There were 4 safety incidents between 1998-2000, but diabetes was not a contributing factor to any incidents. This report demonstrated that FAA protocols for screening and monitoring are safe in the context of recreational flight.

In November 2019, the FAA extended the privilege of class 1 licences (commercial) to insulin-treated pilots. The FAA acknowledged that advances in diabetes technology and management have augmented their capacity to assess medical certification for insulin-treated individuals and have made CGM a compulsory glucose monitoring method. To our knowledge, there are no formal plans to prospectively audit individuals who will be newly issued class 1 licences following the recent protocol change.

3.2.3 Conclusion

Overseas data support careful screening to effectively exclude persons at significant risk of hypoglycaemia related incapacitation, and the existing stringent in-flight monitoring protocols are sound. Incapacitation risk of <1% is readily achieved by implementing similar screening and monitoring protocols and likely <0.1% risk can be achieved with the addition of CGM monitoring. The evidence supports persons with insulin-treated diabetes as suitable for Class 1 certification in Australia provided stringent monitoring guidelines are followed.

3.3 Literature describing the safety of insulin pump devices and continuous glucose monitoring (CGM)

3.3.1 Principles of diabetes management using insulin pumps and CGM

An insulin pump is a small electronic device that is programmed to continuously deliver rapid-acting insulin through a Teflon or metal cannula that is inserted below the skin. When instructed by the user, the pump delivers extra insulin at meal times, or to correct a high glucose level. The newest devices (hybrid closed loop) can automatically increase or reduce insulin delivery rates to bring glucose readings into a target range and have been demonstrated to increase glucose time in range (4-10mmol/L) and reduce hypoglycaemia severity and frequency. Insulin pumps can replace insulin delivery by needle injections but with the capacity for micro-adjustment of insulin doses. They can be used by any individual that requires insulin treatment. However, in Australia most users have type 1 diabetes rather than type 2 diabetes.

CGM is a real-time glucose monitoring tool that can be used in conjunction with insulin injections, or an insulin pump. CGM devices measure interstitial glucose every few minutes via an electrode inserted in a separate location under the skin and can alert the user with an alarm when the glucose levels reach levels outside target ranges, or if it is predicted that the user will breach the target range in the next 30 minutes. These target ranges can be pre-set by the user. CGM can be used by persons on multiple daily insulin injections or insulin pump administration of insulin.

3.3.2 Insulin pump and CGM use at altitude

In Australia, insulin pumps were banned from inflight use due to concerns that changes in altitude could cause unintended insulin delivery. In 2012, a study reported the impact of pressure changes on insulin pumps placed in a hypobaric chamber under conditions that mimicked various flight situations.[7] A change in pressure from 760 to 560mmHg over 20 minutes (to mimic ascent) caused delivery of an excess of 0.7 units of insulin, and from 560 to 760mmHg (to mimic descent) delivered 0.5 units less insulin than expected. During simulation of catastrophic depressurisation, (760 to 260mmHg over 1 minute), plunger movement led to more than 8 units of unexpected insulin delivery. Gas bubbles appeared in the tubing but dissolved once pressure normalised. Experts advised cautious interpretation of these data given the small sample size (n=10) and recommended that firm conclusions should not be drawn from this study.[16] The CAA, FAA and Transport Canada accept insulin pumps but with the advice to disconnect during episodes of rapid decompression. There are no reports of insulin pumps causing an adverse inflight event, although the number of pilots in the UK, US and Canada who have used insulin pumps in flight is not reported.

The performance of CGM sensors has also been tested in hyper- and hypo-baric conditions. Medtronic Enlite sensors were tested in a healthy individual wearing multiple sensors, placed in a pressure chamber for 105 minutes.[17] Sensor readings were compared to plasma glucose readings. The investigators reported more accurate sensor readings during hyperbaric (mean absolute relative difference [MARD] 6.7%) then hypobaric conditions (mean MARD 14.4%). MARD values are a measure of accuracy. Under hypobaric conditions, 5/24 sensors failed but the authors concluded that this was related to prototype firmware that is not present in commercially available sensors. For the general public, a sensor glucose MARD value of <15% is accepted as the upper limit of accuracy for safe adjustment of insulin dosing. For aviation use US FAA protocols accept devices with MARD <10%. It is also difficult to draw conclusions from this study as it was a performed in a single individual, without diabetes, with euglycaemic glucose ranges. To our knowledge, there are no other published studies examining inflight CGM performance in a person with diabetes. However, we note that Dexcom CGM sensors are certified for use up to 13,800 feet, which is within the usual operating cabin pressure of commercial aircraft (<10,000 feet).

3.3.3 Overseas guidelines and use of CGM

Overseas guidelines vary in their acceptance of CGM as a monitoring tool (Table 6).

Table 6. A comparison of how international guidelines address CGM use.

	Australia	UK	US	Canada
Initial certification	Not discussed	Not discussed	Compulsory for commercial flight, optional for private/ recreational flight	Not discussed
Ongoing certification	Not discussed	Not discussed	Compulsory for commercial flight, optional for private/ recreational flight	Not discussed
In-flight monitoring	Preferred but not discussed in detail	Accepted but does not replace finger prick glucose measurement	Compulsory for commercial flight, optional for private/ recreational flight	Not discussed

In Australia, pilots must use two glucose recording devices in flight but a CGM system used with a back-up finger prick glucose meter would be an equivalent alternative. Use of CGM data for initial and ongoing certification is not addressed in CASA guidelines. This contrasts with the updated US FAA guidelines that require compulsory submission of CGM data for first- and second-class certification (commercial), recertification and inflight monitoring.[18] The FAA retained a non-CGM option for private licensing certification.[18] The 2019 FAA guidelines quote that CGM is *more* accurate than finger stick blood glucose testing. It is their preferred monitoring tool for multiple reasons: convenience (it is difficult to obtain finger stick glucose levels during turbulence), the capacity for alerts when glucose levels breach target range, the capacity to predict glucose trends, the ability to communicate with an insulin pump to provide insulin adjustment to prevent hyper-or hypoglycaemia, and the capacity to provide reports that accurately quantify glucose trends (% time below, within and above target range).

Only US Food and Drug Administration (FDA) approved devices are accepted, and must meet the following requirements:

- Report demonstrates daily trends (not only averages)
- Pilots must demonstrate consistent effective ongoing use
- Device can identify low (<3.9mmol/L) or high values (>13.9mmol/L) with alarms and reports include percentage time in range
- Accuracy rating with Mean Absolute Relative Difference (MARD) <10%

Under these guidelines, CGM can be used with either insulin injections or insulin pumps, but insulin pumps should be used in conjunction with its compatible CGM device and allow predictive low-glucose suspend (PLGS) functionality.

3.3.4 Diabetes technologies and hypoglycaemia risk

Current CASA guidelines only accept insulin injections for the inflight management and certification of insulin-treated diabetes. CGM is accepted as an appropriate inflight monitoring tool. Advanced diabetes technologies now offer safe alternatives for insulin delivery and glucose monitoring. We present data reviewing the hypoglycaemia risk with insulin pumps compared to multiple daily insulin injections (MDI), and insulin pumps with CGM-sensor augmentation, with threshold-based insulin-suspend functions, predictive low-glucose suspend functions and hybrid closed-loop capability (HCL).

There is sound evidence demonstrating that hypoglycaemia is not increased by use of diabetes technologies, and that the risk may be reduced. A systematic review of 25 trials determined that there was no significant difference in the likelihood of minor or severe hypoglycaemic events in individuals treated with an insulin pump vs MDI.[19] However, insulin pump use without CGM was associated with less overnight hypoglycaemia than MDI users. This suggests that there is no greater risk of hypoglycaemia with insulin pumps over that with insulin injections.

Real-time CGM can reduce hypoglycaemia risk when used with MDI or insulin pumps. A study of persons with type 1 diabetes and hypoglycaemia unawareness (and therefore higher rates of hypoglycaemia so that benefit could be assessed) who used CGM for 12 months demonstrated significant reductions in the number of low glucose events <3.0 mmol/L.[20] This cohort included people with type 1 diabetes managed with injections or with insulin pumps, the latter with and without insulin suspend features. Its small study size (35 subjects only) and retrospective study design limits the strength of this evidence, but it is one of the few studies done in persons with high rates of hypoglycaemia. A trial comparing sensor-augmented pump (SAP) therapy (without suspend function) with multiple daily injection therapy found that there was no significant difference in severe hypoglycaemia between groups at 12 months, with an event rate of 13 cases per 100 person years (equivalent to 0.13 cases per year).[21]

Insulin pumps can be programmed to interrupt insulin delivery when the CGM sensor glucose value meets a preset low value (threshold-suspend). In individuals with documented nocturnal hypoglycaemia, those randomised to sensor-augmented insulin pump therapy with suspend function had 31.8% less frequent hypoglycaemia than those without suspend function during the 3-month study period.[22] In this study there were no episodes of severe hypoglycaemia in the suspend function group, and 0.13 events/person week in the control group. This trial did not use pumps with predictive low glucose suspend feature (that is the insulin delivery suspends before low blood glucose target is reached), which is available in some current insulin pump models.

Pumps with predictive low glucose suspend features can interrupt insulin when the device's algorithm predicts hypoglycaemia will occur thus preventing a hypoglycaemic event. Algorithms used across different manufacturers have demonstrated reduced hypoglycaemia without increasing hyperglycaemia.[23]

The newest insulin pump technology provides a further degree of automation of insulin delivery. This capacity, termed 'hybrid closed-loop' capability, refers to the modulation of basal insulin (increase or decrease) according to sensor measured blood glucose levels. A recently published trial reported 70% time in range in the closed loop group, and 59% in the control group (sensor augmented pump) during daytime (6AM to midnight) and 76% vs 59% time in range overnight (midnight to 6AM).[24] Time in hypoglycaemia (<3.9mmol/L) reduced in both groups (-0.88% adjusted treatment difference closed loop minus control group). In this cohort, the time < 3.0mmol/L was low at baseline (<1%) and reduced by -0.1% with closed loop technology. Severe hypoglycaemia (need for external assistance because of altered consciousness) did not occur in either group in the 6-month trial period.

3.3.5 Conclusion – diabetes technologies and hypoglycaemia risk

Diabetes technologies are evolving rapidly and offer options for both quantification of hypoglycaemia frequency and opportunities to reduce hypoglycaemia risk. The presented data suggest that hypoglycaemia risk is not increased by insulin pump use and may be decreased by insulin pumps combined with CGM with predictive low glucose suspend functions. It should be noted that hypoglycaemia rates reported in these studies come from populations often with hypoglycaemia unawareness or high risk of hypoglycaemia and research populations are inherently different to the expected characteristics of pilots with diabetes. Hypoglycaemia risk in pilots may be lower due to the stringent certification criteria applied to ensure that only pilots with retained hypoglycaemic awareness and free of diabetes complications are certified to fly. Furthermore, pilots have more stringent monitoring protocols than would otherwise be expected in the usual person with diabetes.

We conclude that there is no evidence to support the exclusion of insulin pump therapy, including insulin pumps integrated with CGM to have predictive low glucose suspend or hybrid closed loop functionality. There is evidence to support benefit of continuous glucose monitors and efficacy at altitude to allow use in pilots with insulin-treated diabetes.

4 Proposed ADS Recommendations

In view of the above evidence, the ADS suggest the following recommendations for the medical certification of insulin-treated pilots. These recommendations are divided into:

1. Initial certification guidelines (including changes to class exclusion criteria)
2. Inflight glucose monitoring and management guidelines
3. Ongoing certification guidelines
4. Insulin pump and CGM use
5. Other recommendations

Where applicable, a comment regarding a change from current guidelines is marked by the * symbol.

Expected outcomes for pilots if the recommendations are adopted:

1. Enable pilots with insulin-treated diabetes to use insulin pumps to manage their diabetes inflight.
2. Enable pilots with insulin-treated diabetes to fly commercial aircraft in a multi-crew environment.
3. Enhance certification and operational requirement guidelines by providing clear recommendations on the role of CGM in both quantifying incapacitation risk, and as a risk-mitigating strategy in flight.
4. Include CGM as a required in-flight monitoring tool for class 1 certification, and as a recommendation for class 2 certification.

4.1 Initial certification guidelines

Certification restrictions for applicants with insulin-treated diabetes

Class	Existing Allowance	Proposed Certification Allowance
1 – commercial	Unfit	Case-by-case assessment by CASA Av Med, multi-crew operations only
2 – recreational	Safety pilot restriction for at least 15 flights then restriction lifted following review to allow solo flight	As per current protocol, and allow the option of solo-flight with insulin pumps or MDI combined with CGM
3 – air traffic	Unfit	Case-by-case assessment by CASA AvMed

- Definition of severe hypoglycaemia: a low glucose level resulting in loss of consciousness, seizure or requiring the assistance of another individual (*specific definition of severe hypoglycaemia is missing from current CASA guidelines. This definition also aligns with the definition of 'level 3' hypoglycaemia)
- Exclusion criteria
  - History of any severe hypoglycaemia in the last 12 months or 2 or more episodes in the last 5 years
  - Presence of complications: autonomic neuropathy, cardiovascular disease, retinopathy with impact on visual acuity, renal disease with eGFR <60/ml/min
- Requirements for initial certification:
  - HbA1c <8.0% (**removal of 6.5% lower limit of HbA1c*)
  - Absence of complications of diabetes

- For class 1 or class 2 certification without a safety pilot: CGM data demonstrating
  - time in range 3.9-13.9mmol/L ≥70% (*current protocol 5.0-15.0mmol/L, but 13.9mmol/L is standard reporting. Inflight target glucose is kept at 5.0-15.0mmol/L)
  - time <3.9mmol/L that is <4.0%
  - time <3.0mmol/L that is <1.0% for class 1 certification

- Information to be provided
  - A report from the treating Endocrinologist detailing:
    - Current diabetes treatment including specific reference to insulin dosages, and use of insulin pump technology (if applicable), and confirmed ability to determine and administer insulin doses/boluses
    - Hospitalisations in the last 12 months and any relationship to diabetes.
    - Episodes of symptomatic or asymptomatic hypoglycaemia in the preceding 12 months and any alterations to treatment required
    - Assessment of glucose monitoring diary/meter download (where applicable) and confirmed ability to self-monitor accurately
    - Assessment of CGM data for the 3-month period prior to review including summary of mean glucose, time in range (3.9-13.9mmol/L) and time in hypoglycaemia (<3.9 and <3.0mmol/L)
    - Confirming the individual's carbohydrate counting capacity
    - Four HbA1c results over the last 12 months, and not less than 10 weeks apart
    - Pathology results including renal function with eGFR, total cholesterol, triglyceride, LDL and HDL fractions, urine albumin/creatinine ratio
    - Presence or absence of end-organ damage
    - Follow up recommendations
  - A report from an optometrist or ophthalmologist (preferably credentialled optometrist or CASA designated ophthalmologist) detailing
    - the presence or absence of clinically significant eye disease
    - visual acuity (with and without correction)
    - eye pressures (and treatment if required)
  - A report from the DAME assessing cardiac risk according to existing CASA guidelines
  - Report from a flight instructor confirming that management of diabetes does not interfere with the safe operation of the aircraft

4.2 Inflight glucose monitoring and insulin management guidelines

Specific guidelines regarding the management of blood glucose are required for blood glucose levels which impact decision making processes. The impact of high blood glucose levels on cognitive functioning is variable between individuals, but at low levels a blood glucose level <3.0mmol/L is accepted to be associated with altered function.[9] The guidelines therefore are specific to limit the risk of low blood glucose events. CGM is required for class 1 certification and recommended for class 2 certification.

- Carry
  - Two recording devices including one CGM system (including a spare sensor) and a standard glucose meter.

- Use CGM alarms where available: predictive and threshold glucose alarms, and low glucose predictive suspend functions
- Insulin quantity appropriate to the planned duration of flight(s)
- Adequate supply of rapidly absorbable glucose appropriate to the planned duration of flight(s)

- Pre-flight
  - A pilot with a blood glucose <3.9mmol/L must not commence flight operations for 45 minutes from time of correction of blood glucose to >5.0mmol/L.
  - CGM to be operational from 2-hours prior to flight or 1-hour before duty (whichever is the earlier), and calibrated as per manufacturer recommendations
  - All multi-crew pilots to brief their co-pilot prior to the flight, including:
    - nature of their diabetes
    - testing regimen, timing and method of blood glucose testing
    - actions to ensure blood glucose levels remain within an acceptable range
    - medications/treatment that may be required during the flight
    - possible symptoms of high or low blood glucose levels
    - actions to be taken in the event of incapacitation

- In-flight
  (to be defined as the time from when the aircraft first moves under its own power for the purposes of flight until the time at which it comes to rest on completion of the flight)
  - For all flight operations a take-off must not commence with a BGL <5.0mmol/L.
  - Target glucose range: 5.0-15.0mmol/L
  - For multi-crew operations: co-pilots should be informed of blood glucose test results
  - If using an insulin pump: disconnect prior to take-off and reconnect at top of climb
  - Low BGL management in flight:
    - If BGL <5.0mmol/L: confirm with finger-prick glucose meter and take corrective treatment to restore glucose >5.0mmol/L
    - If BGL <3.9mmol/L:
      - confirm with finger-prick glucose meter and take corrective treatment
      - if multi crew: handover duties to second pilot, then can resume duties when BGL ≥5.0mmol/L for at least 45 minutes
      - if single pilot class 2 operation: maintain the aircraft in the lowest workload environment possible and do not commence final approach to land until BGL ≥5.0mmol/L
  - High BGL management:
    - **If BGL >15.0mmol/L:** confirm with finger-prick glucose meter and take corrective treatment
    - **If BGL >20.0mmol/L:**
      - if multi crew: handover duties to second pilot
      - cross check with finger-prick glucose meter and take corrective treatment
      - if using an insulin pump: check for correct functioning
      - if multi crew: resume duties when BGL ≤20.0mmol/L

- Trouble shooting:
  - CGM failure:
    - a new sensor/transmitter must be inserted as soon as operationally practical
    - if CGM data are unavailable (eg: during CGM warm-up period), finger prick glucose should be monitored at least every 30 minutes
  - Rapid decompression event with insulin pump use:
    - disconnect insulin pump as soon as practicable once decompression is identified
    - a precautionary carbohydrate snack should be taken once the emergency has stabilised

- Any crew intervention required to assist a pilot in recognising or treating blood glucose must be reported to CASA and the pilot will declare themselves unfit for flight duties until appropriate specialist and CASA medical review.

4.3 Ongoing certification guidelines

- Immediately cease flying until cleared by CASA if:
  - Severe hypoglycaemia
  - Any involvement in accidents resulting in serious injury (whether or not related to hypoglycaemia)
  - Change in treatment regimen eg change from multiple daily injections to insulin pump therapy or vice versa (recertification will require 3 months meeting the requirements outlined in section 4.4 Protocols with CGM)
  - New diabetes complications
- 3-monthly reports from treating Endocrinologist including details required as per initial certification.
  - Including 3 monthly HbA1c tests
  - Assessment of CGM data for the 3 month period prior to review including summary of mean glucose, time in range (3.9-13.9mmol/L) and time in hypoglycaemia (<3.9 and <3.0mmol/L), using standardised CGM reporting data from the previous 90 days
  - Timing of report: if there is a change in treatment regimen or the Endocrinologist's review indicates deterioration of glycaemic control, the report should be submitted immediately. Otherwise quarterly evaluations can be accumulated and submitted annually.
  - Confirmation of absence of severe hypoglycaemia at any time and of hypoglycaemia unawareness (defined as failure to detect blood glucose <3.0mmol/L while awake)
- Blood glucose monitoring requirements:
  - Submit in-flight protocol records (any CGM, finger prick glucose measurements, insulin doses, carbohydrate intake, take-off and landing times)
  - 12-month glucose log books demonstrating off-duty glucose levels
  - See CGM section 4.4
- An annual report from optometrist or ophthalmologist as per initial certification requirements.
- A report from the assessing DAME regarding cardiac risk as per initial certification requirements

4.4 Insulin pump or MDI to be used in combination with CGM

- Mandatory CGM use for commercial, and recommended CGM use for single pilot recreational flights

- Insulin pump device must be
  - FDA approved
  - Compatible with a CGM device
  - If used for commercial or solo recreational flight, insulin pumps must have predictive low-glucose suspend functions
- CGM must have the following features:
  - FDA and TGA approved
  - Alerts – for notification of high or low glucose readings
  - Predictive arrow trends – to provide warning about potentially dangerous glucose trends
  - MARD <10%
  - Automatic sampling every 5-15 minutes
- Protocols with CGM:
  - Demonstrate effective and consistent use (>95% in flight, and >70% general use)
  - Report time in ranges:
    - % time <3.0mmol/L (<1%)
    - % time <3.9mmol/L (<4%)
    - % time 3.9 –13.9mmol/L (goal >70%)
    - % time >13.9mmol/L
  - Report mean glucose and standard deviation (SD) glucose for 3 months prior to specialist review. CV glucose is to ideally be <36% of mean glucose in non-work environment to ensure stability of blood glucose
  - Note: CGM reports across different manufacturers allow for different degree of customisation of reporting ranges. The 3.9-10.0mmol/L range is the international standard target range.

4.5 Other recommendations

- As per the 2016 Diabetes Australia 'A new language for diabetes' position statement, the term 'diabetic' should be avoided, and replaced with person with diabetes, or person living with diabetes.
- Avoiding ill-defined language such as 'loss of control' of diabetes
- Define severe hypoglycaemia as per section 4.1
- Other industries outside of aviation: the guidelines provided here are specific to CASA but could be adapted and applied to other industries. Other professions may not require the same frequency of monitoring during work related activities, however the same guidelines should apply to general reporting of blood glucose levels in work and non-work environments. CGM can be a useful tool for quantifying risk in these industries, and the % time in range and time <3.9mmol/L and time <3.0mmol/L should be adapted according to acceptable level of risk of hypoglycaemia in the persons work environment. For example, higher readings than 15.0mmol/L may be acceptable for some industries but hypoglycaemia risk is likely to be similar for all high-risk industries
- SGLT2 inhibitors should be added to the list of approved medications for aviators with type 2 diabetes. SGLT2 inhibitors are not discussed in current CASA guidelines but are a commonly prescribed type 2 diabetes medication and do not increase the risk of hypoglycaemia.

5 Concluding Statements

- Diabetes has implications for employment, especially in safety-sensitive industries. Modern treatment and technological advances have changed since CASA last updated its protocols pertaining to pilots with insulin-treated diabetes.
- Overseas, protocol revisions in view of medical advancements have led to certification of individuals with T1D under specific conditions which are now definable using CGM. There is now inflight evidence to support the UK protocol and use of CGM.
- It is important to note that operating target glucose ranges are higher than recommended for optimal long-term health. The main purpose is to reduce risk of hypoglycaemia. Consistently maintaining elevated glucose levels may lead to HbA1c levels above the threshold for certification. The ADS supports different target glucose levels in-flight vs on-ground, to balance the competing demands of minimized hypoglycaemia risk and avoidance of chronic complications of diabetes
- The proposed protocol is to assist in the identification of low risk people with insulin-treated diabetes and who would be suitable for being issued with aviation licenses. Documentation is to remain rigorous, but we provide detailed guidance regarding the use of insulin pumps and CGM criteria for assessment.
- Pilots with diabetes will continue to be afforded individual assessments so that those who are fit to fly are able to do so. With rigorous monitoring protocols, it is expected that the likelihood of hypoglycaemia inflight will be very low, and within the accepted <1% risk thus consistent with capacity for commercial flight licensing.
- Future guidelines may need revision with the inevitable further evolution of diabetes technologies
- Other occupations may not require the <1% incapacitation risk relevant to the aviation environment. Appropriate adaptation of CGM criteria should be made for such occupations

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