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DIABETES MELLITUS [EASA.2022.C20]

D7.4 Final report

An Agency of the European Union

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ABBREVIATIONS

ACRONYM	DESCRIPTION
ADA	American Diabetes Association
AID	Automated Insulin Delivery
A/HCL	automated or hybrid closed-loop systems
APS	Artificial Pancreas System
ARA.MED.330	Diabetes Protocol
ATC	Air Traffic Control
ATCO	Air Traffic Controller
CAA	Civil Aviation Authority (UK)
CAN	Cardiovascular Autonomic Neuropathy
CGM	Continuous Glucose Monitoring
CSII	Continuous Subcutaneous Insulin Infusion
CV	Cardiovascular
CVD	Cardiovascular Disease
DKA	Diabetic Ketoacidosis
DM	Diabetes Mellitus
DPP4	Dipeptidyl Peptidase-4
DSPN	Distal Symmetrical Polyneuropathy
EASA	European Union Aviation Safety Agency
EASD	European Association for the Study of Diabetes
EGP	Endogenous Glucose Production
EU	European Union
FAA	Federal Aviation Administration (USA)
FAQ	Frequently asked questions
FPG	Fasting Plasma Glucose
GLP1	Glucagon-Like Peptide-1
HCL	Hybrid Closed Loop
IAA	Irish Aviation Authority
ICAO	International Civil Aviation Organisation
IU	International Unit
MARD	Mean Absolute Relative Difference
MDI	Multiple Daily Injections
MUG	Medical University of Graz
OGTT	Oral Glucose Tolerance Test
OOR	Out of Range
RR	Relative Risk

SGLT	Sodium-Glucose Cotransporter
SMBG	Self-Monitoring of Blood Glucose
SU	Sulfonylurea
TAR	Time Above Range
TBR	Time Below Range
TIR	Time In Range
TITR	Time In Tight Range
UACR	Urinary Albumin-to-Creatinine Ratio

1. Introduction

1.1 Diabetes in aviation and the “Pilot and ATCO Aeromedical Fitness-Diabetes Mellitus” project

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by disturbances in glucose homeostasis, requiring the achievement of adequate diabetes control without causing relevant hyperglycaemia and hypoglycaemia. Of these, hypoglycaemia, the most critical adverse effect of insulin and other antihyperglycaemic therapies, can result in acute cognitive dysfunction and incapacitation. This poses a significant challenge in safety-critical occupations such as piloting and air traffic control (ATC), where sustained cognitive function and precision are paramount. For decades, international aviation standards, including those from the International Civil Aviation Organization (ICAO) and EASA, have generally deemed individuals with insulin-treated diabetes as medically unfit.
However, advancements in diabetes technology and treatment have dramatically improved glycaemic control and reduced the risks of severe hypo- and hyperglycaemia. Technologies like continuous glucose monitoring (CGM) systems, modern insulin pumps, and (advanced) hybrid closed-loop ((A)HCL) systems offer more precise, real-time management of insulin doses achieving near-normal glucose levels. Similarly recent developments on insulins as ultra-rapid insulins and stable once daily or even once weekly insulins show promising results. For people with type 2 diabetes, new oral and injectable antihyperglycaemic medication without risk of hypoglycaemia but providing cardiovascular benefits have been on the market and been prescribed for several years. These developments warrant a re-evaluation of existing aeromedical regulations and practices.

The "Pilot and ATCO Aeromedical Fitness – Diabetes Mellitus" project, funded by the EU's Horizon Europe Programme, was initiated by EASA to address these evolving medical capabilities by reviewing current regulations and the state of knowledge on diabetes mellitus, and by developing recommendations on aviation safety in the context of modern diabetes therapies and technology. This work, based on literature reviews, hypobaric chamber flight simulations, and real-time studies including two mid-haul flights in Europe, is intended to support EASA in determining whether modifications to the current medical assessment rules for applicants with diabetes could be considered.

1.2 Diabetes – Fundamentals and Treatment Options

HbA1c:
HbA1c reflects the mean blood glucose over the preceding ~8–12 weeks, representing glycation of hemoglobin. A commonly accepted therapeutic goal is < 7% for most adults with diabetes, though individualized goals (e.g., < 6.5% or < 8%) may apply depending on age, comorbidities, and hypoglycaemia risk (ADA Standards of Care, 2024).

Time in Range (TIR):
TIR describes the percentage of time that a person’s glucose levels remain within the defined target range (typically 70–180 mg/dL). Higher TIR correlates with improved glycaemic control and reduced risk of both microvascular and macrovascular complications.

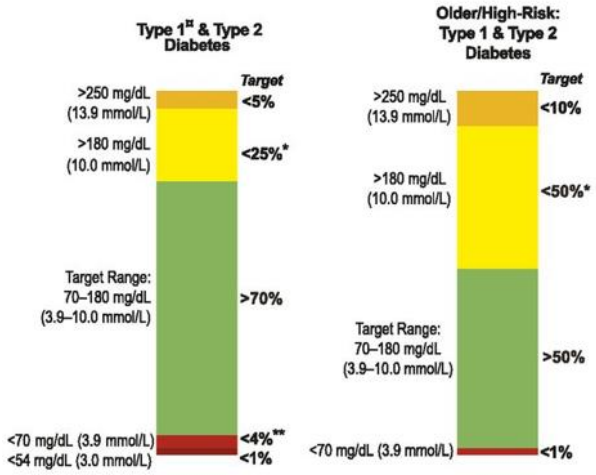

Fig. 1: CGM-based targets for different diabetes populations
From: Clinical targets for continuous glucose monitoring: recommendations from the international consensus on time in range. Diabetes Care. 2019;42(8):1593-1603. doi:10.2337/dci19-0028

Glucose-lowering therapies:

- Metformin – suppresses hepatic gluconeogenesis; modest HbA1c reduction (+).
- SGLT2 inhibitors (e.g., empagliflozin, dapagliflozin) – enhance renal glucose excretion; HbA1c reduction (+).
- GLP-1 receptor agonists (e.g., demaglutide, liraglutide) – stimulate glucose-dependent insulin secretion, inhibit glucagon, and slow gastric emptying; HbA1c reduction (+/++)
- DPP-4 inhibitors (e.g., sitagliptin, linagliptin) – prolong endogenous incretin action; modest HbA1c reduction (/+).
- Sulfonylureas (e.g., glimepiride, glipizide, gliclazide) – stimulate insulin secretion independent of glucose; HbA1c reduction (+) but increased hypoglycaemia risk. (Not recommended in aviation)
- Thiazolidinediones (TZDs; e.g., pioglitazone, rosiglitazone) – enhance insulin sensitivity via PPARγ activation; HbA1c reduction (+) but associated with weight gain and fluid retention. (Not recommended in aviation)

Insulin therapy:

- Ultra-rapid acting analogues: Faster Aspart (Fiasp), Ultra-rapid Lispro (Lyumjev).
- Rapid-acting analogues: Lispro, Aspart, Glulisine.
- Short-acting: Regular insulin (not recommended in aviation)
- Intermediate-acting: NPH (not recommended in aviation)
- Long-acting basal insulins:
  - First generation: Glargine U100, Detemir (not recommended in aviation)
  - Second generation: Glargine U300, Degludec.
- Premixed insulins: Combinations of short-/rapid-acting with intermediate-acting insulin (e.g., 70/30 NPH/Regular, biphasic Aspart, Lispro mix). (not recommended in aviation)

Treatment goals in diabetes care

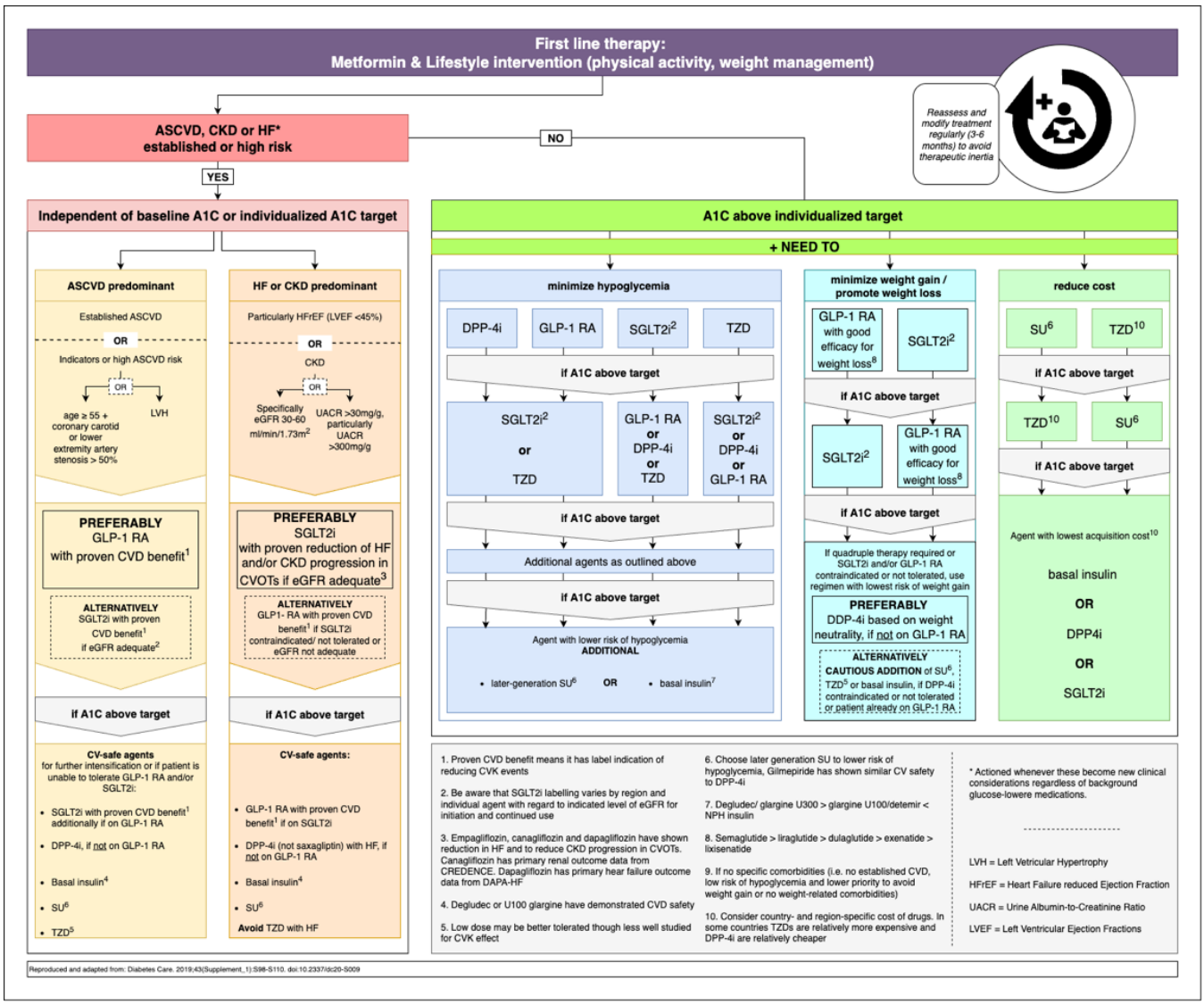

Fig. 2: Treatment goals in diabetes care.

ASCVD = atherosclerotic cardiovascular disease; CKD = chronic kidney disease; CVD = cardiovascular disease; CVOTs = cardiovascular outcomes trials; eGFR = estimated glomerular filtration rate; HF = heart failure;

Adapted from ADA Standards of Medical Care in Diabetes 2020; Diabetes Care. 2019;43(Supplement_1):S98-S110. doi:10.2337/dc20-S009

Use of glucose-lowering medications in the management of type 2 diabetes (1)

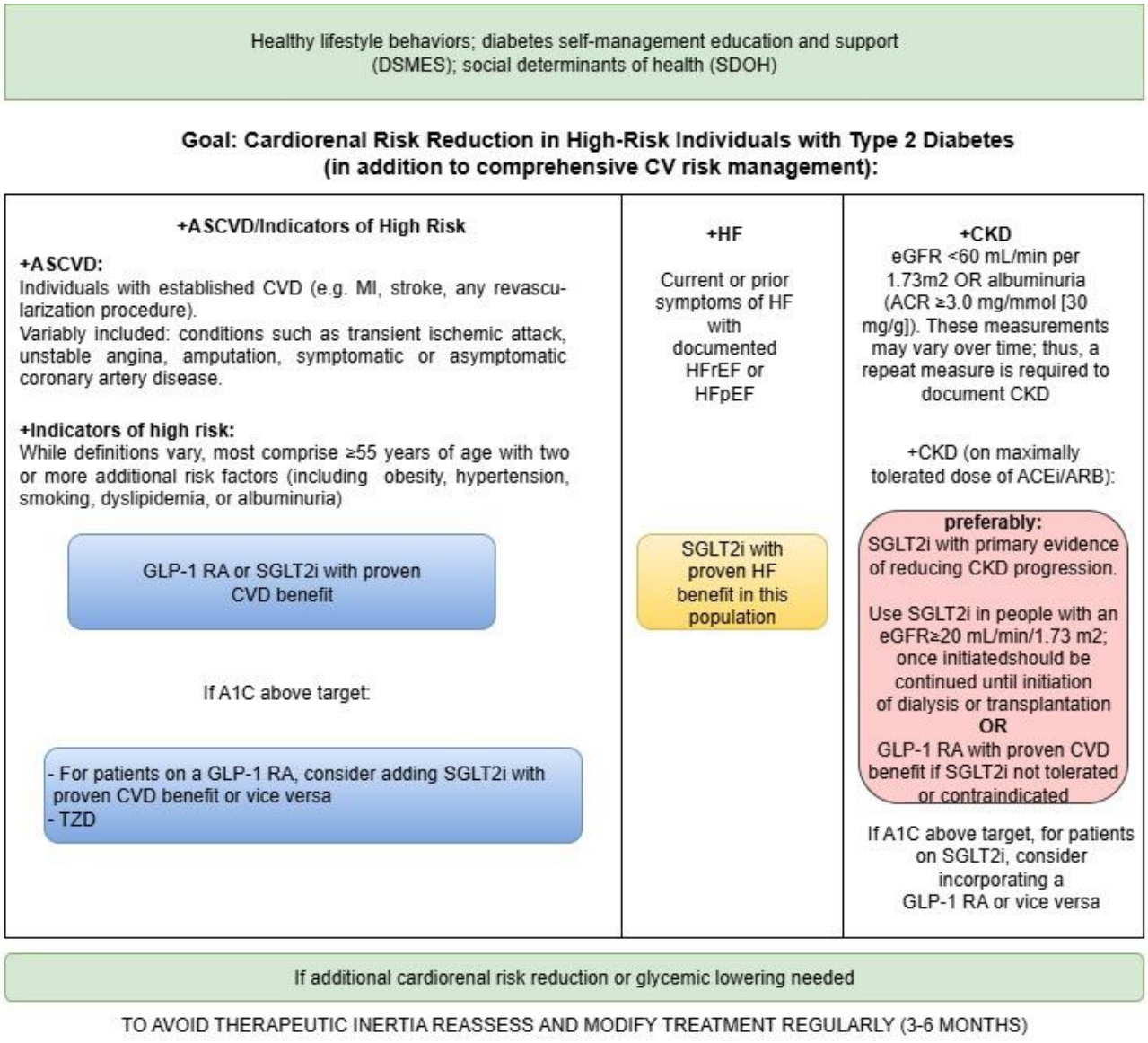

Fig.3: Use of glucose-lowering medications in the management of type 2 diabetes (1)

ASCVD = atherosclerotic cardiovascular disease; CKD = chronic kidney disease; CVD = cardiovascular disease; CVOTs = cardiovascular outcomes trials; eGFR = estimated glomerular filtration rate; HF = heart failure; CKD = chronic kidney disease.

Adapted from Davies et al. (84). Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2024. American Diabetes Association, Professional Practice Committee. Diabetes Care 2024;47(Suppl. 1):S158–S178 | https://doi.org/10.2337/dc24-S009

Use of glucose-lowering medications in the management of type 2 diabetes (2)

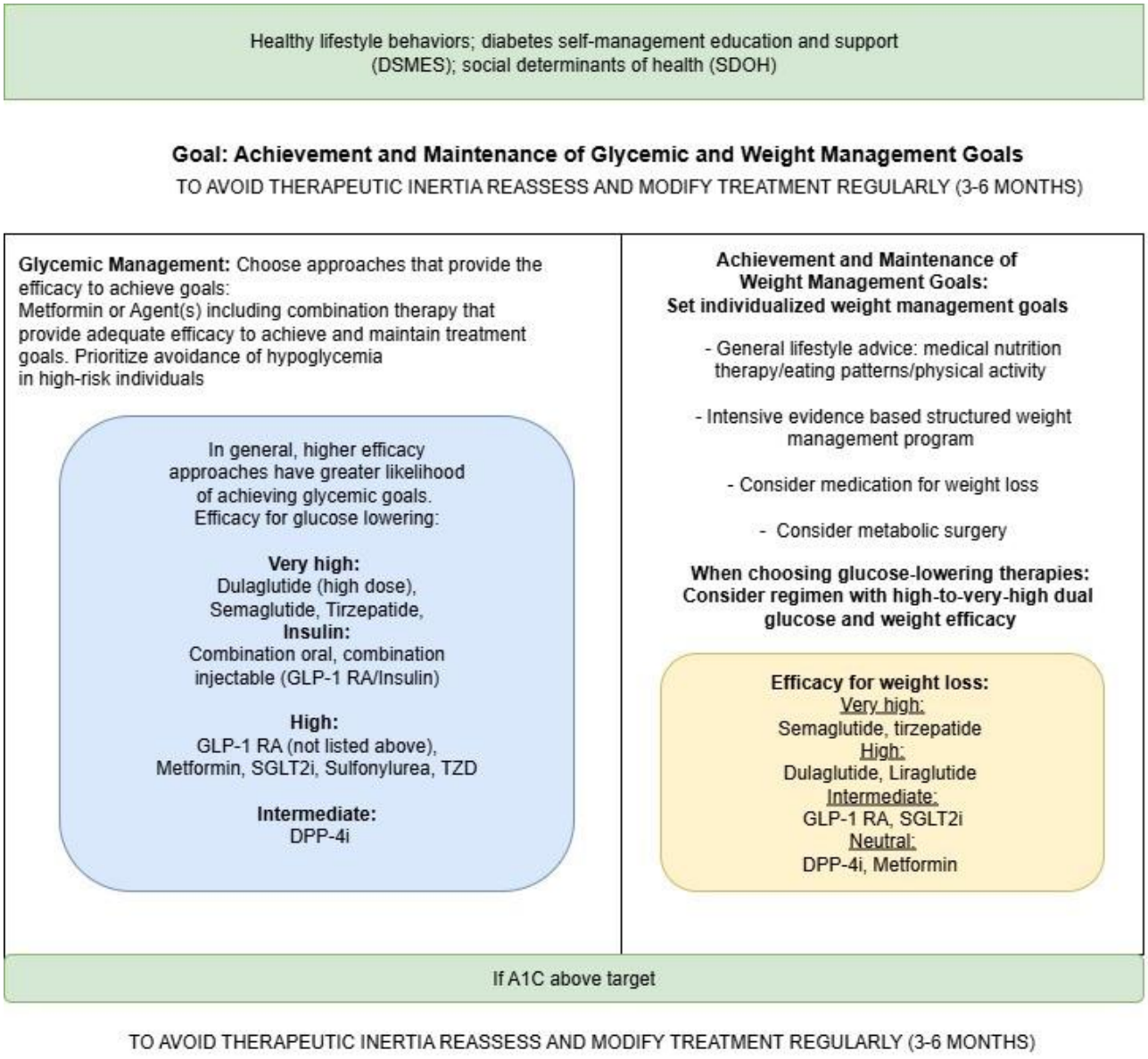

Fig. 4: Use of glucose-lowering medications in the management of type 2 diabetes (2)
ASCVD = atherosclerotic cardiovascular disease; CKD = chronic kidney disease; CVD = cardiovascular disease; CVOTs = cardiovascular outcomes trials; eGFR = estimated glomerular filtration rate; HF = heart failure; CKD = chronic kidney disease.
Adapted from Davies et al. (84). Pharmacologic Approaches to Glycemic Treatment: Standards of Care in Diabetes—2024. American Diabetes Association, Professional Practice Committee. Diabetes Care 2024;47(Suppl. 1):S158–S178 | https://doi.org/10.2337/dc24-S009

Effectiveness of glucose lowering drugs

Medication	Glucose lowering effect	Hypo risk	Weight effect	CVD/HF	CKD	MASH
Metformin	+	No	Neutral	+/Neutral	Neutral	Neutral
SU	+	Yes	Neutral	Neutral	Neutral	Unknown
TZD	+	No	Gain	+/-	Neutral	Potential benefit
DPP4-i	Intermediate	No	Neutral	Neutral (cave: saxagl.)	Neutral	Unknown
GLP-1-RA	+/++	No	Loss	+/Neutral	Neutral (Sema: +)	Potential benefit
SGLT2-i	+	No	Intermediate loss	+/+	+	Unknown
Insulin	+/++	Yes	Gain	Neutral	Neutral	Unknown

Adapted from Diabetes Care 2025;48(Supplement_1):S128–S145 https://doi.org/10.2337/dc25-S006.

Table 1: Effectiveness of glucose lowering drugs
Adapted from Diabetes Care 2025; 48 (Supplement_1): S128-S145 https://doi.org/10.2337/dc25-S006.

2. Summary of literature reviews

2.1 Literature Review D1.1: Review of Diagnostic Measures

This literature review provides a comprehensive overview of the classification, diagnosis, and screening of diabetes mellitus and its complications, primarily based on guidelines from the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD).

Classification and Diagnosis: Diabetes is categorized into four main types: type 1 diabetes, type 2 diabetes, specific types and gestational diabetes. Diagnosis can be established using fasting plasma glucose (FPG), an oral glucose tolerance test (OGTT), or the HbA1c value. For pilots and Air Traffic Control Officers (ATCOs), HbA1c is considered the most practical screening test because it does not require fasting and is less affected by daily variations in glucose levels caused by stress or illness.

Screening: The review recommends screening for prediabetes and type 2 diabetes in asymptomatic adults who have risk factors (e.g., overweight, family history) or are over the age of 35.

Screening for complications:

Diabetic neuropathy: annual screening for peripheral (DSPN) is recommended, starting at diagnosis of type 2 diabetes and five years after diagnosis of type 1 diabetes. This includes clinical tests for small- and large-fiber function (e.g., pinprick, temperature, vibration, 10-g monofilament).

Diabetic retinopathy: an initial dilated eye exam is recommended at the time of diagnosis (type 2 diabetes) or within five years (type 1 diabetes), followed by exams every 2 years depending on glycaemic control and initial findings.

Diabetic Nephropathy: annual assessment of the urinary albumin-to-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR) is advised.

Cardiovascular Disease: See EASA CVD group.

Relevance for pilots and ATCOs: the review emphasizes that aeromedical fitness is determined less by the diabetes diagnosis itself and more by the quality of glycaemic control, the type of therapy, and the presence of complications. Any complications should be assessed according to standard EU regulations (e.g., MED.B.010 for cardiovascular issues) just as they would be for individuals without diabetes.

2.2 Literature Review D1.2: Review of Treatment Options

This literature review focuses on diabetes management and treatment strategies, based on consensus reports by the EASD and ADA.

Management of type 1 diabetes (T1D):

Goals: the primary aims are to prevent acute events like hypoglycaemia and to prevent long-term vascular complications.

Insulin therapy: as insulin is essential for survival of T1D, modern therapies include multiple daily injections (MDI) of insulin or continuous subcutaneous insulin infusion (CSII) via an insulin pump. (A)HCL systems, which combine an insulin pump with a control algorithm and a CGM sensor to automate insulin delivery, are the preferred therapeutic option as they have been shown to dramatically reduce the risk of hypoglycaemia. As of yet, under EU regulations, pilots on insulin therapy are deemed unfit to fly.

Core Principles: The review emphasizes that comprehensive education of people with diabetes, self-monitoring (ideally with CGM and the “time in range” metric), diet, and physical activity are fundamental pillars of successful T1D management.

Management of type 2 diabetes (T2D):
Foundation of treatment: lifestyle changes, including diet, weight reduction, and physical activity, form the cornerstone of all T2D management.
Pharmacotherapy: a critical distinction is made based on hypoglycaemia risk, which is paramount for the safety of pilots,ATCOs and passengers:
Medications without significant hypoglycaemia risk (highly recommended): this group includes metformin, GLP-1 receptor agonists (GLP-1 RAs), SGLT-2 inhibitors, and DPP-4 inhibitors. These are considered safe for use in aviation. GLP-1 RAs and SGLT-2 inhibitors provide over their glucose lowering effect additional proven cardiovascular and renal protective benefits.
Medications with hypoglycaemia risk: insulin and sulphonylureas are the primary agents that can induce hypoglycaemia. Their use in pilots and ATCOs should be avoided or managed only with glucose monitoring, preferably with CGM.

Implications in treating pilots and ATCOs with diabetes - take home message

The unique environment that pilots and ATCOs work in provides greater challenges for the management and treatment of diabetes. In addition, safety concerns in general must be taken into consideration. The risk of hypoglycaemia and incapacitation is the most widely quoted reason for a blanket ban policy preventing safety-critical operations being performed by people with diabetes managed with insulin or oral antihyperglycaemic agents that can cause hypoglycaemia. Advances such as new oral antihyperglycaemic medications and modern insulin analogues with a low risk of hypoglycaemia, as well as the use of modern technologies such as CGM and automated or hybrid closed-loop (A/HCL) systems, have significantly improved glycaemic control in people with insulin-treated diabetes.
There has been a reduced frequency of severe hypoglycaemia events and a delay in diabetes-related comorbidities and complications. It is thus possible to re-appraise the relative risks and extend the boundaries of what is state of the art, practical, and safe.

2.3 Literature Reviews from D2.1: Analysis of the Suitability of Diagnostic Tests

This is a summary of three literature reviews:

Workstream 2.1: review of diagnostic methods for long-term diabetes control
This review outlines the goals of glycaemic monitoring: the long-term prevention of microvascular complications and the short-term goal of achieving adequate glycaemic control while avoiding hypoglycaemia.
It identifies two main components of monitoring: HbA1c to assess average glycaemic control over the preceding ~90 days, and regular glucose measurements (either preferentially CGM or alternatively SMBG) for daily medication adjustments.

The review highlights that CGM would greatly improve the practicability of pre- and in-flight glycaemic control for pilots, providing valuable trend information, early warnings and an effective method to share results with medical examiners.

Workstream 2.2b: Review of Aero-medical Certification Strategies Worldwide

This section reviews existing aeromedical protocols for pilots with diabetes, tracing the development of the UK Civil Aviation Authority (CAA) protocol and its evolution into the EASA ARA.MED.330 protocol, operated jointly by the UK, Ireland, and Austria.
It details the core features of the ARA.MED.330 protocol, such as mandatory pre-flight and hourly in-flight glucose testing using SMBG and a "traffic-light system" to interpret results, where the acceptable "green" range is 5.0-15.0 mmol/L (90–270 mg/dL).
The protocols of other key nations are summarized, including Canada (testing every 30 minutes in-flight), the USA (strong reliance on CGM data and specific time in range targets), and Australia (specific HbA1c goals).
A key finding from the review of published data on the ARA.MED.330 protocol is its high level of safety. Over 22,000 flying hours, pilots maintained stable HbA1c levels, and over 97% of in-flight glucose measurements were in the acceptable "green" range, with no reported incapacitations. The rate of out-of-range readings also decreased over time, a trend possibly linked the increasing adoption of CGM technology.

Workstream 2.5: review of diabetes complications

This review details the methods for assessing macro- and microvascular complications based on ADA standards.
Macrovascular complications: routine screening for coronary artery disease in asymptomatic individuals is not considered cost-effective. Screening for peripheral artery disease should involve assessing lower-extremity pulses and potentially an ankle-brachial index.
Microvascular complications:

- Diabetic retinopathy: the review describes screening timelines (initial and follow-up eye exams) and the classification of disease stages.
- Diabetic kidney disease: it explains the need for annual screening using the urinary albumin-to-creatinine ratio (UACR) and the estimated glomerular filtration rate (eGFR).
- Diabetic neuropathy: it details the annual assessment for peripheral neuropathy using simple clinical tests (e.g., 10-g monofilament, tuning fork) and reviewing specific symptoms.

Consequences for pilots and ATCOs:
Macrovascular complications: aeromedical examiners and medical assessors should manage cardiovascular problems, following MED.B.010 and ATCO.MED.B.010 rules, as they do with the other flight professionals by considering that diabetes makes them more severe and paying special attention to coronary artery disease and arrhythmias. For cardiovascular problems also see the results of the EASA CVD group.
Diabetic retinopathy: aeromedical examiners and medical assessors should manage eye defects, as expected in people without diabetes following MED.B.070 and ATCO.MED.B.070 rules, paying special attention to visual acuity and diplopia.
Diabetic kidney disease: aeromedical examiners and medical assessors should manage renal problems as expected in people without diabetes, following MED.B035 and ATCO.MED.B.035 rules by considering that diabetes makes them worsen more rapidly except for treatment regimens including kidney-protective drugs (like gliflozins or GLP1-receptor agonists).
Diabetic neuropathy: Aeromedical examiners and medical assessors should manage following MED.B.065 and ATCO.MED.B.065 rules paying special attention to recurring episodes of cerebral dysfunction due to hypoglycaemia unawareness, dysesthesia, vascular dysregulation symptoms, and recurrent tachyarrhythmic episodes.

3. Summary of studies

3.1 Summary: Metabolic Study on the Impact of Aviation on Glucose Metabolism

Details see D 3.1.

Objective: this study aimed to investigate the effects of flight-associated atmospheric pressure changes on glucose kinetics in pilots with type 1 diabetes (T1D). The study used a dual-stable isotope technique during hypobaric flight simulations to evaluate fasting and postprandial glucose metabolism.

Methodology: the research was designed as a randomized crossover study comparing two conditions: a simulated flight in a hypobaric chamber (550 mmHg, equivalent to ~2,500 m or 8,200 ft) and a control test at ground level (750 mmHg). Six male, insulin pilots with T1D treated with AID systems participated.

Results: *Increased glucose disposal*: The peripheral glucose disposal rate (Rd) was significantly higher under hypobaric flight conditions compared to ground-level conditions, particularly 120-180 minutes after the meal. *Insulin concentration:* Insulin concentrations were slightly but significantly higher in the late postprandial phase (120-180 minutes) during the flight simulation. *No Change in endogenous glucose production (EGP)EGP and Ra:* There were no significant differences in EGP or in the rate of glucose appearance from the meal (Ra) between the two conditions. *No Stress Response*: Concentrations of stress hormones (catecholamines, cortisol) and glucagon did not differ between the two settings.
The study demonstrates that during simulated flight, pilots with T1D experience an increase in peripheral glucose uptake. This effect was not fully explained by the slightly higher insulin concentrations or a hormonal stress response, as EGP was unaffected.

3.2 CGM vs. SMBG on a simulated flight (with Plasma Glucose as reference standard).

Details see D 2.1.

Objective: To assess the use and accuracy of CGM systems compared to plasma glucose and SMBG during simulated flights, specifically evaluating their safety and reliability under atmospheric pressure changes.

Methodology: six male pilots, with a median age of 40 years (range 20-61), participated in a simulated flight environment. They were equipped with three different CGM systems: Dexcom G7, Guardian 4 (both real-time CGMs), and Libre Freestyle Flash (an intermittently scanned CGM). SMBG measurements were taken using Abbott Freestyle Precision Pro and Libre Flash Capillary, while plasma glucose served as the reference. Measurements were recorded at various time points before and after a meal, under both ground-level and simulated altitude conditions. Pearson correlation coefficients and mean absolute relative difference (MARD) were calculated to assess accuracy. The study was conducted as part of the SUNDIF metabolic study, including Protocol A (insulin-pump treatment) and Protocol B (closed-loop systems).

Results: the study found a strong correlation between both SMBG and the different CGM systems against plasma glucose levels. The correlation strengths remained similar between ground and simulated flight conditions. Specifically, SMBG showed a Pearson correlation of 0.96 (ground) and 0.94 (simulated flight), while Libre Flash (interstitial fluid) showed 0.95 (ground) and 0.88 (simulated flight). The overall MARD for aggregated data from CGM, SMBG, and plasma glucose measurements ranged between 12-17%. CGM measurements closely correlated with SMBG, indicating that CGM is a viable alternative to SMBG at high altitudes. A small postprandial lag was observed between CGM and SMBG. Overall glucose values were similar across fasting and postprandial periods, and this was consistent across all five devices tested.

3.3 Observational Study of ARA.MED.330 Protocol (UK, Ireland, Austria) Outcomes (2012-2015).

Details see D 2.1.

Objective: To evaluate the safety and feasibility of the EASA ARA.MED.330 protocol for insulin-treated commercial pilots, specifically focusing on blood glucose measurements and their consequences.

Methodology: This was a review of medical records for 26 Class 1 pilots with insulin-treated diabetes certified by the UK Civil Aviation Authority between 2012 and 2015. Data collected included demographic information, diabetes history, management details, HbA1c values, and pre- and in-flight blood glucose monitoring results. Pilots used SMBG and followed a traffic light system for glucose interpretation.

Results: The study reported no safety issues, and the protocol was found to be both feasible and practical. HbA1c levels remained unchanged pre- and post-certification, indicating that overall diabetes control did not deteriorate. From 8,897 pre- and in-flight blood glucose values recorded over 4,900 flying hours, only 186 readings were out of range (181 in the "amber" caution range and 5 in the "red" immediate action range). Appropriate corrective actions were taken for all out-of-range values, and no adverse safety events were reported.

3.4 Follow-on Study of ARA.MED.330 Protocol (UK, Ireland, Austria) Outcomes (2012-2019).

Details see D 2.1.

Objective: to systematically collect and evaluate blood glucose measurements and their trends, time course within flight, and consequences.

Methodology: an observational study involving 49 pilots (84% T1D, 16% T2D) who held Class 1 or Class 2 medical certificates and participated in the ARA.MED.330 protocol from May 2012 to December 2019. Pilots performed capillary blood glucose measurements via finger-prick using an ISO 9000 certified meter. Measurements were mandatory pre-flight (1-2 hours before duty, then 30 minutes before take-off), hourly in-flight, and 30 minutes before landing. A traffic light system categorized glucose values: Green (5.0-15.0 mmol/L; 90–270 mg/dL), Amber (4.0-4.9 mmol/L; 72–88 mg/dL and 15.1-20.0 mmol/L; 272–360 mg/dL), and Red (<4.0 mmol/L; <72 mg/dL or >20.0 mmol/L; >360 mg/dL). Co-pilots cross-checked measurements, and data was recorded in logbooks and captured by cockpit voice recorders. Regular clinical reviews were conducted by a CAA diabetes specialist.

Results: the mean pre- and post-certification HbA1c remained stable at 7.2% (55.0-55.1 mmol/mol) over a median diabetes duration of 10.9 years. A total of 38,621 blood glucose values were recorded during 22,078 flying hours. 97.7% of measurements were within the satisfactory green range, 1.4% were in the low amber range, 0.8% in the high amber range. Only 0.1% were in the low red range, and 0.02% in the high red range. Out-of-range readings significantly declined from 5.7% in 2013 to 1.2% in 2019. This decline was possibly attributable to the widespread introduction of CGM systems used by most pilots in parallel with finger-prick monitoring. No pilot incapacitation or safety concerns were reported, and appropriate corrective actions were taken for all out-of-range values. The lowest in-flight glucose was 3.1 mmol/L, and the highest was 21.1 mmol/L. No new clinically significant micro- or macrovascular complications were identified during the follow-up period.

3.5 Questionnaire and Time Measurement Study on SMBG vs. CGM (SUNDIF Trial Pilots)

Details see D 2.1.

Objective: to investigate the practical operation and consequences of different glucose measurement techniques (SMBG and CGM) from the pilots' perspective, assessing their opinions, preferences, and the time required for measurements.

Methodology: six male pilots (median age 40 years, range 20-61), all routine CGM users (3 with Guardian 4, 3 with Dexcom G6) and insulin pump users, participated in the SUNDIF trial. They completed a 25-item questionnaire covering attitudes towards CGM and SMBG (overall satisfaction, effort, ease of use, convenience, accuracy), the value of information provided by each, and trust in the results. The time taken for glucose checks using both methods was objectively recorded in a hypobaric chamber simulating flight conditions.

Results: CGM systems were most valued for their convenience, all users preferred CGM over SMBG. Pilots reported greater confidence in acting upon CGM results and generally had higher overall trust in CGM. The glucose monitoring time for CGM was significantly shorter, with a mean of 6 ± 4.8 seconds compared to 47 ±28 seconds for SMBG. This equates to a saving of approximately 5 minutes over a five-hour flight, minimizing distraction from piloting duties. Overall, CGM was perceived as a tool contributing to safe and efficient glucose monitoring in aviation.

3.6 DEXFLY 1 (Real-world feasibility study of CGM by insulin-treated pilots within the ARA.MED.330 Diabetes protocol)

Details see D 3.1.

Objective: to conduct a real-world study comparing the Dexcom G6® CGM system with fingerprick SMBG for pilots flying under the EASA ARA.MED.330 diabetes protocol.

Methodology: this was a prospective observational study involving 8 pilots (all male, 100% Class 1 medical certificates, 7 with type 1 diabetes, 1 with type 3c diabetes). The median age was 48.5 years, and the mean HbA1c was 53.9 mmol/mol. Participants continuously wore Dexcom G6® systems for a planned 6-month

period (but the study was terminated early due to the Covid-19 pandemic). SMBG measurements, performed according to the ARA.MED.330 protocol (pre-flight, 30 minutes before take-off, hourly in-flight, and 30 minutes before landing), were recorded concurrently with CGM values. The MARD was calculated, with a value <10% considered an acceptable safety threshold.

Results: A total of 874 paired SMBG and CGM measurements were analysed. A strong positive correlation (r=0.843, p<0.001) was observed between the two methods. The mean glucose values were very similar: 8.78 mmol/L (158 mg/dL, SMBG) and 8.71 mmol/L (157 mg/dL CGM). The MARD between the methods was 9.39%, demonstrating satisfactory concordance. Few glucose values were recorded at the extremes (<5 mmol/L [<90 mg/dL] or >15 mmol/L [>270 mg/dL]). The lowest readings were 4.6 mmol/L (83 mg/dL SMBG) and 4.4 mmol/L (79 mg/dL CGM), all falling within the FAA's acceptable glycaemic range (4.4–10.0 mmol/L; 79–180 mg/dL). No SMBG value was below 5 mmol/L (<90 mg/dL) when the corresponding CGM reading was within the protocol's satisfactory range.

3.7 DEXFLY 2 Study (Real-world prospective cohort study of CGM use by insulin-treated pilots within the ARA.MED.330 Diabetes Protocol).

Details see D 3.1.

Objective: to build upon the DEXFLY 1 study by providing definitive real-world data on the performance of the Dexcom G6® CGM system against fingerprick SMBG in commercial pilots with insulin-treated diabetes during normal flying duties, particularly focusing on measurements at the extremes of glucose concentrations and out-of-range (OOR) values.

Methodology: This was an international, multicentred, prospective observational study. Data from 17 male pilots (all Class 1 medical certificates, 16 type 1 diabetes, 1 type 3c diabetes) were collected and analyzed. Participants had a median age of 42.0 years, mean HbA1c of 50.2 mmol/mol (6.8 %) and median diabetes duration of 7.7 years. Pilots wore Dexcom G6® systems continuously for 12 months, and SMBG measurements were performed in accordance with the ARA.MED.330 protocol, with co-pilot validation and logbook recording. MARD was used to assess concordance.

Results: A total of 11,918 paired SMBG and Dexcom G6® CGM values were analysed. 8.4% (SMBG) and 98.1% (CGM) of values were within the satisfactory green range (5.0–15.0 mmol/L; 90 mg/dL-270 mg/dL). No high red range values (>20.0 mmol/L; >360 mg/dL) were recorded by either method. A strong positive correlation (r=0.857, p≤0.001) was found between SMBG and CGM measurements. Mean glucose values were similar: 8.3 ± 2.0 mmol/L; 149.4± 3.6 mg/dL (SMBG) and 8.4 ± 2.0 mmol/L; 51.2±3.6 mg/dL (CGM). The lowest glucose value was 2.7 mmol/L (48.6 mg/dL) for both, and the highest were 18.9 mmol/L; 340.2 mg/dL (SMBG) and 18.6 mmol/L; 334.8 mg/dL (CGM). The MARD was 9.6%, confirming good concordance. OOR analysis showed CGM sensitivity 47.3% and specificity 98.9%. CGM tended to lag slightly behind SMBG after meals but tracked closely before, during, and after OOR events.

3.8 In Vitro Simulation and Real-World Observational Study on Insulin Pump Performance.

Details see D 3.1.

Objective: to comprehensively evaluate the effects of atmospheric pressure changes during flights on modern insulin pump delivery in vitro and to explore the clinical implications of these changes in real-world settings by analysing glycaemic control in pilots using insulin pumps.

Methodology:
In vitro simulation: a hypobaric chamber was used to simulate standard flight protocols (ground level, ascent, cruise, descent). Modern insulin pumps (Medtronic MiniMed 780G, Tandem t:slim X2, Omnipod DASH) with open cannulas, set to deliver basal insulin at 0.6 IU/h, were tested. Triplicate simulations were conducted for 26 pumps, and rapid decompression scenarios were also simulated to assess fluid expulsion.
Real-world observational study: this retrospective study analysed 4,656 capillary blood glucose values recorded by 7 pilots using CSII from May 2012 to December 2019, as part of the EASA diabetes protocol in the UK, Ireland, and Austria.

Results:
In vitro simulation: full insulin pump cartridges demonstrated small over- and under-deliveries during ascent and descent. For pumps set at a basal rate of 0.6 IU/h, measured delivery was 0.75 IU during ascent and -0.38 IU (under-delivery) during descent. These findings represented a worst-case scenario. During rapid decompression, an average of 5-6 units of dyed fluid and bubbles were expelled from the infusion sets.
Real-world observational study: there was no evidence that repeated flights or repeated exposure to ambient pressure changes adversely affected glycaemic control in pilots using insulin pumps. Pilots using CSII had fewer out-of-range (OOR) values (0.7% amber, 0.02% red) compared to those on MDI therapy (2.4% amber, 0.2% red) and demonstrated tighter glycaemic control. Most OOR values (90.9%), including all in-flight OOR values, occurred during the first flight duty period.

3.9 Hypobaric Simulation Study on Closed-Loop Insulin Delivery Systems.

Details see D 3.1.

Objective: to evaluate the performance and safety of AID systems in a simulated hypobaric flight environment.

Methodology: Six participants with type 1 diabetes (median age 47 years, HbA1c 50 mmol/mol) were included. The study tested various HCL algorithms and device pairings: Medtronic Guardian 4-Medtronic 780G-SmartGuardTM (n=4), Dexcom G6-Omnipod DASH®-Android APS (n=1), and Dexcom G6-Ypsomed Pump-CamAPS FX (n=1). Interstitial glucose and oxygen saturation measurements were recorded every 15 minutes, with SMBG also used.

Results: CGM glucose measurements mirrored SMBG measurements with a 5-minute lag. HCL systems were able to administer insulin as expected and maintain a tight fasting and post-prandial glucose range across different pressure altitudes, with no apparent safety issues demonstrated. Two participants experienced hypoglycaemia during an extended 16-hour fast, likely due to the fast itself rather than inappropriate insulin administration.

3.10 Evaluation of cardiovascular risks of pilots and ATCOs

Details see D 3.1.

Objective: to estimate the risk of cardiovascular disease (CVD) in pilots and ATCOs) with type 1 and type 2 diabetes using established risk calculators to determine if any increased risk to flight safety can be identified in advance and managed.

Methodology: this was a retrospective, multi-centred, observational study using longitudinal data from the UK Civil Aviation Authority (CAA), Irish Aviation Authority (IAA), and Austrocontrol for pilots and ATCOs with insulin-treated diabetes certified under the ARA.MED.330 protocol from May 2012 to April 2024. The study included 90 individuals with diabetes and a control group of 90 age, gender, and license-class matched pilots and ATCOs without diabetes. Three different risk calculators were used to estimate the 5- and 10-year risk of a cardiovascular event:

- QRisk®3: Calculated for all individuals with type1, type 2 and without diabetes.
- Steno1: Calculated for all individuals with type 1 diabetes (T1D).
- Score2-Diabetes: Calculated for all individuals with type 2 diabetes (T2D).

Results:

- *Overall Risk:* pilots and ATCOs with diabetes had a greater relative risk (RR) of a future CVD event compared to both the pilot control group and the risk engine's healthy control population.
- QRisk®3 Score: at the time of their initial license application, the mean 10-year CVD risk for the diabetes group was significantly higher (7.5%) compared to the pilot control group (1.9%). The initial relative risk was 4.0 times greater than that of the pilot control group. However, this increased risk diminished over time; at the most recent medical review (after a mean follow-up of 5.8 years), the RR of the diabetes group over the pilot control group had reduced to 1.5.
- Steno1 Score (T1D): this calculator, which incorporates diabetes duration and HbA1c, showed that pilots with T1D had only a slightly elevated 10-year CVD risk (6.7%) compared to the risk engine's control group (6.1%), resulting in a much lower relative risk of 1.1.
- Score2-Diabetes Score (T2D): the mean 10-year risk for pilots and ATCOs with T2D was 8.0% at initial assessment, increasing to 10.6% at the latest follow-up.
- Discussion on risk calculators: the study suggests that the QRisk®3 calculator may overestimate the CVD risk in pilots with diabetes who maintain excellent glycaemic control, as it does not account for HbA1c or diabetes duration. The Steno1 calculator, which does include these critical factors, provided a much lower risk estimate.

Conclusion: Risk assessment tools are a useful component in evaluating a pilot's future risk of a CVD event. However, it is crucial that medical examiners consider both the duration of the diabetes and the individual's long-term glycaemic control (HbA1c), as these factors have a strong impact on CVD risk. It is recommended that all pilots with diabetes over the age of 40 should be screened for CVD risk, and those identified with an elevated risk should be referred to a cardiologist for a thorough assessment.

3.11 Real-World Comparative Pilot Study of CGMs on Commercial Flights.

Details see D 3.1.

Objective: to provide the first within-subject, head-to-head comparative evaluation of four widely available continuous glucose monitoring (CGM) systems during real-world commercial airline flights in adults with type 1 diabetes, focusing on accuracy and clinical reliability under flight conditions.

Methodology: a prospective, monocentric, observational study with 20 experienced CGM users with type 1 diabetes. Four CGM systems (Dexcom G7, Abbott Libre 3, Sinocare iCan, Medtronic Simplera) were simultaneously tested during commercial airline flights (Vienna-Reykjavik-Vienna, ~4:20 hours duration) and matched ground conditions. Capillary glucose measurements were used as accuracy checks. Accuracy and clinical reliability were assessed using MARD, Clarke error grid analysis, and Parkes error grid analyses across all flight phases.

Results: Dexcom G7 (9.5% ± 3.3%) and Abbott Libre 3 (9.6 ± 3.8%) demonstrated the lowest MARD values and consistently performed well across all flight phases, showing mean MARD values below 10%. These two systems also showed the highest clinical agreement in Clarke Error Grid (98.5% and 98.2% in Zones A and B, respectively) and highest clinical accuracy in Parkes Error Grid (99.0% and 98.9% in Zones A and B). The consistent performance of G7 and Libre 3 supports that these sensors are largely unaffected by moderate changes in ambient pressure and oxygen in the cabin.

3.12 In-Flight Glycaemic Control Using AID Systems: A Within-Subject Comparative Pilot Study.

Details see D 3.1.

Objective: to provide foundational evidence on the feasibility, safety, and glycaemic performance of AID systems in a real-world commercial flight environment.

Methodology: a single-center, non-randomized pilot study comparing four widely used AID systems. Twenty participants with type 1 diabetes were included. The study used a within-participant design, evaluating AID systems under commercial mid-haul flight and control conditions on ground, in both fed and fasting states. The primary outcome was time in range (70–180 mg/dL/3.9-10 mmol/L). Secondary outcomes included time in tight range (=TITR, which means time spent within the range of 70-140mg/dl/3.9–7.8 mmol/L), time below range 1 (=TBR1, which means time spent within the range of 54-69 mg/dl/3.0–3.8 mmol/L, time below range 2 (=TBR2, which means time spent within the range of <54mg/dl/<3.0 mmol/L), and Time Above Range (TAR1 181-250 mg/dl/10.1–13.9 mmol/L, TAR2 >250mg/dl/>13.9 mmol/L). Safety endpoints were also monitored.

Results: The overall TIR during flights was 88.2 ± 13.5% (95% CI: 82.1–94.2%), compared to 82.1 ± 17.7% (95% CI: 74.4–89.9%) on the ground. The mean difference in TIR between in-flight and ground phases was 4.6 ± 21.9% (95% CI: –5.0 to 14.2), suggesting no clinically relevant impairment or reduced efficacy in-flight performance. During fasting conditions, TIR was similarly high: 93.1 ± 8.2% in-flight (95% CI: 89.4–96.8%) and 92.6 ± 11.3% on the ground (95% CI: 87.5–97.7%), with a mean difference of 0.5 ± 12.5% (95% CI: –5.0 to 6.0). Under non-fasting conditions, TIR averaged 82.3 ± 23.8% in-flight (95% CI: 71.4–93.3%) and 75.0 ± 24.1% on-ground (95% CI: 64.4–85.5%).
In-flight TITR averaged 67.7 ± 19.4% (95% CI: 58.9–76.4%), while on-ground TITR was 64.2 ± 18.1% (95% CI: 56.2–72.1%).
TBR1 4.7 ± 7.2% (95% CI: 1.5–8.0%) in-flight versus 5.9 ± 15.7% (95% CI: –1.0 to 12.8%) on ground, and TBR2 was 1.5 ± 5.6% (95% CI: –1.0 to 4.0%) in-flight versus 2.0 ± 8.5% (95% CI: –1.8 to 5.7%) on ground, indicating good control and potentially even less time in hypoglycaemia during flight. For TAR1, the systems showed a mean of 7.1 ± 10.5% in-flight (95% CI: 2.4–11.8%) and 12.0 ± 13.8% on-ground (95% CI: 5.9–18.0%). Level 2

hyperglycaemia (TAR2) remained low throughout, with 0.2 ± 0.7% (95% CI: –0.1 to 0.5%) in-flight and 2.1 ± 4.8% (95% CI: 0.0–4.2%) on-ground.
The mean total insulin dose administered during in-flight conditions was 25.4 ± 17.6 IU (95% CI: 17.2 – 33.5), an increase compared to 18.7 ± 11.6 IU (95% CI: 13.3 - 24.1) on ground. No diabetic ketoacidosis or device malfunctions affecting pumps or CGM systems were reported. The study demonstrated that AID systems can deliver reliable and safe glycaemic management during commercial flights.

Take-home message from the above studies: *Details see D 2.1. and D 3.1.*
The conducted studies assessed the suitability of modern diabetes technologies in simulated and real-world aviation environments.

• **CGM:** CGM systems demonstrated a strong correlation with SMBG and plasma glucose values in both simulated and real flights. The accuracy, measured by the MARD, remained comparable between flight and ground conditions. Specific CGM models (Dexcom G7, Abbott Libre 3) showed high accuracy (MARD <10%). Pilots reported a strong preference for CGM systems due to the significantly shorter time required for measurements (an average of 6 vs. 47 seconds) and greater convenience, which minimizes distraction.

• **Insulin Pumps:** in-vitro simulations suggest that insulin pumps can deliver small, unintended amounts of insulin due to pressure changes during ascent and descent (approx. 0.6 units with full cartridges on ascent). A rapid decompression event led to an over-delivery of an amount equivalent to 5-6 units of insulin. However, in real-world applications, pilots using insulin pumps showed equivalent or even better glycaemic control and no more hypoglycaemia than pilots on multiple daily injections. The release of hormones such as adrenaline in stress situations, which leads to glucose release from the liver, might help to counteract inadvertent insulin bolus.

AID: in both simulated and real-world flights, AID systems were able to maintain stable glycaemic control. For release of insulin in rapid decompression events see above. TIR was comparable during flight (88.2%) and on the ground (82.1%), and no device-related safety issues or malfunctions were observed.

4. Summary: Review of Aeromedical Safety Regulations and Risks for individuals with Diabetes Mellitus

For details see D 4/5.

This report (deliverable 4/5) presents a comprehensive review of the existing aeromedical regulations and safety risks for pilots and ATCOs with diabetes mellitus. It proposes a modern, evidence-based, and harmonized risk-assessment framework to allow for the safe certification of individuals with diabetes, including those treated with insulin.

Core aeromedical risk assessment: the "1% rule"
The 1% rule was developed to provide an objective, quantitative limit for the maximum acceptable risk of a pilot suffering a medical incapacitation that could lead to a fatal accident.

The rule originates from an overall target fatal accident rate of 1 in 10 million flying hours. It was decided that medical issues should account for no more than 10% of crew-related failures, setting the target for a fatal accident from medical causes at 1 in 1 billion flying hours. The most critical factor is the presence of a second pilot. Studies suggested a second pilot could prevent an accident in 99 out of 100 incapacitations during critical flight phases (take-off and landing). This second pilot mitigation effect reduces the overall risk of a fatal accident by a factor of approximately 1,000. Because of this 1,000-fold risk reduction, the acceptable incapacitation risk for an *individual pilot* in a multi-pilot crew can be 1,000 times higher than the target for a fatal accident. This leads to a maximum acceptable risk of incapacitation of approximately 1% per year.
Modern aircraft, technologies, and procedures suggest that a higher risk threshold could be acceptable today.

Modernizing Risk Assessment Frameworks
The report advocates for evolving beyond a single rule towards more systematic approaches. It highlights the Aeromedical Risk Assessment Matrix (ARA-Matrix), which assesses risk by combining the likelihood of a medical event occurring with the severity of its potential harm.

Diabetes-Specific Risks and Certification Pathways
The primary aeromedical risks associated with diabetes are acute events from inadequate glycaemic control and long-term complications.
• Hypoglycaemia is the main concern, as it can cause sudden and subtle cognitive impairment, confusion, or complete incapacitation due to unconsciousness.
• Hyperglycaemia can also impair cognitive function and, in the long term, accelerates the development of micro- and macrovascular complications, which themselves increase incapacitation risk.
To manage these risks, the report goes on explaining the EU's ARA.MED.330 protocol and a similar system by the FAA in the United States, which – for class 1 pilots - are both based on the following safety pillars: a) glucose monitoring and a traffic-light system, b) widespread use of CGM as a better option compared to SMBG, c) an operational multi-pilot limitation (=a second qualified pilot is always at the controls), d) mandatory regular reviews by diabetes specialists and screening for long-term complications.

The report recommends, among others:
• Updating and harmonizing regulations based on a systematic, risk-matrix approach *(suggestion see further down in this report).*
• Formally incorporating the use of modern technologies like CGM and AID into the regulatory framework.
• Developing standardized medical report templates and follow-up requirements to ensure consistent and safe decision-making across all member states.

5. Key Recommendations for EASA

For details see D.6.1.

1. Consider updating the implementing rules, acceptable means of compliance and guidance material for the medical certificate assessments of applicants with diabetes to reflect the latest diagnostic tests and modern diabetes therapies available.

2. Consider permitting the use of insulin and other oral antihyperglycaemic medication with low risk of hypoglycaemia in pilots and ATCOs subject to individual assessment by or under the supervision and

guidance of the medical assessor of the licensing authority, involving clinical specialists and operational experts as necessary, and applying appropriate operational limitations (e.g. Operational Multi-Pilot Limitation).

3. The detailed assessment and follow-up requirements for each class of medical certificate and type of diabetes should be proportionate to the risk of complications and hypo-/hyperglycaemia and the applicability of suitable operational limitations

4. Define the overall acceptable safety targets for the management of medical risk as part of the overall safety system, then consider aeromedical risk through a (semi-) quantitative mathematical approach using standardized risk acceptability criteria matrices and the application of epidemiological/ research/existing protocol data.

5. EASA should decide on the level of oversight required both in terms of clinical surveillance for good control and complication prevention and operational testing and who should be responsible.

6. EASA should consider what level of rulemaking is required in the operations areas to ensure that the operational aspects of required testing are within operations manuals and other colleagues are aware of the requirements for the relevant applicants to test during flight.

7. Medical Assessors, aeromedical examiners, and clinical specialists should be provided with training on the aeromedical aspects of the latest diagnostic, investigative and treatment options in order to determine the fitness of applicants and understand the interaction of the condition and operational effects.

6. Take-home messages (based on overall results of the research)

1. Diabetes Screening:
   The suggested test to screen for diabetes is the measurement of an HbA1c value, as the HbA1c is a stable parameter not influenced by acute changes in glucose and not requiring any specific pre-condition such as fasting. In case of an abnormal HbA1c value, a second confirmatory test (e.g. HbA1c on a second sample or another test such as an oGTT) needs to be performed to establish or rule out diabetes diagnosis.
   In pilots and ATCOs with an established diagnosis of diabetes, HbA1c monitoring should follow a structured schedule.
   - If glycaemic control is stable and within target, HbA1c should be assessed every 6 months, ideally aligned with the specialist clinic review.
   - If glycaemic control is suboptimal, both HbA1c measurement and specialist review should be performed every 3 months.
   - In exceptional cases with long-term stability under no or minimal therapy ("exemplar cases"), extending the interval to 12 months may be justifiable.

   In people using AID/CGM systems additionally TIRs and ambulatory glucose profiles should be considered as they allow deeper insights into glycaemic control and enable adjustments.

2. Diabetes medication:
   Medication with low risk of hypoglycaemia and CV benefits should be used whenever possible. Sulfonylurea should be avoided.

   Medication with low risk of hypoglycaemia: this group includes metformin, GLP-1-RAs, SGLT-2 inhibitors, and DPP-4 inhibitors. Due to their glucose lowering effect without causing hypoglycaemia they are considered safe to be prescribed and use in pilots and ATCOs. Moreover, GLP-1-RAs and SGLT-2 inhibitors also have proven cardiovascular and renal protective benefits.

   Medication with high risk of hypoglycaemia:

   a) Oral antihyperglycaemic agents:

   Sulfonylureas (e.g., glimepiride, glipizide, gliclazide) – stimulate insulin secretion independent of glucose; HbA1c reduction (+) but increased hypoglycaemia risk. (Not recommended in aviation)

   Thiazolidinediones (TZDs; e.g., pioglitazone, rosiglitazone) – enhance insulin sensitivity via PPARγ activation; HbA1c reduction (+) but associated with weight gain and fluid retention. (Not recommended in aviation - no cardiovascular benefit and with potential harm)

   b) Insulins:

   Pilots/ATCOs requiring insulin therapy should use modern insulin analogues with low risk of hypoglycaemia. Human insulins, pre-mixed insulins, NPH insulins and first-generation basal insulin analogues are not recommended due to their pharmacodynamic and pharmacokinetic profiles that have a higher risk of unwanted hypo- and hyperglycaemic excursions.

In type 2 diabetes in case insulin therapy is needed, basal insulin therapy using a second-generation insulin should be the first insulin to be initiated. In people with type 1 diabetes or diabetes requiring basal-bolus insulin therapy, AID using rapid acting insulin analogues should be preferred. In case this is not an option (e.g. allergy towards adhesive material) basal- bolus insulin therapy using rapid-acting and second generation basal insulin analogue should be used.

3. Diabetes technology:

3.1. All pilots/ATCOs treated with agents that have a hypoglycaemia risk (insulin, SU) should monitor their glucose via CGM, with SMBG as backup. CGM should also be used to manage the insulin therapy and assess the achievement of treatment goals.

Pilots and ATCOs requiring intensive insulin therapy should use AID systems with proven safety (see above).

3.2. Precaution for emergencies:
Readily absorbed carbohydrates must be carried at all times when on duty.
If an AID system is used, an emergency kit (pens, blood glucose meter, and insulin) must be carried at all times when on duty in case the AID system fails.

3.3. Insulin pumps (as part of AID) :
Insulin pumps should not be used as stand-alone devices. In case of a rapid decompression, an over-delivery of insulin due to sudden loss of cabin pressure can potentially happen. Due to its pharmacokinetic properties, the onset of insulin action will be only after 10-15 minutes following (involuntary) bolus insulin administration, thus there will be sufficient time to take countermeasures such as carbohydrate intake. In addition, the release of stress hormones (e.g. adrenaline) will result in an increase in blood glucose levels due to glucose release from the liver and will additionally counteract the glucose lowering effect caused by the insulin over-delivery.
Action: In the event of a sudden loss of cabin pressure at high altitude the insulin pump should be switched off or disconnected immediately and 15g carbohydrate ingested as soon as possible (at least within 20 minutes of the decompression).

4. Aeromedical assessments:
- In all pilots with diabetes, HbA1c and TIRs should be assessed for diabetes control according to the scheme mentioned in “Take Home Messages 1”
- Regular diabetes checkup (nephropathy, retinopathy, kidney disease) should be performed according to current diabetes guidelines
- Minimum criteria for vision accuracy should be set according with EASA regulation.
- Blood pressure and lipid management should be optimized meeting the current guidelines
- People with neuropathy are unfit to fly, for retinopathy and CVD the current EU regulations should apply.

CV risk assessment should be performed as follows:
- Type 1 diabetes: use the Swedish National Diabetes Register to obtain individualized 10-year ASCVD risk predictions (McGurnaghan et al., 2021 –- https://diabepi.shinyapps.io/cvdrisk/). If high risk is identified, a cardiologist review is required.
- Type 2 diabetes: use SCORE2-Diabetes to obtain individualized 10-year ASCVD risk predictions. If high risk is identified, a cardiologist review is required.

- Any type of diabetes: if there are symptoms or signs of cardiovascular disease (CVD), a cardiologist review is mandatory.
- Other forms of diabetes: an individualized CV risk management plan must be developed.
- For further details, refer to *CV Risk Diabetes – CV Group*.

For aeromedical assessments, see also section 5 (p. 45 ff) of the teaching material slides (D 7.3.) for the following topics: a) medical reports required to complete an assessment; b) suggestion for contents of medical report; c) features of a medical flight test; d) current functional ability; e) risk of aeromedically relevant incapacitation; f) assessment of fitness; g) limitations; h) change in fitness; i) practical sessions.

4. Suggested risk-matrix approach for diabetes:

A risk matrix has been developed, inspired by the U.S. Air Force and MESAFE models, combining a numerical scale for likelihood (1–5) and an alphabetical scale for severity (A–E). This allows comparison with the original 1% rule.
Instead of treating diabetes risk as a single event (e.g., acute myocardial infarction) as in the 1% rule, it should be considered a multifactorial condition. Risks may be acute (e.g., hypoglycaemia) or gradual, depending on treatment.

Diabetes Aeromedical Risk Assessment Matrix (ARA-Matrix)				Harm				
				Negligible - A	Minor - B	Major - C	Hazardous - D	Catastrophic E
Likelihood				Minimal impact on flight safety Minimal impact on performance and able to continue duties	Reduced effectiveness and capacity to adapt to operational requirement Minor to moderate performance compromise and able to continue duties	May compromise flight safety Major decrement in performance	May cause flight safety critical event Severe incapacitation	Always cause catastrophic event Complete incapacitation
Likelihood	Annual event Frequency	Flight hours between events (approx.)*	Diabetes Review	Nil or Insignificant	Hypo/hyperglycaemia action levels reached	Hypo/hyperglycaemia action levels reached + mild symptoms	Symptomatic Hypo/hyperglycaemia requiring intervention	Hypoglycaemia Unconscious (Or DKA/HONK)
Frequent - 5	>10 (>99%)	100 – 1,000	Weekly					
Likely - 4	1 – 10 (90-99%)	1,000 – 10,000	Monthly					
Occasional – 3	0.1 – 1 (10-90%)	10,000 – 100,000	< Once per year					
Improbable - 2	1 – 10%	100,000 – 1,000,000	< Once per 1-10 years					
Very Improbable - 1	<1%	>1,000,000	< Once per decade					

* In context of random onset of events that are unconnected to flight. If event is connected to flying activity, e.g. murder, suicide, or flight anxiety, use career frequency rather than yearly.

** Operational risk reduction could be in the form of co-pilot, back-up crew, and time window to land (e.g. helicopter). Personal risk factors could be closely followed-up by psychologist and peer support, etc. Formalised risk reduction is documented and required in the certificate.

	Risk Unacceptable	Not appropriate to proceed
	Unmitigated risk unacceptable	May be deemed acceptable in some cases after thorough review and specific mitigation measures
	Risk may be acceptable	May require additional operational and/or personal risk reduction**
	Risk acceptable	No additional action needed

Table 2: Suggested risk matrix for diabetes *(for details see D4/5)*

Example: A weekly “major” event (C5) would be unacceptable. A catastrophic event occurring every 2 years (E2) might be acceptable if mitigations are in place and confirmed by the NAA.

The risk matrix approach can be further adapted to add (plot) epidemiological or research data. Data from in-flight monitoring could also be plotted onto the matrix to inform risk assessment.
For more details concerning the risk matrix, see: D4/5 Review of existing aeromedical safety regulations and risks for the aeromedical certification of pilots and ATCOs with diabetes, EASA.2022.C20.

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