Cureus
Part of SPRINGER NATURE

Open Access Review Article

Published via AstroMedica: Advances in Transportation Medicine, Flight, Spaceflight, and Microgravity

GLP-1 Receptor Agonists in Civil Aircrew: Evidence, Regulatory Divergence, and a Proposal for Harmonized Certification

Review began 11/05/2026
Review ended 11/12/2026
Published 11/17/2026

© Copyright 2026
Minoretti. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

DOI: 10.7759/cureus.119808

Piercarlo Minoretti [1]

1. Occupational Health, Studio Minoretti, Oggiono, ITA

Corresponding author: Piercarlo Minoretti, scientific.direction@studiominoretti.it

Abstract

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), including the dual agonist tirzepatide and the oral agents semaglutide and orforglipron, are increasingly prescribed for obesity, a condition common among airline pilots. Civil aviation authorities now accept these drugs in aircrew, but their guidance differs and has not been compared with the pharmacology of each agent. The evidence on the pharmacology, benefits, and adverse effects of GLP-1 RAs relevant to flight and on their interactions with the flight environment was reviewed. The guidance of civil aviation authorities in the United States, the United Kingdom, the European Union, New Zealand, Australia, and Canada was also compared. The half-life of the regulated agents ranges from two to three days for orforglipron to about one week for semaglutide, so that exposure approaches steady state between one and five weeks after each change in dose. Gastrointestinal adverse events are frequent and cluster during dose escalation, whereas acute kidney injury, pancreatitis, and gallbladder disease may also occur later in treatment. Signals for nonarteritic anterior ischemic optic neuropathy, increased heart rate, and vestibular symptoms carry low absolute risks but are relevant to flight duty. Benefits include fewer major adverse cardiovascular events (MACE) and less severe obstructive sleep apnea (OSA). Cabin altitude, low humidity, and circadian disruption may add to the gastrointestinal effects of these drugs, although no study has tested them in flight. Observation periods ranged from one to four weeks after initiation and from 48 hours to five days after a dose increase, and none of the guidance documents stated a pharmacokinetic basis for them. The Federal Aviation Administration halved its observation period after initiation within one year; no authority addressed reinitiation after missed doses, and only one explicitly covered cabin crew. A phase-based protocol is proposed in which stand-down periods follow the half-life of each agent, with four weeks after initiation and seven days after each dose increase for the weekly agents, and two weeks and three days, respectively, for orforglipron. A multi-pilot limitation would apply until the maintenance dose reaches steady state, followed by periodic review of weight, heart rate, blood pressure, and symptoms. Specific rules address missed doses, switches between agents or formulations, and cabin crew. A harmonized approach grounded in pharmacology may protect flight safety while allowing aircrew to benefit from treatment and to disclose it.

Categories: Occupational Health, Pharmacology
Keywords: aeromedical certification, aviation medicine, cabin crew, glp-1 receptor agonists, obesity, pilots, semaglutide, tirzepatide

Introduction And Background

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have changed the pharmacological treatment of obesity, as once-weekly subcutaneous semaglutide and tirzepatide produced sustained weight loss in large randomized trials [1,2]. These drugs act on the receptor of the gut hormone GLP-1, and they increase glucose-dependent insulin secretion, reduce glucagon release, delay gastric emptying, and suppress appetite through central pathways [3]. Oral agents have since entered the field, and both a once-daily 25-mg formulation of semaglutide and orforglipron, a nonpeptide small molecule, reduced body weight in phase 3 trials of adults with obesity [4,5]. Overweight and obesity are also common among airline pilots [6], so the use of these drugs in aircrew is likely to grow.

The aeromedical relevance of these drugs rests on the principle that the medical condition of a crew member should keep the annual risk of sudden incapacitation within a low tolerance [7]. This tolerance is conventionally expressed as the 1% rule, under which a crew member is considered unfit when the annual risk of an incapacitating medical event exceeds 1% [8]. The adverse effects of treatment bear directly on this assessment. Nausea, vomiting, or dizziness may distract a crew member from safety-critical duties or, when sudden and severe, cause incapacitation in flight, and civil aviation authorities have raised these concerns for GLP-1 RAs [9,10]. Cardiovascular disease is the most frequent cause of grounding among pilots assessed under European rules [11]. In addition, many pilots report avoiding medical care for fear of losing their certificate [12], and undisclosed conditions or medications have been documented in fatal transportation accidents with medical causes [13]. Comparable questions arise in other safety-sensitive transport occupations, where fitness standards classify glucose-lowering drugs mainly by their potential to cause hypoglycemia [14].

Civil aviation authorities have issued guidance on GLP-1 RAs that differs in the length of the observation

period at initiation and after dose increases, and in the respective roles of the medical examiner and of the authority [9,15,16]. Within Europe, the European Union Aviation Safety Agency (EASA) has not published common guidance on these drugs for obesity, and national authorities have adopted procedures of their own [17,18]. Divergence among regulators has also been described for other conditions relevant to flight safety, such as post-traumatic stress disorder [19]. Evidence specific to aviation, however, remains scarce, and the only review on the topic identified by the literature search addressed military aircrew, who in the United States are not authorized to use these medications [20].

In the present narrative review, the term aircrew designates pilots and cabin crew, in the sense of the European regulation that sets medical requirements for both groups in civil aviation [21]. Cabin crew are considered alongside pilots because their health determines the performance of safety duties, although no harmonized international approach to their fitness to fly exists [22]. The term GLP-1 RAs is also used to include tirzepatide, a dual agonist of the glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptors with a half-life of about five days [23]. The half-life of a drug is the time needed for its plasma concentration to fall by one half, and with repeated dosing, a stable level of exposure, the steady state, is approached after four to five half-lives [24]. Observation periods are the intervals during which a crew member may not operate after starting a drug or changing its dose. Current periods are fixed in hours or weeks, whereas the half-life of the regulated agents ranges from about one week for subcutaneous semaglutide to two to three days for orforglipron at steady state [25,26]. Oral semaglutide, in particular, combines the long half-life of the parent molecule with a bioavailability that varies widely from one dose to the next [27]. The working hypothesis is that the present observation periods were set without reference to the time course of drug exposure and of adverse events for each agent. A common protocol based on the phases of treatment might then be derived from the available clinical evidence. In light of this hypothesis, the burden of obesity in aircrew and the pharmacology, benefits, and adverse effects of GLP-1 RAs relevant to flight are examined first. The interactions of these drugs with the flight environment and the guidance of civil aviation authorities are then considered, and a phase-based protocol for the harmonized certification of treated aircrew is finally discussed.

Review

Literature search and sources

PubMed was searched from inception to November 2026, with two core searches whose complete strings are given in the Appendix. The first, which retrieved 14 records, combined terms for GLP-1 RAs and other weight-loss medications with terms for aviation and aircrew, including pilots, cabin crew, flight attendants, cabin altitude, hypobaric hypoxia, medical certification, and incapacitation. The second, which retrieved 622 records, combined terms for pilots and cabin crew with terms for obesity and related conditions, such as overweight, body mass index (BMI), obstructive sleep apnea (OSA), fatty liver, type 2 diabetes, cardiovascular disease, and loss of license. After the removal of two duplicates, the titles and abstracts of 634 records were screened against the eligibility criteria, and 186 records met them, 47 of which had been published from 2020 onward. The other 448 records did not concern aircrew or aviation (n=110), concerned military aircrew only (n=110), addressed other topics (n=180), were case reports, narrative reviews, letters, or conference abstracts (n=44), or were animal studies (n=4). No record of the first search reported original data on GLP-1 RAs in civil aircrew.

The remaining sources were identified by targeted PubMed searches for each domain of the review, namely pharmacokinetics, cardiovascular and metabolic benefits, adverse effects, and the effects of cabin altitude, low humidity, and circadian disruption. Title and author queries were added for phase 3 trials and consensus documents, and the reference lists of retrieved articles were examined. In each domain, a dedicated search was run for studies that did not support the hypothesis, including null trials, reports of persistent or serious adverse events, and surveys describing a low prevalence of obesity among pilots. Of the 137 references cited, 17 were retrieved by the core searches, 105 by targeted searches and reference lists, and 15 are guidance documents and other sources not indexed in PubMed.

Guidance documents on GLP-1 RAs and obesity in aircrew were retrieved between October 25 and 27, 2026, from the websites of civil aviation authorities. The authorities consulted were the Federal Aviation Administration (FAA) of the United States, the UK Civil Aviation Authority (UK CAA), EASA, and the national authorities of New Zealand, Australia, Canada, and European Union (EU) member states. Only the versions in force on the retrieval dates were compared, and earlier versions were recorded when pilot associations had documented their content.

Randomized controlled trials, meta-analyses, cohort and case-control studies, pharmacokinetic studies, pharmacovigilance analyses, cross-sectional surveys of aircrew, and consensus documents were eligible. Case reports were considered only for questions that no other study addressed, such as reinitiation after a lapse in treatment. Human data were given priority, and animal studies were considered only for mechanistic questions, such as the brainstem pathways of nausea, that human studies have not addressed. Studies of military aircrew were included only when no study of civil aircrew addressed the same question. Conference abstracts, preprints, and retracted articles were excluded. To reflect current formulations, treatment patterns, and regulatory practice, priority was given to articles published from 2020 onward, and earlier studies were retained only when no recent study addressed the same question. Overweight and obesity were recorded as defined by each study, in most cases by BMI thresholds. Pharmacokinetic

parameters and the timing of adverse events after initiation or dose escalation were extracted whenever reported, because these variables underlie the proposed certification protocol. Retractions, expressions of concern, and corrections were screened in Crossref and PubMed, and 10 of the cited articles had a published correction.

Records were screened, and data were extracted by a single reviewer (P.M.). Because the evidence combined randomized trials, observational and pharmacovigilance studies, pharmacokinetic studies, surveys, and regulatory documents, no formal risk-of-bias tool was applied. The design, population, and, where available, the sample size of the main studies are reported instead with their findings. Where studies disagreed, randomized trials and their meta-analyses were given precedence over observational studies, and pharmacovigilance analyses were used to describe the timing of adverse events and to identify signals rather than to estimate risk. Effect estimates are reported as in the original studies, with their 95% CIs when these were available, and estimates from different designs or populations were not pooled or compared directly. Regulatory documents were compared on predefined items that included the observation period at initiation and after dose changes, the clearing authority, and the treatment of oral formulations.

Obesity and metabolic disease in aircrew

Prevalence of Overweight and Obesity in Pilots and Cabin Crew

A systematic review of 48 studies from 20 countries, with a pooled sample of 36,958 airline pilots, reported a prevalence above 50% for overweight and obesity, as well as for physical inactivity, fatigue, and regular alcohol intake [6]. Smaller cohorts have shown a similar pattern, as 53.6% of 304 Spanish male commercial pilots had excess weight, including 6.4% with obesity, and 64.6% had abdominal obesity [28]. Among 140 male airline pilots, overweight was present in 43.6%, and overweight pilots had a greater carotid intima-media thickness than normal-weight pilots irrespective of sleep quality ($p<0.001$) [29]. Hepatic steatosis was detected by transient elastography in 24.8% of 137 apparently healthy male pilots; 5.1% had significant fibrosis, and BMI was the only independent predictor of both measures [30].

Cabin crew face a different occupational profile, and flight attendants reported more frequent standing, lifting, pushing and pulling, and bending than teachers [31]. A scoping review of 27 studies also described a high prevalence of fatigue, sleepiness, and poor sleep quality in cabin crew, with an increased susceptibility to sleep disorders [32]. Because the health of cabin crew determines their ability to perform safety duties, the reliance of their fitness-to-fly assessments on self-reported data has been questioned [22].

OSA and Cardiometabolic Risk

OSA may go unrecognized in pilots, and daytime polysomnography after long-haul night flights showed moderate-to-severe OSA in 70.9% of 103 pilots without a known diagnosis, with BMI among the significant contributors [33]. In a matched case-control study of 74 pilots, BMI was likewise an independent predictor of polysomnography-confirmed OSA (OR=3.43, 95% CI=1.97, 8.77) [34]. Among 749 French aircrew members, 10.5% screened positive for sleep apnea syndrome, 15.5% had excessive daytime sleepiness, and 24.6% reported falling asleep in flight while on duty [35]. Standard questionnaires for OSA screening discriminated poorly in pilots and air traffic controllers, with areas under the receiver operating characteristic curve between 0.49 and 0.58 [36]. When the disorder is treated, most affected crew members return to duty, and 83.1% of 138 aircrew members with OSA were assessed as fit to fly after the evaluation of residual sleepiness [37].

Type 2 diabetes adds a further layer of risk, as 28 of 59 commercial pilots with the disease (47.5%) developed at least one complication, such as coronary artery disease, retinopathy, or stroke, over nine years of follow-up [38]. Obesity therefore links several conditions that may compromise aeromedical certification, whereas its surgical treatment carries micronutrient deficiencies and neurological complications that may also be relevant to flight safety [39].

Medical Incapacitation, Loss of License, and the 1% Rule

Cardiovascular disease leads the medical causes of grounding in civil aviation, accounting for 19% of unfit assessments among 82,435 cases evaluated by six European authorities [11]. Circulatory diseases were also the most common reason for both permanent (24%) and temporary (17.9%) disqualification among Turkish civil pilots, whose overall rates of permanent and temporary disqualification were 1.3% and 6.6% [40]. The contribution of cardiovascular causes rose with age in the European data, reaching 48% of unfit assessments beyond 65 years of age [11]. In the United Arab Emirates, the annual rate of temporary license suspension among commercial airline pilots was 2.8%, and 8.1% of 1233 suspensions recorded between 2018 and 2021 became permanent [41].

The 1% rule remains the conventional threshold for aeromedical fitness, and it has been applied in particular to the risk of cardiovascular events [42,43]. Risk matrices that weigh the probability of an event against its operational consequence have been proposed as an alternative, and their dispositions agreed with those of the legacy approach in 88 of 99 adjudicated cases [8]. Within this engineering approach to risk [7], a treatment may change fitness in two directions, lowering the long-term risk of cardiovascular incapacitation

while adding short-term risks of its own during initiation and dose escalation.

Pharmacology relevant to flight operations

Agents and Formulations

Subcutaneous semaglutide and tirzepatide are given once weekly, and their maintenance doses of 2.4 mg and 5-15 mg, respectively, are reached after dose-escalation periods of 16 weeks and of up to 20 weeks, respectively [2,44]. Oral semaglutide is the same peptide coformulated with the absorption-promoting excipient sodium N-(8-[2-hydroxybenzoyl] amino) caprylate, which raises the local gastric pH and limits the degradation of the peptide in the stomach [45]. Once-daily doses of 25 mg and 50 mg of oral semaglutide have been tested in adults with obesity [4,46]. Orforglipron, by contrast, is a nonpeptide small molecule designed for once-daily oral administration without food or water restrictions [47].

Half-Life, Dose Escalation, and Time to Steady State

Subcutaneous semaglutide 2.4 mg has a half-life of 145-165 hours [25], so that exposure approaches steady state only four to five weeks after each change in dose [24]. Tirzepatide has a half-life of about five days [23], whereas orforglipron has a half-life of 48.1-67.5 hours at steady state [26], which corresponds to roughly eight to 14 days of accumulation after a dose change. Oral semaglutide shares the slow elimination of the parent peptide, which buffers day-to-day differences in absorption and yields relatively stable exposure at steady state [45]. Dose escalation therefore produces a sequence of overlapping accumulation phases, each lasting several weeks for the weekly agents, and a longer half-life may be associated with a higher risk of adverse events [48]. Consistent with this time course, adverse events reported for tirzepatide to the Food and Drug Administration Adverse Event Reporting System had a median onset of 23 days (interquartile range, six to 90 days) [49]. Current observation periods after a dose increase, by contrast, range from 48 hours to five days (Figure *1*) [15,16,18].

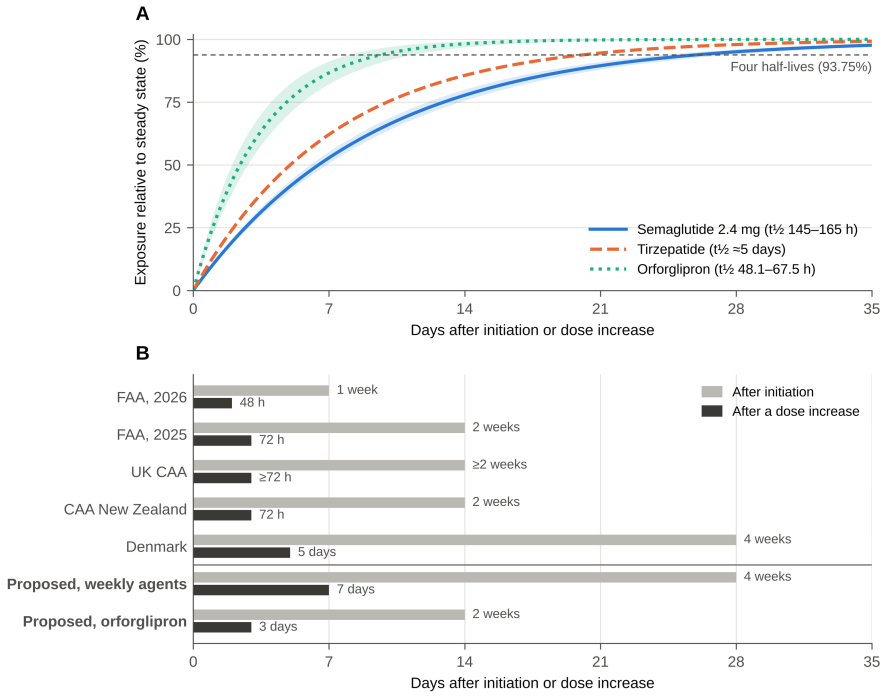


FIGURE 1: Approach to steady state of GLP-1 receptor agonists compared with the observation periods of civil aviation authorities and of the proposed protocol.

(A) Exposure relative to steady state after initiation or a dose increase, calculated from the reported half-lives of subcutaneous semaglutide 2.4 mg (145–165 h) [25], tirzepatide (about five days) [23], and orforglipron at steady state (48.1–67.5 h) [26], assuming linear pharmacokinetics and first-order elimination. The curves describe trough concentrations at successive doses relative to steady state, the shaded bands span the reported range of half-lives, and the dashed line marks four half-lives. Oral semaglutide shares the half-life of the subcutaneous peptide. (B) Observation periods after initiation and after a dose increase required by the FAA in 2026 and 2025, the UK CAA, the CAA of New Zealand, and the Danish authority, compared with those of the proposed protocol [9,15,16,18,50]. Minimum periods are shown for the UK CAA.

CAA, Civil Aviation Authority; FAA, Federal Aviation Administration; GLP-1, glucagon-like peptide-1; h, hours; t½, half-life.

Image credits: Original figure created by the author from the pharmacokinetic parameters and regulatory documents cited in this legend. The curves were computed and plotted using Python (developed and maintained by the Python Software Foundation, Wilmington, Delaware, USA) with the assistance of Claude Opus 5.5 (developed by Anthropic, Inc., San Francisco, California, USA). The author independently verified all plotted values against the cited sources.

Absorption of Oral Semaglutide and Orforglipron

Oral semaglutide has a bioavailability of 0.8% under the recommended dosing conditions, which include no more than 120 mL of water and a post-dose fast of at least 30 minutes [27]. Exposure was limited or absent when the tablet was taken after a meal, and it increased with longer post-dose fasting [51]. Shorter pre-dose fasts of two to six hours, compared with an overnight fast, reduced the area under the concentration-time curve to 12%-43% of the reference value after 10 days of dosing [52]. Within-subject variability in bioavailability reached 137%, although the long half-life reduced the variability of steady-state exposure to 33% [27]. In addition, co-administration with five placebo tablets lowered semaglutide exposure by 34%, and oral semaglutide increased total thyroxine exposure after levothyroxine by 33% [53]. Orforglipron showed modest food effects, with fed-state reductions in the area under the curve of 17.6-23.7% and an unchanged half-life [54].

Gastric Emptying and Drug Interactions

Delayed gastric emptying is a class effect of GLP-1 RAs, and a meta-analysis of scintigraphic studies estimated a mean delay in gastric half-emptying time of 36.0 minutes (95% CI=17.0, 55.0) compared with placebo [55]. At week 20 of treatment with semaglutide 2.4 mg, the absorption of acetaminophen after a standardized meal increased by only 8% relative to placebo, a difference that lost significance after adjustment for body weight [56]. Tirzepatide delayed gastric emptying after a single dose, whereas the effect diminished with repeated dosing in healthy participants [57]. Because slower gastric emptying may alter the

absorption of oral drugs, a systematic review of 22 reports examined co-administered medications and found reduced or unchanged peak concentrations and delayed times to peak, without clinically significant changes in overall exposure [58]. Tirzepatide, however, reduced the area under the curve and the peak concentration of an oral hormonal contraceptive [59], whereas oral semaglutide did not affect ethinylestradiol or levonorgestrel exposure [60].

Discontinuation and Reinitiation

Treatment interruptions are frequent in routine care, and among 125,474 US adults who started a GLP-1 RA, one-year discontinuation reached 64.8% (95% CI=64.4%, 65.2%) in those without type 2 diabetes [61]. Weight returns after withdrawal, as participants regained 11.6 percentage points of a 17.3% weight loss within one year of stopping semaglutide [62]. In randomized withdrawal trials, a switch to placebo after the escalation phase was followed by weight gains of 6.9% with semaglutide and 14.0% with tirzepatide, whereas continued treatment maintained or extended weight loss [44,63]. Occasional missed doses appear to have limited consequences, since pharmacokinetic and pharmacodynamic modeling indicated that 80% adherence to semaglutide or tirzepatide preserved about 90% of the expected weight loss [64]. Longer lapses raise a different problem, because reinitiation of semaglutide at the maintenance dose after a seven-week gap was followed by recurrent nausea and vomiting that required medical care [65].

Aeromedically relevant benefits

Major Adverse Cardiovascular Events (MACE) and Heart Failure

Semaglutide 2.4 mg reduced MACE from 8.0% to 6.5% in 17,604 adults with overweight or obesity and established cardiovascular disease without diabetes (HR=0.80, 95% CI=0.72, 0.90) [66]. Oral semaglutide at doses up to 14 mg also reduced MACE in type 2 diabetes with atherosclerotic disease, chronic kidney disease, or both (HR=0.86, 95% CI=0.77, 0.96) [67]. Tirzepatide, in turn, was noninferior for MACE to dulaglutide, an agent with established cardiovascular benefit, in type 2 diabetes with atherosclerotic disease (HR=0.92, 95.3% CI=0.83, 1.01) [68]. Across 21 randomized trials with 99,599 participants, GLP-1 RAs reduced MACE (incidence rate ratio=0.87, 95% CI=0.83, 0.91) as well as cardiovascular death, myocardial infarction, and heart failure [69].

Heart failure outcomes point in the same direction, as semaglutide reduced cardiovascular death or worsening heart failure in a pooled analysis of 3743 participants with heart failure with preserved or mildly reduced ejection fraction (HFpEF) (HR=0.69, 95% CI=0.53, 0.89) [70]. Tirzepatide likewise lowered the rate of cardiovascular death or worsening heart failure from 15.3% to 9.9% in obesity-related HFpEF (HR=0.62, 95% CI=0.41, 0.95) [71]. Across 24 trials in overweight or obesity, GLP-1 RAs and co-agonists reduced incident atrial fibrillation by 18% (RR=0.82, 95% CI=0.70, 0.96) [72]. Systolic blood pressure fell by 4.95 mmHg (95% CI=4.05, 5.86) more with semaglutide than with placebo in an individual participant data meta-analysis of three trials [73]. Functional capacity also improved, as the 6-minute walk distance increased by 20.3 m (95% CI=8.6, 32.1) more with semaglutide than with placebo in obesity-related HFpEF [74]. In the STEP 1 trial, a meaningful improvement in physical functioning was reached by 39.8% of participants receiving semaglutide compared with 24.1% of those receiving placebo [75].

Obstructive Sleep Apnea

In two 52-week trials in adults with moderate-to-severe OSA and obesity, tirzepatide reduced the apnea-hypopnea index (AHI) by 20.0 (95% CI=−25.8, −14.2) and 23.8 (95% CI=−29.6, −17.9) events per hour more than placebo [76]. Participants also reported less sleep-related impairment and sleep disturbance, and those not using positive airway pressure reported improvements on the Epworth Sleepiness Scale [77]. A meta-analysis of six studies with 1067 participants found a class effect on the AHI (mean difference=−9.48 events per hour, 95% CI=−12.56, −6.40), with a larger reduction for tirzepatide than for liraglutide [78]. Because untreated OSA and excessive sleepiness are common in aircrew, these effects may lower the risk of falling asleep on duty, which was reported by about one in four crew members in a large aeromedical cohort [35].

Glycemic Therapy Without Hypoglycemic Agents

For pilots with type 2 diabetes, a report commissioned by EASA classified GLP-1 RAs among the agents with a low risk of hypoglycemia that may be used safely in aviation, and it advised against sulfonylureas [79]. In head-to-head trials, incretin-based agents lowered glycated hemoglobin (HbA1c) by 0.48% (95% CI=0.45%, 0.52%) more than basal insulin while reducing hypoglycemia and body weight [80]. In the SURPASS-4 trial, hypoglycemia (glucose <54 mg/dL or severe) occurred in 6%-9% of participants receiving tirzepatide compared with 19% of those receiving insulin glargine, and in 1%-3% of tirzepatide-treated participants who were not taking a sulfonylurea [81]. Fitness-to-drive rules for diabetes similarly exempt GLP-1 RAs from the license limitations applied to insulin, sulfonylureas, and glinides [14].

Alcohol Use

Regular alcohol intake is common among airline pilots [6], which gives aeromedical relevance to the effects of GLP-1 RAs on drinking. In treatment-seeking adults with alcohol use disorder (AUD) and obesity,

semaglutide 2.4 mg added to cognitive behavioral therapy reduced heavy drinking days by 13.7 percentage points more than placebo over 26 weeks (95% CI=5.4, 22.0) [82]. Low-dose semaglutide also reduced drinks per drinking day and craving in non-treatment-seeking adults with AUD [83]. In a Swedish nationwide cohort of 227,866 individuals with AUD, periods of semaglutide use were associated with the lowest risk of AUD hospitalization (adjusted HR=0.64, 95% CI=0.50, 0.83) [84].

Aeromedically relevant adverse effects

Across 21 randomized trials, GLP-1 RAs increased gastrointestinal disorders by 63% and gallbladder disorders by 26% compared with controls, and these and other adverse effects of potential relevance to flight duty are summarized with their timing in Table *1* [69].

Adverse effect	Magnitude	Timing	Relevance to flight duty
Gastrointestinal			
Nausea, vomiting, and diarrhea	Semaglutide 2.4 mg, nausea 43.9% vs 16.1% and vomiting 24.5% vs 6.3% [85]; tirzepatide, gastrointestinal events 27.8%–72.8% vs 12.2%–32.5% [86]; oral semaglutide 25 mg, 74.0% vs 42.2%[4]	During or shortly after dose escalation; mostly mild to moderate and transient [85]	Sudden incapacitation or distraction; fluid loss
Severe constipation, gastroparesis, and obstruction	1.02 vs 0.75 per 100 person-years compared with SGLT-2 inhibitors in type 2 diabetes (HR=1.37, 95% CI=1.30, 1.45) [87]	During treatment	Acute abdominal pain
Residual gastric contents	OR=5.96 (95% CI=3.96, 8.98) despite appropriate fasting, without more pulmonary aspiration [88]	During treatment	Nausea worsened by turbulence and maneuvering [9]
Metabolic			
Hypoglycemia	Excess of 17 events per 1000 persons over two years without diabetes [89]; higher with insulin or secretagogues[14]; lower symptom scores at the glucose nadir with tirzepatide [90]	Any time; mainly in combination therapy	Sudden or subtle incapacitation
Ocular			
NAION	OR=1.70 (95% CI=1.23, 2.36); absolute risk 0.09%, number needed to harm about 2700 [91]	Not reported	Sudden, painless loss of vision
Proliferative diabetic retinopathy	1.1% vs 0.5% with tirzepatide in type 2 diabetes (OR=2.15, 95% CI=1.24, 3.74) [92]	Early worsening after initiation	Visual standards
Neuropsychiatric			
Suicide, self-harm, and mood changes	Suicide or self-harm, 0.047 vs 0.042 events per 100 person-years in trials [93]; ROR=1.45 (95% CI=1.18, 1.77) for suicidal ideation with semaglutide [94]	Not reported	Impairment; underreporting of mood symptoms by pilots [95]
Pancreatobiliary and renal			
Gallbladder and biliary disease	RR=1.37 (95% CI=1.23, 1.52) overall and 2.29 (95% CI=1.64, 3.18) in weight-loss trials [96]	Higher with higher doses and longer use [96]	Biliary colic
Acute pancreatitis	Attributable excess of drug-induced cases[97]	42% of attributable events of the first year in the first three months [97]	Severe abdominal pain
Acute kidney injury	Hospitalization in 45.3% of reported cases[98]; number needed to harm 357 with tirzepatide 10–15 mg [99]	Median onset 63 days[98]	Interaction with dehydration
Body composition and cardiovascular			
Loss of lean mass	About 25% of weight lost with tirzepatide[100]; 25%–39% across incretin agonists [101]	Parallel to weight loss	Muscle strength; tolerance to acceleration [9]
Increase in heart rate	+3.47 beats per minute overall (95% CI=2.65, 4.29); +9.29 (95% CI=4.45, 13.86) with orforglipron 36 mg [102]	During treatment	Cardiovascular assessment

Neurological			
Dizziness, presyncope, and vestibular disorders	Vestibular disorders, HR=4.02 (95% CI=3.33, 4.86) at six months with semaglutide [103]; hypotension and syncope in US veterans [104]	Neurological events, median onset 32 days, 45.3% within 30 days [105]	Balance and spatial orientation; presyncope
Product quality			
Compounded and unlicensed products	Semaglutide 28.6–38.7% above the labeled amount but 7.7%–14.4% of the powder, endotoxin in all three samples [106]; preparation errors, ROR=48.92 (95% CI=12.63, 189.6) [107]	Any time	Overdose and contamination

TABLE 1: Adverse effects of GLP-1 receptor agonists relevant to flight duty

NAION, nonarteritic anterior ischemic optic neuropathy; ROR, reporting odds ratio; SGLT-2, sodium-glucose cotransporter-2; vs, versus.

Gastrointestinal Events and Their Time Course

In the pooled STEP 1-3 trials, nausea occurred in 43.9% of participants receiving semaglutide 2.4 mg compared with 16.1% of those receiving placebo, and vomiting in 24.5% compared with 6.3% [85]. Tirzepatide showed a similar pattern, with gastrointestinal events in 27.8%-72.8% of treated participants compared with 12.2%-32.5% of placebo recipients, most of them during dose escalation [86]. With semaglutide, 98.1% of gastrointestinal events were mild to moderate, and most were transient and clustered during or shortly after dose escalation [85]. Oral agents carry the same profile, as gastrointestinal events affected 74.0% of participants receiving oral semaglutide 25 mg compared with 42.2% of those receiving placebo [4]. In a direct comparison in type 2 diabetes, orforglipron caused more gastrointestinal events than oral semaglutide, and 9%-10% of participants discontinued orforglipron for adverse events compared with 4%-5% of those receiving oral semaglutide [47].

Severe gastrointestinal motility events have been examined in adults with type 2 diabetes. In this population, the composite rate of severe constipation, gastroparesis, and gastrointestinal obstruction was 1.02 per 100 person-years among new users of GLP-1-based therapies and 0.75 among new users of sodium-glucose cotransporter-2 (SGLT-2) inhibitors (HR=1.37, 95% CI=1.30, 1.45) [87]. Food also remains in the stomach for longer, as GLP-1 RA exposure increased the odds of residual gastric contents before anesthesia despite appropriate fasting (OR=5.96, 95% CI=3.96, 8.98), without a detectable increase in pulmonary aspiration [88]. For aircrew, the clustering of gastrointestinal events around dose escalation may define the period in which sudden nausea or vomiting on duty is most likely [86].

Hypoglycemia in Combination Therapy

Hypoglycemia is uncommon when GLP-1 RAs are used alone, and in people with obesity but without diabetes the excess over placebo was estimated at 17 events per 1000 persons treated for two years [89]. The risk rises when these drugs are combined with insulin or insulin secretagogues, the agents to which fitness standards for road transport attach license limitations because of their intrinsic hypoglycemic potential [14]. During clamp-induced hypoglycemia, tirzepatide preserved the glucagon response but delayed the cortisol and noradrenaline responses and lowered symptom scores at the glucose nadir, whereas the proportion of participants aware of hypoglycemia did not differ from placebo [90].

Ocular Events

Nonarteritic anterior ischemic optic neuropathy (NAION) was associated with GLP-1 RA use in a meta-analysis of 15 longitudinal studies with more than 1.5 million patients (OR=1.70, 95% CI=1.23, 2.36) [91]. In Danish and Norwegian registries of people with type 2 diabetes, semaglutide was associated with NAION compared with SGLT-2 inhibitors (HR=2.81, 95% CI=1.67, 4.75), with an incidence difference of 1.41 per 10,000 person-years (95% CI=0.53, 2.29) [108]. The absolute risk nonetheless remains low, as the meta-analysis estimated an absolute risk of 0.09% in treated patients and a number needed to harm of about 2700 [91]. Early worsening of diabetic retinopathy has also been described, and new-onset proliferative retinopathy occurred in 1.1% of tirzepatide-exposed compared with 0.5% of unexposed individuals with type 2 diabetes (OR=2.15, 95% CI=1.24, 3.74) [92].

Neuropsychiatric Signals

In randomized trials, suicide or self-harm events were very rare and did not differ between GLP-1 RAs and placebo (0.047 compared with 0.042 per 100 person-years) [93]. In Swedish and Danish registers, suicide death occurred at 0.23 compared with 0.18 events per 1000 person-years among users of GLP-1 RAs and SGLT-2 inhibitors (HR=1.25, 95% CI=0.83, 1.88) [109]. After adjustment for confounding, suicidality was not

associated with GLP-1 RA use compared with dipeptidyl peptidase-4 inhibitors (HR=1.02, 95% CI=0.85, 1.23) [110]. A disproportionality signal for suicidal ideation emerged, however, for semaglutide in the World Health Organization pharmacovigilance database (reporting OR (ROR)=1.45, 95% CI=1.18, 1.77) [94]. Mood symptoms may also be underreported in aviation, since 25% of Australian commercial pilots met the threshold for depression on an overt questionnaire and 41% on the same measure presented as a life-stress survey [95].

Pancreatobiliary Events and Kidney Injury

Gallbladder and biliary disease is a well-documented adverse effect, with a higher risk across 76 trials (RR=1.37, 95% CI=1.23, 1.52) and a greater risk in weight-loss trials (RR=2.29, 95% CI=1.64, 3.18) [96]. Acute pancreatitis followed a different time course, because drug-induced events attributable to GLP-1 RAs clustered early, with 42% of them in the first three months, whereas one-year rates of all-cause pancreatitis were similar to those of sulfonylurea users [97]. Acute kidney injury reported to pharmacovigilance had a median onset of 63 days and led to hospitalization in 45.3% of cases [98]. In a network meta-analysis, only high-dose tirzepatide (10-15 mg per week) increased the risk of acute kidney injury, with a number needed to harm of 357 [99].

Lean Mass, Heart Rate, and Vestibular Symptoms

Lean mass accounted for about 25% of the weight lost with tirzepatide in a body composition substudy of SURMOUNT-1, a proportion similar to that observed with placebo [100]. Across trials, lean mass made up 25%-39% of the weight lost with incretin agonists, a share comparable to that of lifestyle intervention (26.2%) and greater than that of lifestyle intervention with resistance training (17.5%) [101]. GLP-1 RAs increased resting heart rate by 3.47 beats per minute (95% CI=2.65, 4.29) in people with overweight or obesity without diabetes, with the largest increase for orforglipron 36 mg (9.29 beats per minute, 95% CI=4.45, 13.86) [102]. In a large real-world cohort, semaglutide was associated with new vestibular disorders at six months (HR=4.02, 95% CI=3.33, 4.86) and at 3 years (HR=4.95, 95% CI=4.51, 5.43), although their cumulative incidence remained below 0.5% [103]. Pharmacovigilance reports identified dizziness and presyncope among neurological signals, and neurological events as a whole had a median onset of 32 days, with 45.3% of them within 30 days of initiation [105]. A systematic analysis of 175 outcomes in US veterans with diabetes also linked GLP-1 RA use to hypotension and syncope compared with usual care [104].

Compounded and Unlicensed Products

Products obtained outside approved channels add risks unrelated to the active molecule. In three vials bought from illegal online pharmacies, semaglutide exceeded the labeled amount by 28.6%-38.7% but made up only 7.7%-14.4% of the powder instead of the claimed 99%, and endotoxin was detected in all samples [106]. Compounded GLP-1 RAs also had higher reporting odds of preparation errors (ROR=48.92, 95% CI=12.63, 189.6) and hospitalization (ROR=2.35, 95% CI=1.94, 2.83) than approved products in the Food and Drug Administration reporting system [107]. The UK CAA has accordingly classified the use of peptide products obtained outside licensed prescribing pathways as disqualifying for all classes of medical certification [111].

Interactions with the flight environment

Cabin Altitude and Gastric Function

At a cabin pressure equivalent to 8000 ft, oxygen saturation fell by 4.4 percentage points (95% CI=3.9, 4.9) in a 20-hour chamber study of 502 adults, and discomfort increased after three to nine hours [112]. Long-haul crew of a charter airline reported more bloating than short-haul crew and ground personnel (51% compared with 36%), and gastric emptying of a high-fiber meal was delayed at a simulated cabin altitude of 2500 m [113]. Hypoxia also slowed gastric emptying after endurance exercise (maximum 13C excretion time 45.5 compared with 38.5 minutes) and increased nausea [114]. Over four days at a simulated altitude of 3500 m, hypobaric hypoxia reduced body mass and acylated ghrelin and increased satiety and fullness [115]. Functional gastrointestinal disorders were already present in 39.2% of 212 Chinese male civil pilots, with diet and sleep among the associated factors [116]. Because GLP-1 RAs also delay gastric emptying [55] and suppress appetite [56], their effects might add to those of cabin altitude during long flights.

Low Cabin Humidity and Fluid Intake

The air of an aircraft cabin is dry and recirculated, and prolonged flights combined with immobility may promote fluid shifts and dehydration [117]. In healthy volunteers, dulaglutide lowered 24-hour urine output compared with placebo (median 1250 compared with 1680 mL, p=0.04) and tended to reduce ad libitum fluid intake (1300 compared with 1600 mL, p=0.06) [118]. In treated aircrew, reduced drinking during duty periods may therefore coincide with the gastrointestinal fluid losses that are most frequent during dose escalation [86].

Circadian Disruption, Meal Timing, and Rest

GLP-1 secretion follows circadian rhythms, and incretin rhythms are vulnerable to the circadian disruption caused by shift work, nocturnal light exposure, and sleep loss [119]. Among 22,617 Chinese airline personnel, dinner after 8 pm on morning-shift days was associated with anxiety (adjusted OR=1.78, 95% CI=1.53, 2.05) and depression (adjusted OR=2.01, 95% CI=1.78, 2.27) [120]. In nine participants, simulated night shifts also raised the postprandial insulin response to identical meals, and the glucose response rose with borderline significance [121]. During in-flight rest, sleep at a simulated cabin altitude was shorter and contained less deep sleep, and participants spent 69.7% of the sleep period below 90% oxygen saturation [122]. Irregular schedules also bear on drug administration, since oral semaglutide requires a fasting state and a post-dose wait [51], whereas orforglipron can be taken with or without food [54].

Shared Pathways of Nausea and Motion

In mice, area postrema neurons expressing the GLP-1 receptor mediated both the weight-lowering and the aversive effects of GLP-1 RAs, so that nausea could not be separated from efficacy at the circuit level [123]. The same hindbrain region processes emetic stimuli, and GIP receptor signaling attenuated GLP-1 receptor agonist-induced nausea-like behavior in mice and rats and emesis in musk shrews (*Suncus murinus*) [124]. Provocative motion increased neuronal activation in the nucleus tractus solitarius and the medial vestibular nucleus of the musk shrew, which suggests a partial overlap with the pathways engaged by GLP-1 RAs [125]. Turbulence and maneuvering may therefore worsen drug-induced nausea, a concern that the Civil Aviation Authority of New Zealand has raised in its guidance [9].

Regulatory approaches

The guidance of civil aviation authorities on GLP-1 RAs differed in the agents accepted, the length of the observation periods, the treatment of oral formulations, and the respective roles of the medical examiner and of the authority (Table *2*) [9,16,17]. After initiation, the observation period ranged from one to four weeks, and after a dose increase from 48 hours to five days [15,18].

Authority (document, version)	Agents accepted	Oral agents	Period after initiation	Period after dose increase	Clearance and follow-up	Cabin crew and certificate limitations
Authorities with specific guidance						
FAA, United States (weight loss management worksheet, September 2026) [15,50,126]	One agent only: metformin, liraglutide, semaglutide, tirzepatide, or orforglipron	Permitted; 48 h after a change of formulation	One week (two weeks in 2025)	48 h (72 h in 2025)	AME; progress note within 90 days; no side effects; no hypoglycemia requiring intervention in 12 months; HbA1c never ≥6.5%; annual documentation for Class 1 and 2	Not addressed; no limitation
UK CAA (guidance material; obesity information sheet v3.1, July 2026) [10,16]	GLP-1 RAs and GIP/GLP-1 RAs prescribed for obesity	Permitted	≥2 weeks, then AME assessment	≥72 h, no AME assessment	Obesity follow-up at each periodic examination; medical flight test if BMI >35 kg/m²	Not addressed; no limitation
CAA of New Zealand (medical manual, developed with CASA; undated) [9]	GLP-1 RAs prescribed for obesity	Not mentioned	Two weeks; examiner clearance and letter to the authority	72 h; examiner clearance if related to side effects	BMI ≥25 kg/m²; diabetes excluded within three months; authority clearance for complications or persistent side effects	Not addressed; no limitation
Swedish Transport Agency (March 2026) [17]	GLP-1 analogues with a weight-reduction indication; no off-label use	Not mentioned	Grounding; duration not stated	Grounding; duration not stated	Documented clinical follow-up at renewal; further evaluation if BMI ≥35 kg/m²	Published with requirements for cabin crew; multi-pilot limitation possible for Class 1
Danish Civil Aviation and Railway Authority (flowchart,	Liraglutide, semaglutide, or tirzepatide as a single	Not mentioned	Four weeks	Five days	Before treatment, fundoscopy and HbA1c, no mental disorder in 24 months, no thyroid or pancreatic disease; at four	Covered; limitation requiring medical records to be copied to the

June 2025) [18]	agent; weight loss only				weeks, blood pressure, heart rate, and fundoscopy; reassessment at ≥2-week intervals if side effects	AME, removed after discontinuation >2 weeks
Authorities without specific guidance						
EASA, European Union (Part-MED and acceptable means of compliance; diabetes training material for AMEs, November 2025) [21,79,127,128]	No common guidance for obesity; GLP-1 RAs among preferred non-hypoglycemic agents in diabetes; GIP/GLP-1 RAs listed as non-hypoglycemic agents	Not addressed	Not addressed	Not stated for obesity; in diabetes, unfit after any change of medication or dosing, duration not stated	Further evaluation if BMI ≥35 kg/m²	Part-MED applies to cabin crew; no specific provision
CASA, Australia (obesity guideline, October 2021) [129]	GLP-1 RAs not mentioned; appetite suppressants disqualifying	Not addressed	Not addressed	Not addressed	Two-week ground trial for drugs reducing fat absorption	Not addressed
Transport Canada (handbook for civil aviation medical examiners) [50,130]	No specific guidance found; general criteria for medications not otherwise listed	Not addressed	Not addressed	Not addressed	Not addressed	Not addressed

TABLE 2: Guidance of civil aviation authorities on GLP-1 receptor agonists for obesity in aircrew

AME, aviation medical examiner; BMI, body mass index; CAA, Civil Aviation Authority; CASA, Civil Aviation Safety Authority; EASA, European Union Aviation Safety Agency; FAA, Federal Aviation Administration; GIP, glucose-dependent insulinotropic polypeptide; GLP-1 RAs, glucagon-like peptide-1 receptor agonists; HbA1c, glycated hemoglobin; h, hours.

United States

In the United States, the FAA allows aviation medical examiners (AMEs) to certify applicants who use one of five weight-loss agents, namely metformin, liraglutide, injectable or oral semaglutide, tirzepatide, or orforglipron [15]. Two glucose-lowering agents used together require a special issuance by the FAA, whereas sympathomimetic agents and the combination of bupropion and naltrexone are not acceptable [126]. Under this pathway, the AME must verify an observation period of one week after initiation and of 48 hours after each dose increase or change of medication or formulation [15]. The same worksheet requires a clinical progress note issued within the previous 90 days, the absence of side effects, and no hypoglycemic event requiring intervention in the previous 12 months. Applicants who have ever had an HbA1c of 6.5% or higher are excluded from this pathway, and holders of first- or second-class certificates must renew the documentation every year [15].

United Kingdom

The UK CAA considers GLP-1 RAs and dual GIP and GLP-1 receptor agonists prescribed for obesity compatible with all classes of medical certification, and it permits both subcutaneous and oral formulations [16]. Gastrointestinal adverse effects at initiation or after a dose increase could theoretically worsen with exposure to pressure change, which is the only rationale that the authority gives for its observation periods [10]. Pilots are accordingly assessed as unfit for at least two weeks after initiation, whereas one week may be considered for air traffic controllers, who are not exposed to pressure change [16]. A subsequent assessment by an AME must confirm the absence of side effects that could impair fitness, and after a dose adjustment the unfit period is at least 72 hours without a further AME assessment. Follow-up then proceeds under the general requirements for obesity, with a review at each periodic examination until the BMI falls below 35 kg/m^2 and a medical flight test above this threshold [10].

EASA and Member States

Within the EU, Part-MED, the annex of the aircrew regulation that sets medical requirements, applies to both pilots and cabin crew [21]. The acceptable means of compliance to Part-MED allow pilots with a BMI of 35 kg/m^2 or higher to be assessed as fit only after further evaluation [127]. No common EASA guidance on GLP-1 RAs for obesity could be identified, and a research report commissioned by the agency considered these drugs within the treatment of diabetes [79]. The AME training material produced by the same project lists GLP-1 RAs among the preferred non-hypoglycemic agents in diabetes and also describes dual GIP and

GLP-1 receptor agonists as non-hypoglycemic agents [128]. The same material treats any change in medication or dosing regimen in pilots with diabetes as a reason for unfitness, without stating its duration. The Swedish Transport Agency accepts only GLP-1 analogues with an approved indication for weight reduction, excludes off-label use, and requires grounding at initiation and after each dose change, for a period that it does not specify [17]. The Swedish guidance also makes renewal conditional on documented clinical follow-up and allows a multi-pilot limitation on Class 1 certificates according to risk factors and side effects.

The Danish authority has issued a flowchart, last revised in June 2025, that accepts liraglutide, semaglutide, or tirzepatide as single agents for weight loss and applies to pilots of all classes and to cabin crew [18]. The flowchart requires the AME to document visual acuity with fundoscopy before treatment and to exclude diabetes, thyroid or pancreatic disease, and any mental disorder in the previous 24 months. New users are grounded for four weeks, after which the AME reviews blood pressure, heart rate, and fundoscopy and issues a certificate that requires all medical records to be copied to the examiner [18]. Side effects defer certification, with reassessment at intervals of at least two weeks, whereas each dose increase entails five days of unfitness and discontinuation for more than two weeks leads to a certificate without limitations.

New Zealand, Australia, and Canada

The Civil Aviation Authority of New Zealand, in guidance developed with the Civil Aviation Safety Authority (CASA) of Australia, requires pilots to stop flying for two weeks after initiation and for 72 hours after any dose change [9]. The return to flying after initiation requires clearance by the medical examiner and a letter to the authority, whereas persistent or severe side effects and any complication of treatment require clearance by the authority itself. The medical examiner must also confirm a BMI of at least 25 kg/m^2, the absence of diabetes on testing in the previous three months, the absence of nutritional deficiencies, and counseling on hydration and nutrition [9]. Among its concerns, the guidance lists a lower tolerance to acceleration due to loss of muscle mass, a higher risk of fracture due to bone loss, and presyncope from restricted intake of food and fluids.

In Australia, the clinical practice guideline of CASA on obesity, last updated in October 2021, does not mention GLP-1 RAs and classifies appetite suppressants as disqualifying [129]. The same guideline requires a two-week ground trial for drugs that reduce the absorption of dietary fat and grounding for up to three months after bariatric surgery. No guidance specific to GLP-1 RAs could be found in the handbook for civil AMEs of Transport Canada [130], whose examiners assess these drugs with general criteria for medications not otherwise listed [50].

Shared Gaps

None of the documents reviewed stated a pharmacokinetic basis for its observation periods, which were applied in the same way to agents with different half-lives and routes of administration [9,16,18]. The periods have also been revised without a stated rationale, since the FAA shortened them from two weeks and 72 hours in late 2025 to one week and 48 hours in 2026 [15,50]. Reinitiation after missed doses or an interruption of treatment was not addressed by any authority, and only the Danish flowchart defined the certification status after discontinuation [18]. Oral formulations were explicitly permitted by the FAA and the UK CAA, but only the FAA attached an observation period to a change of formulation [15,16]. Cabin crew were covered explicitly only by the Danish flowchart [18]. The Swedish guidance, published on a page shared by pilots, air traffic controllers, and cabin crew, was the only one to foresee an operational limitation of the certificate in the form of a multi-pilot restriction [17].

A proposal for harmonized certification

The protocol proposed here is organized by phase of treatment, and Table *3* sets each proposed standard beside the requirements of the civil aviation authorities whose guidance was compared. The current requirements are those stated by the authorities, whereas the proposed stand-down periods, limitations, and conditions are recommendations of the author that no authority has adopted. The principles behind the protocol and the rationale for each phase of treatment are given in the subsections that follow.

Phase	Current requirements of civil aviation authorities	Proposed: weekly agents and oral semaglutide	Proposed: orforglipron	Proposed conditions and clearance	Basis of the proposal
Phases of treatment					
Before	FAA, HbA1c never ≥6.5% [15]; CAA of New Zealand, BMI ≥25 kg/m² and diabetes excluded within 3	Same for all	Same for all	Licensed product prescribed for weight management, single agent. AME records HbA1c, blood pressure, resting heart rate, visual acuity with fundoscopy, and	Heart rate increase; NAION signal; hypoglycemia

treatment	months [9]; Denmark, fundoscopy and HbA1c, no thyroid or pancreatic disease, no mental disorder in 24 months [18]	agents	agents	history of pancreatitis, gallbladder disease, or mental disorder. Diabetes treated with insulin or insulin secretagogues follows the existing glucose-lowering pathways	in combination therapy; impurities in unlicensed products
Initiation	FAA, one week; UK CAA, ≥2 weeks; CAA of New Zealand, two weeks; Denmark, four weeks; Sweden, duration not stated [9,15-18]	Unfit for four weeks	Unfit for two weeks	AME review; no gastrointestinal symptoms in the previous seven days; stable heart rate, blood pressure, and hydration	At least four half-lives of each agent
Dose increase	FAA, 48 h; UK CAA and CAA of New Zealand, 72 h; Denmark, five days; Sweden, duration not stated [9,15-18]	Unfit for seven days	Unfit for three days	Return without AME review if free of symptoms	First dosing interval at the new dose; about one half-life of orforglipron
Dose escalation	Multi-pilot limitation possible in Sweden [17]; not addressed by the other authorities	Multi-pilot or safety-pilot limitation until four weeks after the last increase	Same limitation until two weeks after the last increase	Cabin crew do not operate as the only cabin crew member on board	Gastrointestinal events cluster during escalation; exposure approaches steady state at the maintenance dose
Maintenance	FAA, progress note within 90 days and annual documentation for Class 1 and 2 [15]; UK CAA, obesity follow-up at each periodic examination [10]; Sweden, documented clinical follow-up at renewal [17]	Unrestricted	Unrestricted	AME review at the end of escalation and at each periodic examination: weight, heart rate, blood pressure, gallbladder and visual symptoms, dizziness, mood, source of medication; HbA1c yearly; sleep testing before changes in positive airway pressure therapy	Later onset of acute kidney injury and pancreatitis; gallbladder risk related to weight loss
Special situations					
Switch of agent or formulation	FAA, 48 h after a change of medication or formulation [15]; not addressed by the other authorities	Managed as a dose increase with the windows of the new agent	Same	Declared to the AME	Different exposure after a change of molecule or route
Missed doses	Not addressed by any authority	One missed dose, no action; two consecutive, managed as a dose increase; three or more, managed as a new initiation	Gap of three to six days, managed as a dose increase; seven days or longer, managed as a new initiation	Declared to the AME	Recurrent vomiting after reinitiation at the maintenance dose; elimination over about three half-lives
Side effects at any phase	FAA and UK CAA, absence of side effects required [15,16]; CAA of New Zealand, authority clearance if persistent or severe [9]; Denmark, reassessment at intervals of ≥2 weeks [18]	Unfit until resolution	Unfit until resolution	AME review before return	Incapacitation from vomiting, presyncope, or abdominal pain
	Denmark, certificate without limitations after >2	No stand-	No stand-	BMI, blood pressure, and OSA	Weight regain within one year

Discontinuation	weeks without treatment [18]; not addressed by the other authorities	down	down	reassessed at the next periodic examination	of stopping treatment

TABLE 3: Current requirements and proposed phase-based protocol for the certification of aircrew treated with GLP-1 receptor agonists for obesity

Current requirements are those stated in the guidance documents of civil aviation authorities, whereas the proposed periods, limitations, and conditions are recommendations of the author. Multi-pilot limitation for commercial pilot licenses and safety-pilot limitation for private pilot licenses.

AME, aviation medical examiner; BMI, body mass index; CAA, Civil Aviation Authority; FAA, Federal Aviation Administration; GLP-1, glucagon-like peptide-1; HbA1c, glycated hemoglobin; h, hours; NAION, nonarteritic anterior ischemic optic neuropathy; OSA, obstructive sleep apnea; UK, United Kingdom.

Principles

The protocol rests on four principles derived from the pharmacology and adverse-effect profile of GLP-1 RAs. First, observation periods should be proportional to the half-life of each agent, because exposure approaches steady state only after four to five half-lives [24]. For subcutaneous semaglutide, this interval equals or exceeds the four-week steps of the usual escalation schedule [25], so that exposure rises almost continuously until the maintenance dose is reached. Second, the period of highest risk extends across the whole escalation phase rather than the first days after each dose change, as most gastrointestinal events with semaglutide and tirzepatide occurred during or shortly after escalation [85,86].

Third, operational mitigation may replace grounding during part of this phase. Risk matrices weigh the probability of an incapacitating event against its operational consequence [42], and a multi-pilot limitation lowers this consequence while the pilot remains in service, an option already foreseen in Swedish guidance [17]. Proportionate measures may also limit the incentive to conceal treatment, since 26.8% of surveyed pilots had withheld information on a health questionnaire for fear of losing their certificate [12]. Fourth, the protocol applies only to licensed products prescribed for weight management and used as a single agent, because products obtained outside approved channels have shown deviations from the labeled content, contamination with endotoxin, and preparation errors [106,107]. Aircrew with diabetes treated with insulin or insulin secretagogues would remain under the existing pathways for diabetes, since fitness standards classify these drugs by their potential to cause hypoglycemia [14].

Initiation and Dose Escalation

Before treatment, the AME should record the HbA1c, blood pressure, resting heart rate, and visual acuity with fundoscopy, as already required in Denmark [18], together with any history of pancreatitis, gallbladder disease, or mental disorder. These baseline values allow later comparison, because GLP-1 RAs raised resting heart rate [102] and were associated with NAION in observational studies [91]. After the first dose, the proposed stand-down lasts four weeks for subcutaneous semaglutide, tirzepatide, and oral semaglutide, and two weeks for orforglipron, periods that cover at least four half-lives of each agent [23,25,26]. Return to duty would require an AME review confirming the absence of gastrointestinal symptoms during the previous seven days, a full dosing interval of the weekly agents, together with stable heart rate, blood pressure, and hydration.

After each dose increase, a stand-down of seven days for the weekly agents and of three days for orforglipron would cover the first dosing interval at the new dose and about one half-life of orforglipron at steady state [26]. In the absence of symptoms, return after a dose increase would not require an AME review, in line with the current practice of the UK CAA [16]. Between dose increases, pilots would fly with a multi-pilot limitation, or a safety-pilot limitation for private licenses, until four weeks after the last increase for the weekly agents and two weeks for orforglipron. At that point, exposure to the maintenance dose has approached steady state, and the escalation phase in which gastrointestinal events cluster has ended [85]. For the weekly agents, the stand-down after a dose increase is longer than the 48 hours to five days now required [15,18], whereas the multi-pilot limitation keeps the pilot in service during most of the escalation phase.

Maintenance and Periodic Review

The maintenance phase would begin when the limitation is removed, and certification would then be unrestricted. Some adverse events have a later onset, such as acute kidney injury [98], and more than half of the drug-induced pancreatitis attributable to GLP-1 RAs in the first year occurred after the first three months [97]. An AME review at the end of escalation and at each periodic examination should therefore address weight trajectory, resting heart rate, blood pressure, and symptoms of gallbladder disease. The same review should cover visual symptoms, dizziness, and mood, together with the HbA1c once a year and the source of the medication. Gallbladder events deserve particular attention, because their risk was greatest in trials of weight loss [96]. The obesity requirements of each authority, such as further evaluation above a BMI of 35 kg/m^2, would continue to apply and might lapse as weight falls [10,127]. Because tirzepatide reduced

the AHI in adults with OSA [76], aircrew treated for OSA should undergo sleep testing before any change in positive airway pressure therapy.

Oral Agents

Oral semaglutide shares the slow elimination of the injectable peptide [45], so the windows proposed for the weekly agents would apply to it. The absorption of oral semaglutide, however, depends on dosing conditions [51]. Aircrew taking oral semaglutide should therefore take the daily dose after an overnight fast and respect the post-dose wait before eating, a requirement that early report times and irregular duty periods may complicate. Because the long half-life dampens the variability of exposure at steady state [27], occasional dosing errors are unlikely to require additional stand-down periods. Orforglipron, by contrast, can be taken with or without food [54], and its shorter half-life justifies the shorter windows proposed for this agent [26]. A switch between injectable and oral formulations, or between agents, would be managed as a dose increase with the windows of the new agent, as the FAA already requires an observation period after a change of formulation [15].

Discontinuation and Reinitiation

Discontinuation of treatment does not require a stand-down for pharmacological reasons, and the Danish authority issues a certificate without limitations after more than two weeks without treatment [18]. Because weight is regained after treatment ends [62], obesity-related conditions such as OSA and hypertension should be reassessed at the next periodic examination. Occasional missed doses have limited effects on efficacy [64], and a single missed weekly dose would not require any action. After a seven-week lapse, reinitiation of semaglutide at the maintenance dose caused recurrent vomiting that required medical care, and three or more missed weekly doses were regarded as a lapse calling for a reduced dose [65]. For the weekly agents, two consecutive missed doses would therefore be managed as a dose increase and three or more as a new initiation. For orforglipron, a gap of three to six days would be managed as a dose increase, and a gap of seven days or longer, about three half-lives [26], as a new initiation.

Cabin Crew

Cabin crew are exposed to the same cabin environment and, in Europe, to medical requirements set by the same regulation as pilots [21], so the pharmacological windows proposed for pilots would apply to them without change. The duties of cabin crew are also physically demanding [31]. Because no multi-pilot limitation exists for cabin crew, an equivalent measure during escalation would be to avoid duty as the only cabin crew member on board. Fitness assessments of cabin crew also rely largely on self-reported information [22], which argues for a structured declaration of the agent, the dose, the date of the last dose increase, and any symptoms at each assessment.

Limitations

To the best of the author's knowledge, no published study has tested GLP-1 RAs in aircrew or under cabin conditions, and their interactions with cabin altitude, low humidity, and circadian disruption were inferred from separate lines of evidence. Of note, some of this evidence points in the opposite direction, since overnight hypoxia near cabin altitude did not change glucose control or appetite hormones, including GLP-1, in adults with type 2 diabetes [131]. Moderate hypoxia combined with sleep restriction also lowered energy intake without gastrointestinal symptoms [132], and the shared pathways of nausea and motion were described only in animal models [123-125]. The population at risk may also differ from that of the trials, because pilots had a lower prevalence of obesity than the general population [133]. Recent data on obesity in cabin crew are lacking, and the only large survey retrieved by the literature search predates the approval of these drugs for weight management [134].

Benefit estimates came from populations older and at higher cardiovascular risk than active aircrew [66], and GLP-1 RAs did not reduce stroke across 21 trials [69]. Pooled randomized trials showed no significant reduction in alcohol consumption, in contrast with observational data [135]. For NAION, a network of 37.1 million people with type 2 diabetes found no difference in the cohort analysis with a sensitive outcome definition, although its self-controlled analysis suggested a modest increase in risk [136]. The certainty of the evidence on this association was rated low to very low [137]. Much of the information on the timing of adverse events derives from pharmacovigilance databases, which are subject to reporting bias [49].

Regulatory guidance is published on web pages that change without notice, and two of the documents reviewed carried no date [9,16]. Unpublished or case-by-case practices of national authorities could not be assessed.

Finally, the proposed protocol has not been tested prospectively in aircrew. The windows proposed for orforglipron rest on phase 1 studies in healthy participants [26], and the thresholds for reinitiation after missed doses rely on modeling and on a single case report [64,65]. A multi-pilot limitation is also unavailable in single-pilot operations, where grounding for the whole escalation phase may remain the only option.

Conclusions

GLP-1 RAs are now accepted for aircrew by several civil aviation authorities, but the observation periods required at initiation and after dose increases differ widely and do not reflect the time course of drug exposure. Weekly agents approach steady state only after several weeks, whereas most current windows after a dose increase last hours or a few days. A protocol organized by phase of treatment, with stand-down periods proportional to the half-life of each agent and a multi-pilot limitation during dose escalation, may reconcile flight safety with the cardiometabolic benefits of treatment. Proportionate rules may also encourage aircrew to disclose their treatment rather than conceal it. Prospective registries of treated pilots and cabin crew, based on a structured declaration of agent, dose, and symptoms, would allow the proposed standards to be tested and refined. The same framework could later be extended to air traffic controllers, who share the demands of sustained vigilance without exposure to pressure changes, and to other safety-sensitive transport occupations. A common position among authorities would end the present situation in which the same pilot, on the same drug, may be fit to fly in one country and grounded in another.

Appendices

PubMed search strings

Search 1, GLP-1 Receptor Agonists and Aviation (14 Records)

("Glucagon-Like Peptide-1 Receptor Agonists"[MeSH] OR "Glucagon-Like Peptide-1 Receptor"[MeSH] OR "Glucagon-Like Peptide 1"[MeSH] OR "glucagon-like peptide-1"[tiab] OR "glucagon-like peptide 1"[tiab] OR GLP-1[tiab] OR GLP1[tiab] OR semaglutide[tiab] OR tirzepatide[tiab] OR liraglutide[tiab] OR orforglipron[tiab] OR dulaglutide[tiab] OR incretin*[tiab] OR "anti-obesity medication*"[tiab] OR "weight-loss medication*"[tiab] OR "weight loss medication*"[tiab]) AND (pilots[tiab] OR "airline pilot*"[tiab] OR "commercial pilot*"[tiab] OR aircrew*[tiab] OR "air crew*"[tiab] OR "cabin crew*"[tiab] OR "flight attendant*"[tiab] OR aviation[tiab] OR aviator*[tiab] OR "Aerospace Medicine"[MeSH] OR Aviation[MeSH] OR Pilots[MeSH] OR "cabin altitude"[tiab] OR hypobaric[tiab] OR "simulated altitude"[tiab] OR "medical certification"[tiab] OR "fitness to fly"[tiab] OR "fit to fly"[tiab] OR incapacitation[tiab])

Search 2, Obesity and Related Conditions in Aircrew (622 Records)

(Obesity[MeSH] OR obes*[tiab] OR overweight[tiab] OR "body mass index"[tiab] OR "sleep apnea"[tiab] OR "sleep apnoea"[tiab] OR "Sleep Apnea, Obstructive"[MeSH] OR "metabolic syndrome"[tiab] OR "fatty liver"[tiab] OR steatosis[tiab] OR "type 2 diabetes"[tiab] OR cardiovascular[tiab] OR "loss of licence"[tiab] OR "loss of license"[tiab] OR disqualification[tiab] OR "unfit"[tiab]) AND (pilots[tiab] OR "airline pilot*"[tiab] OR "commercial pilot*"[tiab] OR aircrew*[tiab] OR "air crew*"[tiab] OR "cabin crew*"[tiab] OR "flight attendant*"[tiab] OR aviator*[tiab] OR Pilots[MeSH])

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Piercarlo Minoretti

Acquisition, analysis, or interpretation of data: Piercarlo Minoretti

Drafting of the manuscript: Piercarlo Minoretti

Disclosures

AI use statement: The authors used Claude Opus 5.5 (Anthropic, Inc., San Francisco, California, USA) as follows: language polishing in the entire paper. During the preparation of this work, the author used Claude Opus 5.5 to improve language, structure, and readability. After using this tool, the author reviewed and edited the content as needed. The authors confirm that they have reviewed and verified all AI-assisted content and take full responsibility for the work. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Wilding JP, Batterham RL, Calanna S, et al.: Once-weekly semaglutide in adults with overweight or obesity . N Engl J Med. 2021, 384:989-1002. 10.1056/NEJMoa2032183
2. Jastreboff AM, Aronne LJ, Ahmad NN, et al.: Tirzepatide once weekly for the treatment of obesity . N Engl J

Med. 2022, 387:205-16. 10.1056/NEJMoa2206038

3. Moiz A, Filion KB, Tsoukas MA, Yu OH, Peters TM, Eisenberg MJ: Mechanisms of GLP-1 receptor agonist-induced weight loss: a review of central and peripheral pathways in appetite and energy regulation. Am J Med. 2025, 138:934-40. 10.1016/j.amjmed.2025.01.021
4. Wharton S, Lingvay I, Bogdanski P, et al.: Oral semaglutide at a dose of 25 mg in adults with overweight or obesity. N Engl J Med. 2025, 393:1077-87. 10.1056/NEJMoa2500969
5. Wharton S, Aronne LJ, Stefanski A, et al.: Orforglipron, an oral small-molecule GLP-1 receptor agonist for obesity treatment. N Engl J Med. 2025, 393:1796-806. 10.1056/NEJMoa2511774
6. Wilson D, Driller M, Johnston B, Gill N: The prevalence of cardiometabolic health risk factors among airline pilots: a systematic review. Int J Environ Res Public Health. 2022, 19:4848. 10.3390/ijerph19084848
7. Syburra T, Nicol ED, Mestres CA, et al.: EACTS expert consensus document on civil aviation following cardiothoracic surgery and transcatheter procedures. Interdiscip Cardiovasc Thorac Surg. 2026, 41:217. 10.1093/icvts/ivag217
8. Mayes RS, Keirns CJ, Hicks AG, Menner LD, Lee MS, Wagner JH, Baltzer RL: USAFSAM Aeromedical Consultation Service Medical Risk Assessment and Airworthiness Matrix. Aerosp Med Hum Perform. 2023, 94:514-22. 10.3357/AMHP.6154.2023
9. Civil Aviation Authority of New Zealand: medical manual, part 3, clinical aviation medicine. Weight loss GLP-1 medication. (2026). Accessed: October 25, 2026: https://www.aviation.govt.nz/licensing-and-certification/medical-certification/medical-examiners/medical-manual/part-....
10. UK Civil Aviation Authority: obesity information for pilots and air traffic controllers (obesity information sheet), version 3.1. (2026). Accessed: October 25, 2026: https://www.caa.co.uk/media/3sckjpyk/20260729-v31-obesity-information-sheet.pdf.
11. Simons R, Maire R, Van Drongelen A, Valk P: Grounding of pilots: medical reasons and recommendations for prevention. Aerosp Med Hum Perform. 2021, 92:950-5. 10.3357/AMHP.5985.2021
12. Hoffman WR, Aden J, Barbera RD, Mayes R, Willis A, Patel P, Tvaryanas A: Healthcare avoidance in aircraft pilots due to concern for aeromedical certificate loss: a survey of 3765 pilots. J Occup Environ Med. 2022, 64:e245-8. 10.1097/JOM.0000000000002519
13. Minsinger KD, Graber JM, Nezam H, Caruth J, Udasin I: Examinee nondisclosure of relevant medical information during transportation-related regulatory examinations: a case series. J Occup Environ Med. 2025, 67:e336-41. 10.1097/JOM.0000000000003346
14. Abrahamian H, Köhler G, Salamon B, et al.: [Diabetes mellitus and road traffic-a position paper of the Austrian Diabetes Association (Update 2026)]. Wien Klin Wochenschr. 2026, 138:373-85. 10.1007/s00508-025-02655-y
15. Federal Aviation Administration: CACI - weight loss management worksheet (use of medication for obesity or overweight). (2026). Accessed: October 25, 2026: https://www.faa.gov/ame_guide/media/CACI_weight_loss_management.pdf.
16. UK Civil Aviation Authority: metabolic and endocrinology guidance material (GM) . (2026). Accessed: October 25, 2026: https://www.caa.co.uk/aeromedical/medical-standards/pilots/medical-conditions/metabolic-and-endocrinology/metabolic-a....
17. Transportstyrelsen (Swedish Transport Agency): overweight (Website in Swedish) . (2026). Accessed: October 25, 2026: https://www.transportstyrelsen.se/sv/luftfart/certifikat-utbildning-och-flygmedicin/flygmedicin/pilot-flygledare-och-....
18. Trafikstyrelsen (Danish Civil Aviation and Railway Authority): medical guidance flowchart. Weight loss, pharmaceutical assisted weight loss (TS10062025). (2025). Accessed: October 27, 2026: https://cdn.trafikstyrelsen.dk/trafikstyrelsen/Media/638852222603301657/Weightloss%20medication%20%20TS10062025.p
19. Vuorio A, Bor R, Budowle B, Gray A, Suhonen-Malm AS: Assessment policy of post-traumatic stress disorder in aviation and its practical application using turbulence-triggered trauma as an example. Front Public Health. 2025, 13:1505004. 10.3389/fpubh.2025.1505004
20. Prokop RL, Stork BF, James LC: Should military aircrew members be allowed to use Food and Drug Administration approved weight loss medications? A review of the literature and recommendations. Mil Med. 2025, 190:e2303-8. 10.1093/milmed/usaf321
21. Commission Regulation (EU) No 1178/2011 of 3 November 2011 laying down technical requirements and administrative procedures related to civil aviation aircrew pursuant to Regulation (EC) No 216/2008 of the European Parliament and of the Council. Off J Eur Union. 2011, L 311:1-193.
22. Grout A, Leggat PA: Cabin crew health and fitness-to-fly: opportunities for re-evaluation amid COVID-19 . Travel Med Infect Dis. 2021, 40:101973. 10.1016/j.tmaid.2021.101973
23. Schneck K, Urva S: Population pharmacokinetics of the GIP/GLP receptor agonist tirzepatide . CPT Pharmacometrics Syst Pharmacol. 2024, 13:494-503. 10.1002/psp4.13099
24. Hall S, Isaacs D, Clements JN: Pharmacokinetics and clinical implications of semaglutide: a new glucagon-like peptide (GLP)-1 receptor agonist. Clin Pharmacokinet. 2018, 57:1529-38. 10.1007/s40262-018-0668-z
25. Enebo LB, Berthelsen KK, Kankam M, Lund MT, Rubino DM, Satylganova A, Lau DC: Safety, tolerability, pharmacokinetics, and pharmacodynamics of concomitant administration of multiple doses of cagrilintide with semaglutide 2·4 mg for weight management: a randomised, controlled, phase 1b trial. Lancet. 2021, 397:1736-48. 10.1016/S0140-6736(21)00845-X
26. Pratt E, Ma X, Liu R, et al.: Orforglipron (LY3502970), a novel, oral non-peptide glucagon-like peptide-1 receptor agonist: a phase 1a, blinded, placebo-controlled, randomized, single- and multiple-ascending-dose study in healthy participants. Diabetes Obes Metab. 2023, 25:2634-41. 10.1111/dom.15184
27. Overgaard RV, Navarria A, Ingwersen SH, Bækdal TA, Kildemoes RJ: Clinical pharmacokinetics of oral semaglutide: analyses of data from clinical pharmacology trials. Clin Pharmacokinet. 2021, 60:1335-48. 10.1007/s40262-021-01025-x
28. Alaminos-Torres A, Martínez-Álvarez JR, López-Ejeda N, Marrodán-Serrano MD: Atherogenic risk, anthropometry, diet and physical activity in a sample of Spanish commercial airline pilots. Int J Environ Res Public Health. 2022, 19:4128. 10.3390/ijerph19074128
29. Minoretti P, Santiago Sáez A, García Martín Á, Liaño Riera M, Gómez Serrano M: Carotid intima-media thickness, overweight, and poor sleep quality in commercial airline pilots: a cross-sectional study. Cureus. 2024, 16:e63552. 10.7759/cureus.63552

30. Minoretti P, Sáez AS, Martín ÁFG, Riera ML, Serrano MG, Emanuele E: Prevalence of hepatic steatosis and fibrosis in apparently healthy airline pilots: a transient elastography study. Hepatol Forum. 2024, 5:7-10. 10.14744/hf.2023.2023.0050
31. Johnson CY, Grajewski B, Lawson CC, MacDonald LA, Rocheleau CM, Whelan EA: Occupational physical demands and menstrual cycle irregularities in flight attendants and teachers. Occup Environ Med. 2024, 81:3-8. 10.1136/oemed-2023-109099
32. Wen CC, Cherian D, Schenker MT, Jordan AS: Fatigue and sleep in airline cabin crew: a scoping review . Int J Environ Res Public Health. 2023, 20:2652. 10.3390/ijerph20032652
33. Han SH, Lee GY, Hyun W, Kim Y, Jang JS: Obstructive sleep apnea in airline pilots during daytime sleep following overnight flights. J Sleep Res. 2021, 30:e13375. 10.1111/jsr.13375
34. Shao Y, Song Z, Fu L, Liu L, Chen Y, Zhou L, Huang J: Metabolic and anthropometric factors outperform psychomotor vigilance task in predicting obstructive sleep apnea in pilots: a LASSO-based analysis. Ear Nose Throat J. 2026, 1455613251413546. 10.1177/01455613251413546
35. Monin J, Guiu G, Reybard C, Bompaire F, Bisconte S, Perrier E, Manen O: Prevalence of sleep disorders in a large French cohort of aircrew members and risk of in-flight sleepiness. Sleep Med. 2022, 100:183-9. 10.1016/j.sleep.2022.08.013
36. Arora T, Al-Houqani M: Comparison of commonly used screening tools for determining obstructive sleep apnea amongst aviation employees. Sleep Med. 2021, 77:332-6. 10.1016/j.sleep.2020.07.008
37. Monin J, Rebiere E, Guiu G, Bisconte S, Perrier E, Manen O: Residual sleepiness risk in aircrew members with obstructive sleep apnea syndrome. Aerosp Med Hum Perform. 2023, 94:74-8. 10.3357/AMHP.6033.2023
38. Demir AE, Ata N, Suzen B, Dogan Yedikardaslar H, Gokkusu S, Ozsari L, Akkan T: Type 2 diabetes-related complications among commercial pilots: aeromedical considerations from a retrospective cohort. J Multidiscip Healthc. 2026, 19:572696. 10.2147/JMDH.S572696
39. Mendoza Mantilla DA, Serna AZ, Delgado AM, Mathers CH: Long-term post-bariatric surgical outcomes for aeromedical certification consideration. Aerosp Med Hum Perform. 2026, 97:524-33. 10.3357/AMHP.6765.2026
40. Gunduz SH, Metin S: Medical reasons for permanent and temporary disqualification of Turkish civil aviation pilots. Arch Environ Occup Health. 2024, 79:113-20. 10.1080/19338244.2024.2359416
41. Hohmann E, Pieterse R: Temporary incapacitation rates and permanent loss of medical license in commercial airline pilots. Aerosp Med Hum Perform. 2023, 94:113-21. 10.3357/AMHP.6071.2023
42. Gray G, Bron D, Davenport ED, et al.: Assessing aeromedical risk: a three-dimensional risk matrix approach . Heart. 2019, 105:s9-s16. 10.1136/heartjnl-2018-313052
43. Rienks R, Buwalda M, Bucx J, Dubois E, Wingelaar T, van Hulst R: Cardiovascular risk assessment in divers: toward safer diving. Undersea Hyperb Med. 2022, 49:355-65.
44. Rubino D, Abrahamsson N, Davies M, et al.: Effect of continued weekly subcutaneous semaglutide vs placebo on weight loss maintenance in adults with overweight or obesity: the STEP 4 randomized clinical trial. JAMA. 2021, 325:1414-25. 10.1001/jama.2021.3224
45. Vahora S, Shah V, Patel B: Semaglutide bioavailability: limitations, formulation innovation and future opportunities. Pharm Res. 2026, 43:2989-3010. 10.1007/s11095-026-04185-2
46. Knop FK, Aroda VR, do Vale RD, et al.: Oral semaglutide 50 mg taken once per day in adults with overweight or obesity (OASIS 1): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2023, 402:705-19. 10.1016/S0140-6736(23)01185-6
47. Rosenstock J, Yabe D, Cox D, et al.: Efficacy and safety of once-daily oral orforglipron compared with oral semaglutide in adults with type 2 diabetes (ACHIEVE-3): a multinational, multicentre, non-inferiority, open-label, randomised, phase 3 trial. Lancet. 2026, 407:1147-60. 10.1016/S0140-6736(26)00202-3
48. Min JS, Jo SJ, Lee S, Kim DY, Kim DH, Lee CB, Bae SK: A comprehensive review on the pharmacokinetics and drug-drug interactions of approved GLP-1 receptor agonists and a dual GLP-1/GIP receptor agonist. Drug Des Devel Ther. 2025, 19:3509-37. 10.2147/DDDT.S506957
49. Chen H, Ding Y, Shan Y: Post-marketing safety monitoring of tirzepatide: a pharmacovigilance study based on the FAERS database. Expert Opin Drug Saf. 2025, 24:959-67. 10.1080/14740338.2025.2468860
50. Air Line Pilots Association, International: what airline pilots need to know about weight-loss medications . (2025). Accessed: October 27, 2026: https://www.alpa.org/articles/2025/11/what-airline-pilots-need-to-know-about-weight-loss-medications.
51. Bækdal TA, Breitschaft A, Donsmark M, Maarbjerg SJ, Søndergaard FL, Borregaard J: Effect of various dosing conditions on the pharmacokinetics of oral semaglutide, a human glucagon-like peptide-1 analogue in a tablet formulation. Diabetes Ther. 2021, 12:1915-27. 10.1007/s13300-021-01078-y
52. van Hout M, Forte P, Jensen TB, Boschini C, Bækdal TA: Effect of various dosing schedules on the pharmacokinetics of oral semaglutide: a randomised trial in healthy subjects. Clin Pharmacokinet. 2023, 62:635-44. 10.1007/s40262-023-01223-9
53. Hauge C, Breitschaft A, Hartoft-Nielsen ML, Jensen S, Bækdal TA: Effect of oral semaglutide on the pharmacokinetics of thyroxine after dosing of levothyroxine and the influence of co-administered tablets on the pharmacokinetics of oral semaglutide in healthy subjects: an open-label, one-sequence crossover, single-center, multiple-dose, two-part trial. Expert Opin Drug Metab Toxicol. 2021, 17:1139-48. 10.1080/17425255.2021.1955856
54. Ma X, Liu R, Pratt EJ, Benson CT, Bhattachar SN, Sloop KW: Effect of food consumption on the pharmacokinetics, safety, and tolerability of once-daily orally administered orforglipron (LY3502970), a non-peptide GLP-1 receptor agonist. Diabetes Ther. 2024, 15:819-32. 10.1007/s13300-024-01554-1
55. Hiramoto B, McCarty TR, Lodhia NA, et al.: Quantified metrics of gastric emptying delay by glucagon-like peptide-1 agonists: a systematic review and meta-analysis with insights for periprocedural management. Am J Gastroenterol. 2024, 119:1126-40. 10.14309/ajg.0000000000002820
56. Friedrichsen M, Breitschaft A, Tadayon S, Wizert A, Skovgaard D: The effect of semaglutide 2.4 mg once weekly on energy intake, appetite, control of eating, and gastric emptying in adults with obesity. Diabetes Obes Metab. 2021, 23:754-62. 10.1111/dom.14280
57. Urva S, Coskun T, Loghin C, et al.: The novel dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 (GLP-1) receptor agonist tirzepatide transiently delays gastric emptying similarly to selective long-acting GLP-1 receptor agonists. Diabetes Obes Metab. 2020, 22:1886-91. 10.1111/dom.14110

58. Calvarysky B, Dotan I, Shepshelovich D, Leader A, Cohen TD: Drug-drug interactions between glucagon-like peptide 1 receptor agonists and oral medications: a systematic review. Drug Saf. 2024, 47:439-51. 10.1007/s40264-023-01392-3
59. Skelley JW, Swearengin K, York AL, Glover LH: The impact of tirzepatide and glucagon-like peptide 1 receptor agonists on oral hormonal contraception. J Am Pharm Assoc (2003). 2024, 64:204-211.e4. 10.1016/j.japh.2023.10.037
60. Jordy AB, Albayaty M, Breitschaft A, et al.: Effect of oral semaglutide on the pharmacokinetics of levonorgestrel and ethinylestradiol in healthy postmenopausal women and furosemide and rosuvastatin in healthy subjects. Clin Pharmacokinet. 2021, 60:1171-85. 10.1007/s40262-020-00976-x
61. Rodriguez PJ, Zhang V, Gratzl S, et al.: Discontinuation and reinitiation of dual-labeled GLP-1 receptor agonists among US adults with overweight or obesity. JAMA Netw Open. 2025, 8:e2457349. 10.1001/jamanetworkopen.2024.57349
62. Wilding JP, Batterham RL, Davies M, et al.: Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension. Diabetes Obes Metab. 2022, 24:1553-64. 10.1111/dom.14725
63. Aronne LJ, Sattar N, Horn DB, et al.: Continued treatment with tirzepatide for maintenance of weight reduction in adults with obesity: the SURMOUNT-4 randomized clinical trial. JAMA. 2024, 331:38-48. 10.1001/jama.2023.24945
64. Cengiz A, Wu CC, Lawley SD: Incretin mimetics for weight loss forgive nonadherence . Diabetes Obes Metab. 2025, 27:4109-17. 10.1111/dom.16438
65. Denny O, Baron J, Albanese NP: Navigating glucagon-like peptide receptor agonist reinitiation amid access barriers: an adverse drug event case report. J Pharm Pract. 2024, 37:1410-3. 10.1177/08971900241256775
66. Lincoff AM, Brown-Frandsen K, Colhoun HM, et al.: Semaglutide and cardiovascular outcomes in obesity without diabetes. N Engl J Med. 2023, 389:2221-32. 10.1056/NEJMoa2307563
67. McGuire DK, Marx N, Mulvagh SL, et al.: Oral semaglutide and cardiovascular outcomes in high-risk type 2 diabetes. N Engl J Med. 2025, 392:2001-12. 10.1056/NEJMoa2501006
68. Nicholls SJ, Pavo I, Bhatt DL, et al.: Cardiovascular outcomes with tirzepatide versus dulaglutide in type 2 diabetes. N Engl J Med. 2025, 393:2409-20. 10.1056/NEJMoa2505928
69. Galli M, Benenati S, Laudani C, et al.: Cardiovascular effects and tolerability of GLP-1 receptor agonists: a systematic review and meta-analysis of 99,599 patients. J Am Coll Cardiol. 2025, 86:1805-19. 10.1016/j.jacc.2025.08.027
70. Kosiborod MN, Deanfield J, Pratley R, et al.: Semaglutide versus placebo in patients with heart failure and mildly reduced or preserved ejection fraction: a pooled analysis of the SELECT, FLOW, STEP-HFpEF, and STEP-HFpEF DM randomised trials. Lancet. 2024, 404:949-61. 10.1016/S0140-6736(24)01643-X
71. Packer M, Zile MR, Kramer CM, et al.: Tirzepatide for heart failure with preserved ejection fraction and obesity. N Engl J Med. 2025, 392:427-37. 10.1056/NEJMoa2410027
72. Karakasis P, Vlachos K, Antoniadis AP, Siontis KC, Patoulias D, Fragakis N, Mantzoros CS: Effect of GLP-1 receptor agonists and co-agonists on atrial fibrillation risk in overweight or obesity: systematic review and meta-analysis of randomized controlled trials. Metabolism. 2026, 175:156463. 10.1016/j.metabol.2025.156463
73. Kennedy C, Hayes P, Cicero AF, et al.: Semaglutide and blood pressure: an individual patient data meta-analysis. Eur Heart J. 2024, 45:4124-34. 10.1093/eurheartj/ehae564
74. Kosiborod MN, Abildstrøm SZ, Borlaug BA, et al.: Semaglutide in patients with heart failure with preserved ejection fraction and obesity. N Engl J Med. 2023, 389:1069-84. 10.1056/NEJMoa2306963
75. Rubino D, Bjorner JB, Rathor N, et al.: Effect of semaglutide 2.4 mg on physical functioning and weight- and health-related quality of life in adults with overweight or obesity: patient-reported outcomes from the STEP 1-4 trials. Diabetes Obes Metab. 2024, 26:2945-55. 10.1111/dom.15620
76. Malhotra A, Grunstein RR, Fietze I, et al.: Tirzepatide for the treatment of obstructive sleep apnea and obesity. N Engl J Med. 2024, 391:1193-205. 10.1056/NEJMoa2404881
77. Kanu C, Shinde S, Chakladar S, Dennehy EB, Weaver TE, Poon JL, Malhotra A: Effect of tirzepatide treatment on patient-reported outcomes among SURMOUNT-OSA participants with obstructive sleep apnea and obesity. Sleep Med. 2025, 134:106719. 10.1016/j.sleep.2025.106719
78. Li M, Lin H, Yang Q, Zhang X, Zhou Q, Shi J, Ge F: Glucagon-like peptide-1 receptor agonists for the treatment of obstructive sleep apnea: a meta-analysis. Sleep. 2025, 48:280. 10.1093/sleep/zsae280
79. European Union Aviation Safety Agency: pilot and ATCO aeromedical fitness, diabetes mellitus (EASA.2022.C20). D7.4 final report. (2025). Accessed: October 25, 2026: https://www.easa.europa.eu/en/downloads/142676/en.
80. Nauck MA, Mirna AE, Quast DR: Meta-analysis of head-to-head clinical trials comparing incretin-based glucose-lowering medications and basal insulin: an update including recently developed glucagon-like peptide-1 (GLP-1) receptor agonists and the glucose-dependent insulinotropic polypeptide/GLP-1 receptor co-agonist tirzepatide. Diabetes Obes Metab. 2023, 25:1361-71. 10.1111/dom.14988
81. Del Prato S, Kahn SE, Pavo I, et al.: Tirzepatide versus insulin glargine in type 2 diabetes and increased cardiovascular risk (SURPASS-4): a randomised, open-label, parallel-group, multicentre, phase 3 trial. Lancet. 2021, 398:1811-24. 10.1016/S0140-6736(21)02188-7
82. Klausen MK, Justesen SK, Pedersen JN, et al.: Once-weekly semaglutide versus placebo in patients with alcohol use disorder and comorbid obesity: a randomised, double-blind, placebo-controlled trial. Lancet. 2026, 407:1687-98. 10.1016/S0140-6736(26)00305-3
83. Hendershot CS, Bremmer MP, Paladino MB, et al.: Once-weekly semaglutide in adults with alcohol use disorder: a randomized clinical trial. JAMA Psychiatry. 2025, 82:395-405. 10.1001/jamapsychiatry.2024.4789
84. Lähteenvuo M, Tiihonen J, Solismaa A, Tanskanen A, Mittendorfer-Rutz E, Taipale H: Repurposing semaglutide and liraglutide for alcohol use disorder. JAMA Psychiatry. 2025, 82:94-8. 10.1001/jamapsychiatry.2024.3599
85. Wharton S, Calanna S, Davies M, et al.: Gastrointestinal tolerability of once-weekly semaglutide 2.4 mg in adults with overweight or obesity, and the relationship between gastrointestinal adverse events and weight loss. Diabetes Obes Metab. 2022, 24:94-105. 10.1111/dom.14551
86. Rubino DM, Pedersen SD, Connery L, et al.: Gastrointestinal tolerability and weight reduction associated with tirzepatide in adults with obesity or overweight with and without type 2 diabetes in the SURMOUNT-1

to -4 trials. Diabetes Obes Metab. 2025, 27:1826-35. 10.1111/dom.16176

87. Alkabbani W, Crisafulli S, Paik JM, et al.: Glucagon-like peptide-1 based therapies and the risk of severe gastrointestinal motility adverse events: a cohort study. Diabetes Obes Metab. 2026, 28:7494-504. 10.1111/dom.70963
88. Elkin J, Rele S, Sumithran P, et al.: Association between glucagon-like peptide-1 receptor agonist use and peri-operative pulmonary aspiration: a systematic review and meta-analysis. Anaesthesia. 2025, 80:846-58. 10.1111/anae.16601
89. Moll H, Frey E, Gerber P, et al.: GLP-1 receptor agonists for weight reduction in people living with obesity but without diabetes: a living benefit-harm modelling study. EClinicalMedicine. 2024, 73:102661. 10.1016/j.eclinm.2024.102661
90. Pieber TR, Svehlikova E, Urva S, et al.: Counterregulatory response to hypoglycemia during a hypoglycemic clamp in people with type 2 diabetes treated with tirzepatide. Front Endocrinol (Lausanne). 2025, 16:1627947. 10.3389/fendo.2025.1627947
91. Nogueira A, Rassi TN, Iqbal A, et al.: Association between GLP-1 receptor agonists and ischemic optic neuropathy: a meta-analysis. Diabetes Care. 2026, 49:724-9. 10.2337/dc25-1238
92. Buckley AJ, Tan GD, Gruszka-Goh M, Scanlon PH, Ansari I, Suliman SG: Early worsening of diabetic retinopathy in individuals with type 2 diabetes treated with tirzepatide: a real-world cohort study. Diabetologia. 2025, 68:2069-76. 10.1007/s00125-025-06466-8
93. Ebrahimi P, Batlle JC, Ayati A, et al.: Suicide and self-harm events with GLP-1 receptor agonists in adults with diabetes or obesity: a systematic review and meta-analysis. JAMA Psychiatry. 2025, 82:888-95. 10.1001/jamapsychiatry.2025.0091
94. Schoretsanitis G, Weiler S, Barbui C, Raschi E, Gastaldon C: Disproportionality analysis from World Health Organization data on semaglutide, liraglutide, and suicidality. JAMA Netw Open. 2024, 7:e2423385. 10.1001/jamanetworkopen.2024.23385
95. Minnock SD, Thomas MJ: Underreporting of depression in Australian commercial pilots . Aerosp Med Hum Perform. 2024, 95:821-5. 10.3357/AMHP.6467.2024
96. He L, Wang J, Ping F, et al.: Association of glucagon-like peptide-1 receptor agonist use with risk of gallbladder and biliary diseases: a systematic review and meta-analysis of randomized clinical trials. JAMA Intern Med. 2022, 182:513-9. 10.1001/jamainternmed.2022.0338
97. Xie Y, Choi T, Al-Aly Z: GLP-1 receptor agonists and risk of all cause and cause specific acute pancreatitis: target trial emulation. BMJ Med. 2026, 5:e002183. 10.1136/bmjmed-2025-002183
98. Dong S, Sun C: Can glucagon-like peptide-1 receptor agonists cause acute kidney injury? An analytical study based on post-marketing approval pharmacovigilance data. Front Endocrinol (Lausanne). 2022, 13:1032199. 10.3389/fendo.2022.1032199
99. Liang CS, Hsu CW, Chen JJ, et al.: Differential acute kidney injury profiles of GLP-1RAs and SGLT2is: a network meta-analysis. Int J Mol Sci. 2026, 27:4137. 10.3390/ijms27094137
100. Look M, Dunn JP, Kushner RF, et al.: Body composition changes during weight reduction with tirzepatide in the SURMOUNT-1 study of adults with obesity or overweight. Diabetes Obes Metab. 2025, 27:2720-9. 10.1111/dom.16275
101. Eisa N, Barood O: Lean mass changes with incretin therapy versus lifestyle intervention: a systematic review and meta-analysis of randomised controlled trials. Diabetes Obes Metab. 2026, 28:4818-27. 10.1111/dom.70666
102. Zhang Y, Zhang C, Gong X, Cheng P, Fu H, Diao L, Song C: Effect of glucagon-like peptide-1 receptor agonists on heart rate in non-diabetic individuals with overweight or obesity: a systematic review and pairwise and network meta-analysis of randomized controlled trials. Eur J Med Res. 2026, 31:318. 10.1186/s40001-026-03933-9
103. Toraih EA, Alenezy A, Hussein MH, et al.: The risk of vestibular disorders with semaglutide and tirzepatide: findings from a large real-world cohort. Biomedicines. 2025, 13:1049. 10.3390/biomedicines13051049
104. Xie Y, Choi T, Al-Aly Z: Mapping the effectiveness and risks of GLP-1 receptor agonists . Nat Med. 2025, 31:951-62. 10.1038/s41591-024-03412-w
105. Chen H, Liu S, Gao S, et al.: Pharmacovigilance analysis of neurological adverse events associated with GLP-1 receptor agonists based on the FDA Adverse Event Reporting System. Sci Rep. 2025, 15:18063. 10.1038/s41598-025-01206-9
106. Ashraf AR, Mackey TK, Vida RG, et al.: Multifactor quality and safety analysis of semaglutide products sold by online sellers without a prescription: market surveillance, content analysis, and product purchase evaluation study. J Med Internet Res. 2024, 26:e65440. 10.2196/65440
107. McCall KL, Mastro Dwyer KA, Casey RT, et al.: Safety analysis of compounded GLP-1 receptor agonists: a pharmacovigilance study using the FDA adverse event reporting system. Expert Opin Drug Saf. 2026, 25:581-8. 10.1080/14740338.2025.2499670
108. Simonsen E, Lund LC, Ernst MT, et al.: Use of semaglutide and risk of non-arteritic anterior ischemic optic neuropathy: a Danish-Norwegian cohort study. Diabetes Obes Metab. 2025, 27:3094-103. 10.1111/dom.16316
109. Ueda P, Söderling J, Wintzell V, et al.: GLP-1 receptor agonist use and risk of suicide death . JAMA Intern Med. 2024, 184:1301-12. 10.1001/jamainternmed.2024.4369
110. Shapiro SB, Yin H, Yu OH, Rej S, Suissa S, Azoulay L: Glucagon-like peptide-1 receptor agonists and risk of suicidality among patients with type 2 diabetes: active comparator, new user cohort study. BMJ. 2025, 388:e080679. 10.1136/bmj-2024-080679
111. UK Civil Aviation Authority: guidance on the use of over-the-counter and direct-to-consumer peptide products, version 1.0. (2026). Accessed: October 25, 2026: https://www.caa.co.uk/media/tyehyb1t/20261013-v10-guidance-on-the-use-of-peptides.pdf.
112. Muhm JM, Rock PB, McMullin DL, et al.: Effect of aircraft-cabin altitude on passenger discomfort . N Engl J Med. 2007, 357:18-27. 10.1056/NEJMoa062770
113. Hinninghofen H, Musial F, Kowalski A, Enck P: Gastric emptying effects of dietary fiber during 8 hours at two simulated cabin altitudes. Aviat Space Environ Med. 2006, 77:121-3.
114. Nomura S, Sumi D, Nagatsuka H, Suzuki T, Goto K: Effects of endurance exercise under hypoxic conditions on the gastric emptying rate and intestinal cell damage. Eur J Appl Physiol. 2025, 125:25-35.

10.1007/s00421-024-05523-1

115. Gatterer H, Roche J, Turner R, et al.: Changes in body mass, appetite-related hormones, and appetite sensation in women during 4 days of hypobaric hypoxic exposure equivalent to 3,500-m altitude. J Appl Physiol (1985). 2023, 134:133-41. 10.1152/japplphysiol.00369.2022
116. Li C, Xu J, Yin D, Zhang Y, Shan D, Jiang X, Shang L: Prevalence and trigger factors of functional gastrointestinal disorders among male civil pilots in China. Sci Rep. 2021, 11:2021. 10.1038/s41598-021-81825-0
117. Zubac D, Buoite Stella A, Morrison SA: Up in the air: evidence of dehydration risk and long-haul flight on athletic performance. Nutrients. 2020, 12:2574. 10.3390/nu12092574
118. Winzeler B, da Conceição I, Refardt J, Sailer CO, Dutilh G, Christ-Crain M: Effects of glucagon-like peptide-1 receptor agonists on fluid intake in healthy volunteers. Endocrine. 2020, 70:292-8. 10.1007/s12020-020-02394-2
119. Gandhi A, Phyu EM, Koom-Dadzie K, Dickson KB, Halm J: GLP-1 receptor agonists at the crossroads of circadian biology, sleep, and metabolic disease. Int J Mol Sci. 2026, 27:2853. 10.3390/ijms27062853
120. Zhang E, Li H, Han H, et al.: Dietary rhythmicity and mental health among airline personnel . JAMA Netw Open. 2024, 7:e2422266. 10.1001/jamanetworkopen.2024.22266
121. Khan Sullivan AM, Isherwood CM, Hassanin H, Skene DJ, van der Veen DR: Diurnal variation and impairment of postprandial glucose-insulin responses and lipid rhythms in simulated shift work. Nutr Bull. 2026, 51:353-65. 10.1111/nbu.70060
122. Elmenhorst EM, Rooney D, Benderoth S, Wittkowski M, Wenzel J, Aeschbach D: Sleep-induced hypoxia under flight conditions: implications and countermeasures for long-haul flight crews and passengers. Nat Sci Sleep. 2022, 14:193-205. 10.2147/NSS.S339196
123. Yacawych WT, Wang Y, Zhou G, et al.: A single dorsal vagal complex circuit mediates the aversive and anorectic responses to GLP1R agonists. J Clin Invest. 2026, 136:e193743. 10.1172/JCI193743
124. Borner T, Geisler CE, Fortin SM, et al.: GIP receptor agonism attenuates GLP-1 receptor agonist-induced nausea and emesis in preclinical models. Diabetes. 2021, 70:2545-53. 10.2337/db21-0459
125. Tu L, Lu Z, Ngan MP, et al.: The brain-penetrating, orally bioavailable, ghrelin receptor agonist HM01 ameliorates motion-induced emesis in Suncus murinus (house musk shrew). Br J Pharmacol. 2020, 177:1635-50. 10.1111/bph.14924
126. Federal Aviation Administration: weight loss medication. Guide for aviation medical examiners . (2026). Accessed: October 25, 2026: https://www.faa.gov/ame_guide/media/Weight_loss_pharm.pdf.
127. European Union Aviation Safety Agency: easy access rules for medical requirements (Regulation (EU) No 1178/2011). AMC1 MED.B.025, metabolic and endocrine system. (2026). Accessed: November 4, 2026: https://www.easa.europa.eu/en/document-library/easy-access-rules/easy-access-rules-aircrew .
128. European Union Aviation Safety Agency: pilot and ATCO aeromedical fitness, diabetes mellitus (EASA.2022.C20). D7.3 aeromedical examiner training material, version 1. (2025). Accessed: October 27, 2026: https://www.easa.europa.eu/en/downloads/142673/en.
129. Civil Aviation Safety Authority: obesity. (2021). Accessed: October 27, 2026: https://www.casa.gov.au/licences-and-certificates/medical-professionals/dames-clinical-practice-guidelines/obesity.
130. Transport Canada: Handbook for civil aviation medical examiners (TP 13312) . (2019). Accessed: October 25, 2026: https://tc.canada.ca/en/aviation/publications/handbook-civil-aviation-medical-examiners-tp-13312.
131. Shepherd AI, James TJ, Gould AA, et al.: Impact of nocturnal hypoxia on glycaemic control, appetite, gut microbiota and inflammation in adults with type 2 diabetes mellitus: a single-blind cross-over trial. J Physiol. 2024, 602:5835-54. 10.1113/JP285322
132. Clavé P, Fabries P, Beauchamps V, et al.: Isolated and combined effects of moderate normobaric hypoxia and sleep restriction on energy intake and food reward. Int J Sport Nutr Exerc Metab. 2025, 35:51-60. 10.1123/ijsnem.2024-0146
133. Wilson D, Driller M, Johnston B, Gill N: The prevalence and distribution of health risk factors in airline pilots: a cross-sectional comparison with the general population. Aust N Z J Public Health. 2022, 46:572-80. 10.1111/1753-6405.13231
134. McNeely E, Gale S, Tager I, Kincl L, Bradley J, Coull B, Hecker S: The self-reported health of U.S. flight attendants compared to the general population. Environ Health. 2014, 13:13. 10.1186/1476-069X-13-13
135. Sinha B, Ghosal S: The effects of glucagon-like peptide-1 receptor agonists (GLP1-RAs) on alcohol-related outcomes: a systematic review and meta-analysis. Addict Sci Clin Pract. 2025, 21:8. 10.1186/s13722-025-00637-z
136. Cai CX, Hribar M, Baxter S, et al.: Semaglutide and nonarteritic anterior ischemic optic neuropathy . JAMA Ophthalmol. 2025, 143:304-14. 10.1001/jamaophthalmol.2024.6555
137. Abdelaal A, Abu Serhan H, Alsaadi M, Yaldo L, Gaier ED, Elhusseiny AM: Semaglutide and the risk of nonarteritic ischemic optic neuropathy: a systematic review and certainty of evidence meta-analysis. Ophthalmology. 2026, 133:799-810. 10.1016/j.ophtha.2026.02.013