

Syncope in Commercial Pilots and New Regulatory Guidance

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- INTRODUCTION:** Syncope is both incapacitating and unpredictable, presenting a significant challenge in aircrew assessment. Previous UK Civil Aviation Authority (CAA) guidance lacked transparency and relied heavily on specialist in-house cardiology and neurology opinion. A new algorithm was developed which elaborated and formalized the decision-making process. An analysis of its impact on historic cases was undertaken to ensure it aligned with previous certificatory outcomes.
- METHODS:** The medical literature on syncope and the approaches of other national aviation authorities were reviewed to help inform the development of a new algorithm. Using syncope cases in the CAA database, regulatory outcomes generated using the new algorithm were compared with previous decisions in terms of time off from flying (TOF) and Operational Multi-Crew Limitation (OML) duration.
- RESULTS:** There were 40 historic syncope cases (25 existing certificate holders, 15 initial applicants) which were ‘reassessed’ using the new algorithm. The mean TOF for existing pilots using the new algorithm was 7.1 ± 9.8 (mean \pm SD) vs. 4.2 ± 3.5 mo under the old guidance with an OML duration of 21.4 ± 34.9 vs. 24.5 ± 25.2 mo. One less initial applicant experienced a delay to certification. Four cases with underlying pathology were detected using old and new guidance.
- DISCUSSION:** The reassessment of cases showed no statistically significant difference in TOF and OML duration; this is a positive finding from a regulatory perspective, enabling algorithm-led decision-making with less reliance on in-house expertise. A similar approach may be useful in future updates to other areas of regulatory practice.
- KEYWORDS:** loss of consciousness, guidance, aircrew, assessment, algorithm.

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Syncope is both incapacitating and unpredictable and is a major aeromedical and regulatory concern, whatever the underlying mechanism. It is, however, a relatively common symptom in the general population and accounts for up to 3% of attendances at emergency departments in the United States, and up to 6% of all hospital admissions.^{6,10} Aircrew experiencing a syncopal event usually require a period of time off flying (TOF) and the application of an Operational Multi-Crew Limitation (OML) which permits flying only as or with a qualified copilot, in order to reduce the risks associated with recurrence. Determining the duration of these risk-mitigating measures is challenging.

The definition of syncope implies an episode of transient loss of consciousness which is both rapid in onset and in resolution. A decrease in cerebral blood flow, usually precipitated by a fall in systemic blood pressure, almost always results in a physical collapse followed by an immediate and spontaneous

recovery. The term ‘global cerebral hypoperfusion’²⁵ might avoid confusion between other forms of ‘collapse’ such as seizure or stroke by unmistakably defining the physiological process involved. In aircrew, the early detection of any underlying pathology, as well as the management of what might be considered a ‘benign event’ in many cases in the general population, is crucial for flight safety. It is estimated that there are between 18.1 and 39.7 events per 1000 patient years in the general population and a cumulative incidence of at least one syncopal

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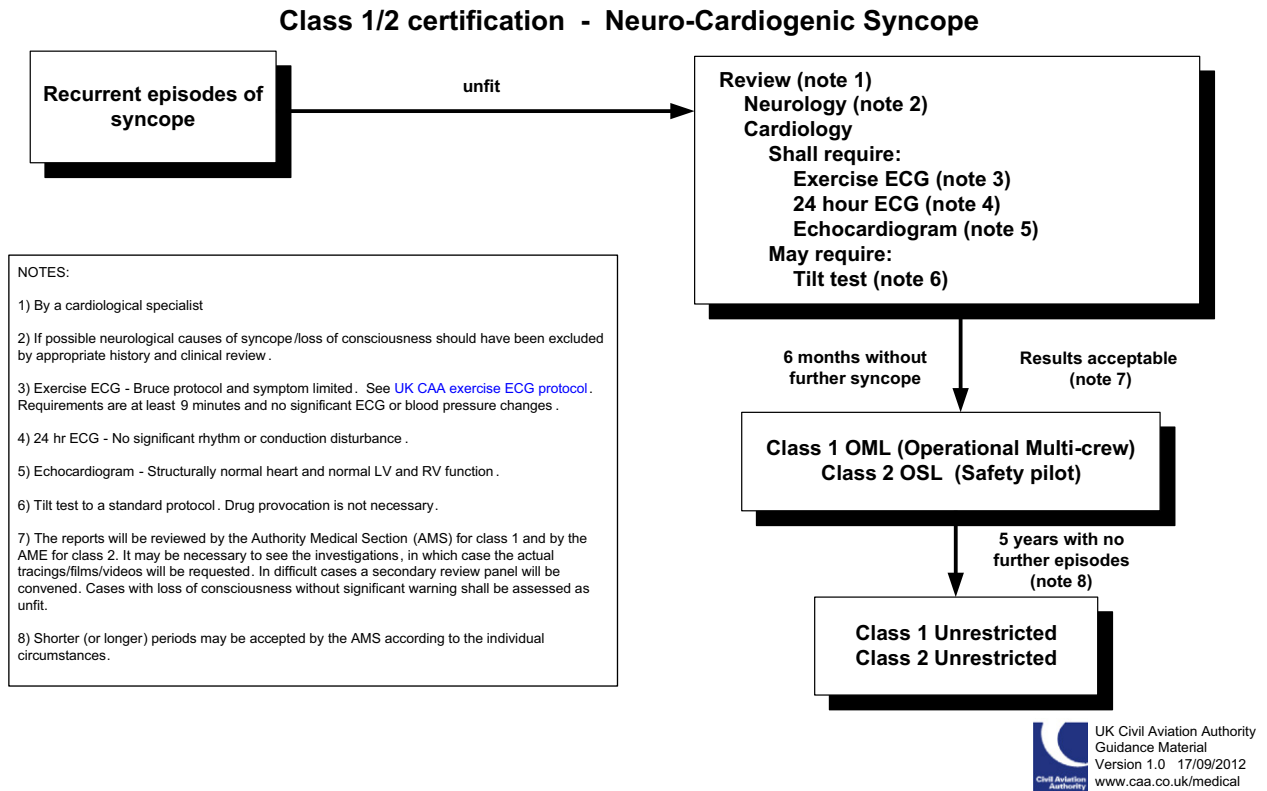


Fig. 1. Old UK Civil Aviation Authority guidance for the assessment of syncope in Class 1/2 pilots (1 = commercial; 2 = private pilot).

episode in 42% of women, and 32% of men by the age of 60.^{9,21,25} Importantly, syncope has a relatively high recurrence rate, with 21% of those who have had one event reporting further events, and just under 1% reporting three or more recurrences.²³

Previous UK CAA guidance on the management of syncope in aircrew, illustrated in Fig. 1, was based mostly on the requirements for investigation stipulated in the aircrew medical regulations and did not address the rationale behind the assessment process. The old algorithm provided a limited range of outcomes in terms of TOF and OML duration, resulting in a majority of decisions which departed from the default recommendations. The aim of developing new guidance was to formalize the decision-making process, making it clear, transparent, consistent and, where possible, evidence-based. This would clarify the process for pilots presenting with syncope, as well as their aeromedical examiners and treating physicians, informing them of the investigations required and the likely regulatory decision outcomes based on the specific circumstances of their case. Having developed the new guidance, the algorithm would be tested using historic cases of pilots with syncope to ensure that future regulatory decisions made using these prespecified parameters would not significantly diverge from decisions made by UK CAA Medical Assessors supported by in-house cardiology and neurology expertise. If the algorithm were found to be sufficiently reliable, this would potentially simplify the decision-making processes and make them less resource intensive.

METHODS

The medical literature was searched for relevant clinical studies relating to the incidence, prevalence, recurrence rate, management and the investigation of syncope. A review of papers published in English was then conducted with databases including PubMed, MEDLINE, Web of Science and Library of Congress. A search for website guidance from other national aviation authorities was carried out and the approach to the management of syncope of another national transport regulatory body, the UK Driver and Vehicle Licensing Agency (DVLA), was also reviewed.²⁷ This is common UK CAA practice when reviewing guidance material, particularly in the absence of comparator guidance material from other aviation regulatory authorities. Using the old guidance as a starting point, the new algorithm was then developed.

Subjects

The UK CAA medical department maintains an electronic database of all pilot medical records, with approximately 20,000 current European Union (EU) Class 1 (commercial) medical certificate holders. The system allows for the recording of diagnostic read-codes as well as 'free text' comments made by an Aeromedical Examiner (AME) or Medical Assessor of the Medical Licensing Authority. This database was searched using COGNOS® software to identify pilots with a read code or free text on their electronic record of

syncope, vasovagal, collapse, faint or loss of consciousness, over a seven-year period (January 1, 2010–December 31, 2017) prior to the development and introduction of the new algorithm. These search terms were identified both empirically and by retrospectively reviewing known cases of syncope to identify the terminology or descriptive terms most frequently used. Collection and use of data was retrospective, anonymized and compliant with all CAA policies on data protection and was considered exempt from research ethic committee approval.

The exclusion criteria included all private pilots (Class 2), cases where the records/medical reports showed that the event diagnosed was not syncopal, such as a loss of consciousness related to head trauma or an epileptic fit, cases with an absence of medical records or insufficient history to support a diagnosis of syncope and cases which had not been reviewed by a CAA Medical Assessor and CAA cardiologist. Cases where pathology was identified from the outset at presentation, e.g., heart block requiring a permanent pacemaker, would automatically follow a different assessment pathway at the point of diagnosis but would still be counted.

Procedure

These 40 cases were divided into existing license holders and initial applicants. All existing license holders were 'reassessed' on paper using the new algorithm. An attempt to apply the new algorithm to the initial applicants, in the same way as existing license holders, resulted in no meaningful comparison due to the considerable variability in time course from the syncopal event(s) to the point of aeromedical assessment at the Authority, so they were considered separately. An Excel spreadsheet was created to capture data from each case, including a description of the event, any underlying pathology, recurrence, precipitants/mitigators and investigations performed. Before applying the new algorithm to the existing certificate-holder cases, the definition of recurrence was established as an individual having more than one distinct episode of syncope, greater than 24 h apart. This meant that individuals who 'fainted' more than once in quick succession or as part of a single 'illness', e.g., gastroenteritis, were classed as having had one event. The final certificatory decision, the TOF and the OML duration under both the old and the new algorithm was tabulated and compared.

Statistical Analysis

As the data relating to the TOF and OML duration were not normally distributed, the descriptive median and upper and lower quartile values were calculated. The significance of differences relating to the TOF and OML duration data using the two assessment protocols was analyzed using the Wilcoxon signed-rank test. This is a nonparametric test used when the difference between pairs of data is nonnormally distributed. It can be used to compare two sets of values which come from the same participant, in this case, the duration of TOF and OML under the old and new guidance.

RESULTS

When the literature on syncope was reviewed, in particular the randomized control trials of intervention, it became clear that the entry criteria for many of these studies identified only those individuals with a very high incidence of syncope, e.g., three attacks in the preceding year which would be very unlikely in a commercial pilot population.¹⁹ The results, therefore, were largely not applicable to our pilot population. Nonetheless, from these data, it was clear that: 1) adequate hydration, avoidance measures, and physical counter-maneuvers used to abort an attack reduced, but did not abolish syncope;²⁸ and 2) the time from the last syncopal episode, rather than lifetime event rate, was a better predictor of future recurrences. This was therefore factored into decisions about required TOF following an event.²⁴ Studies looking for Poisson distribution and evidence of clusters of syncope have also been carried out, but the results have been inconclusive.¹⁶

A search of national aviation authority websites revealed limited guidance for the assessment of syncope in aircrew in other states. The FAA provides limited syncope specific guidance and refers AMEs to the coronary heart disease protocol with the addition of an echocardiogram, 24-h Holter and carotid ultrasounds. They also advise that cases of recurrence, or syncope which is not satisfactorily explained, should be deferred to the FAA for a decision.⁸ The Canadian Aviation Regulations similarly stipulate that aircrew must not suffer from any disturbance of consciousness without satisfactory explanation. Transport Canada have no specific policies for syncope assessment and cases are assessed on an individual basis with Aviation Medical Review Boards being held to facilitate certificatory decision making in some cases.³ CASA (Australia) provides more detailed guidance focusing on medical report specifications and investigations, and provides some insight into favorable/unfavorable indicators of assessment outcomes.⁴ The CAA of New Zealand also recognizes the significance of episodes of loss of consciousness, including syncope as a result of cardiac pathology, but there is no indication of more general syncope assessment pathways.²⁶ So while syncope has been identified as a condition likely to require investigation in these states, there is little or no visibility of assessment criteria or likely certificatory outcomes in terms of TOF and possible restrictions. No information relating to syncope assessment was readily available from other national aviation authority websites, including those in Europe.

With no international regulatory comparatives and a lack of randomized control data relevant to the pilot population, a more pragmatic approach to assessment was necessary. Using the paradigm adopted by the UK Driver Vehicle Licensing Authority (DVLA) of assessing the '3 P's' (posture, provocation, and prodrome),²⁷ but also considering whether the event occurred in an aviation setting, the new algorithm was developed, see **Fig. 2**.

Following development of the algorithm, a total of 290 cases were returned after the initial medical records search, from which 108 private pilots were excluded. Of the remaining

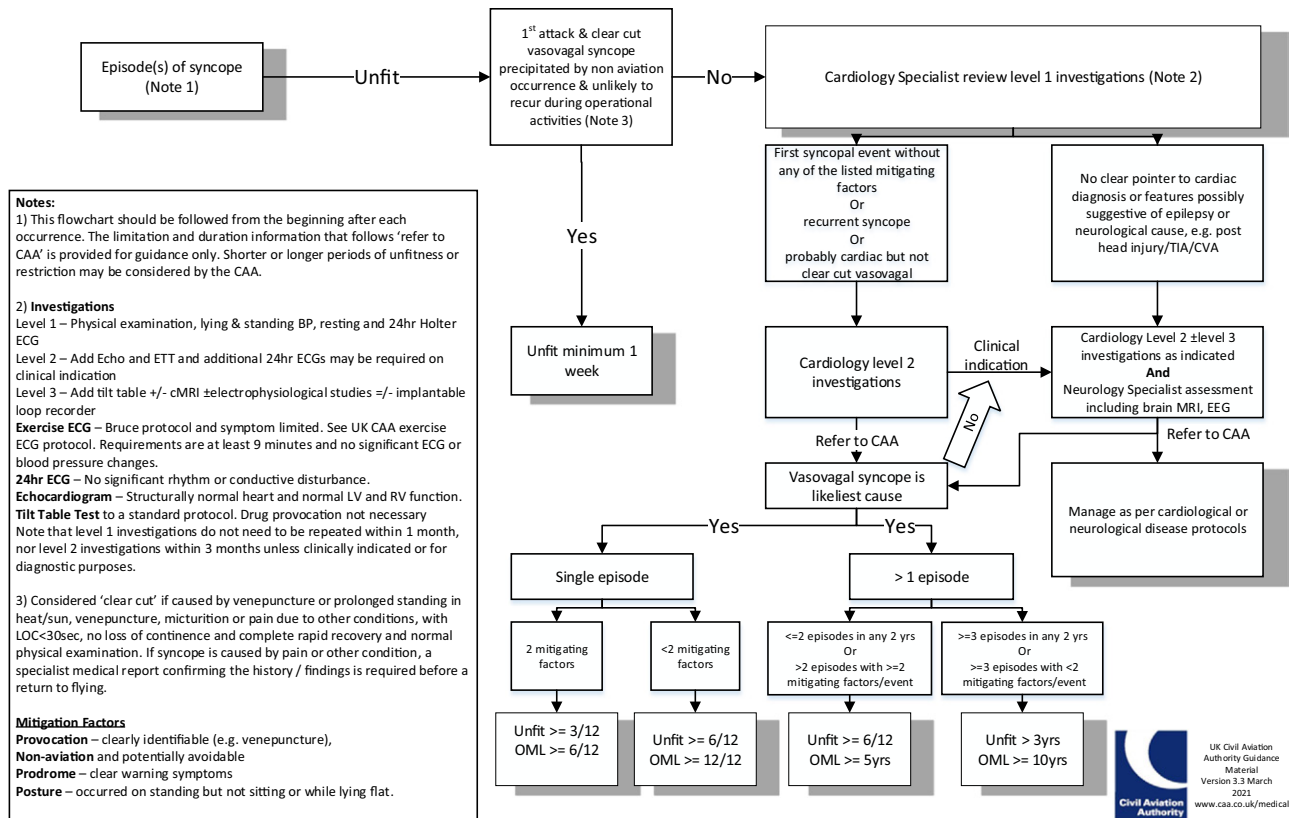


Fig. 2. New UK Civil Aviation Authority algorithm for the assessment of syncope in UK Class 1 (commercial) pilots.

182 cases, 40 cases had medical reports supporting a diagnosis of syncope and had been reviewed at the Medical Licensing Authority by both a Medical Assessor and a cardiologist. Of these, 25 were existing certificate holders and 15 were initial applicants; 36 (90%) were assessed as having vasovagal syncope, without evidence of underlying pathology. This included all subcategories of vasovagal syncope such as situational syncope, e.g., micturition syncope or episodes associated with venepuncture and postural syncope. Of the 25 existing license holders, 4 (16%) were excluded after pathology was identified, leaving 21 cases. Of the four pathology cases excluded, all were existing certificate holders, three were diagnosed with structural heart disease (conducting disease), and one was an anatomical abnormality which induced arrhythmia. Ten individuals experienced an episode of syncope which occurred on the flight deck. Of these, seven were first syncopal attacks and three were recurrences. One of the ten cases demonstrated underlying pathology, and this was also one of the three recurrence cases.

Of the 36 cases, 21 (58%) had true isolated episodes of syncope. Nineteen (53%) individuals had at least two or more events and in all but one of these cases, the events occurred prior to the initial assessment made by the Authority. The one case who had further syncopal events after returning to flying had an OML restriction in place following the previous assessment at the time of recurrence. One individual was unusual in having five episodes of syncope over 6 yr while remaining

fit to fly but had not declared it until the last episode. Two of the four cases where pathology was identified had EKG changes and therefore the simplest of tests was sufficient to trigger further investigations resulting in the early detection of pathology.

The median and modal age of an event was 26 yr, with a mean age of 31.9. The youngest event recorded was at 13 yr of age, the oldest at 61. There was no significant increase in investigation burden when applying the new algorithm versus the old. Two cases would have had fewer investigations, six would have had more and thirty-two the same number. It was apparent that supine and standing blood pressure was not routinely checked or documented; while this was not required under the old guidance, it is stipulated in the new algorithm. The TOF and the duration of the OML using each of the two algorithms are displayed in **Table I**. These data were then displayed in both table and graph form to show the median and upper and lower quartiles, see **Table II** and **Fig. 3**.

Using the new algorithm, the results showed no significant difference in TOF: 7.1 ± 9.8 vs. 4.2 ± 3.5 mo ($P = 0.696$); or the OML duration: 21.4 ± 34.9 vs. 24.5 ± 25.2 mo ($P = 0.158$). Of the 40 cases, 15 were initial applicants. Of these, 11 had experienced recurrent syncope and 4 had single episodes only. Under the old guidance, all 15 gained certifications, with 12 being assessed as fit immediately and 3 with a delay. Using the new algorithm, all 15 would also gain certification, with 13 immediately and 2 after a delay.

Table I. Comparison of Time Off Flying (TOF) and Operational Multi-Crew Limitation (OML) Duration Between the Old Policy and the New Algorithm (in months, mo).

CASE	TOF OLD POLICY (mo)	TOF NEW ALGORITHM (mo)	OML OLD POLICY (mo)	OML NEW ALGORITHM (mo)
1	4	6	18	12
2	6	3	12	6
3	12	6	60	12
5	3	3	48	12
6	4	3	6	6
7	3	0.25	0	0
8	1.5	0.25	7	0
9	3	6	6	12
10	1.5	0.25	0	0
11	1.5	3	3	6
12	15	6	60	12
13	0.75	6	0	12
14	3	6	24	12
15	1.5	3	60	6
16	4	6	18	12
17	6	36	60	120
18	3	6	6	60
19	4	6	2	12
21	3	3	60	6
22	6	36	60	120
24	3	6	6	12

DISCUSSION

The new guidance was designed to formalize the assessment process for syncope and to clearly document the factors likely to affect a pilot’s certification. The old algorithm only specified a 6-mo TOF penalty and an OML duration of 5 yr, though shorter or longer periods were acceptable according to the individual circumstances. In reality, a majority of decisions departed from the default position and were reached ‘outside’ the scope of the algorithm, based on a detailed assessment by a Medical Assessor, supported by in-house cardiology and neurology expertise. By drawing on this in-house expertise in designing the new algorithm, and incorporating the factors likely to influence certification (number of syncopal events and mitigating circumstances), the new algorithm better reflects the range of likely certificatory outcomes, including possible TOF penalties

Table II. Statistical Analysis of the Difference in Time Off Flying (TOF) and Operational Multi-Crew Limitation (OML) Duration Between the Old Policy and the New Algorithm (in months, mo).

	TOF Old Policy (mo)	TOF New Algorithm (mo)	OML Old Policy (mo)	OML New Algorithm (mo)
Highest	15.00	36.00	60.00	120.00
Upper quartile	4	6	60	12
Median	3.00	6.00	12.00	12.00
Lower quartile	3	3	6	6
Lowest	0.75	0.25	0.00	0.00

of 1 wk, 3 mo, 6 mo, or 3 yr and an OML duration of 6 mo, 12-mo, 5 yr, or 10-yr.

The primary finding of this study was that application of the new algorithm resulted in no statistically significant difference in certificatory outcomes. This therefore provides reassurance that future regulatory decision making which is based on the new algorithm should remain consistent and aligned with previous, in-house expert opinion. While the regulator benefits from a simplified decision-making process which is less resource intensive, the benefit to the pilot and the wider aviation community is a more transparent and accountable assessment process which is captured in full. Although not statistically significant, there appeared to be a trend toward less variation in OML duration which may indicate potential for greater consistency in future decision making.

The study found a lower than expected rate of syncope in commercial pilots when compared with the general population, where the incidence of initial episodes was found to be 6.2 per 1000 person-years, or 0.6% per annum.²³ By applying this expected annual rate to the approximately 20,000 Class 1 certificate holders in the UK, one might anticipate 120 reports of syncope over a 12 mo period, far more than the 40 cases reviewed by the Medical Licensing Authority over 7 yr. The reasons for this are likely multifactorial. A modifying factor that influences whether any general population epidemiology is directly relevant to aircrew populations is the ‘healthy-worker effect’.^{12,17} Annual screening in the form of pilot medicals from a starting age of 18–21 is likely to pick up anomalies such as abnormal EKGs indicating the presence of pathology in advance of symptoms, thereby removing some susceptible individuals from the pilot population. It is also impossible to know how many episodes go unreported. Although aircrew have an obligation to report their full medical history and any deterioration in their fitness, various reasons for nonreporting exist. Once familiar with the assessment process and potential consequences of declaration (suspension of a medical certificate, cost of investigations, pressure from an employer to remain operational), aircrew may be less likely to report events. Some may view syncope as a medically insignificant event and in one study, only half of individuals experiencing syncope reported seeing a doctor or visiting a hospital for evaluation.²³ An underestimation of the potential implications of syncope on the flight deck might also contribute to lower levels of reporting. The fact that 10 episodes of syncope over a 7-yr period occurred on the flight deck, where reporting is assumed to be unavoidable, could perhaps be extrapolated to give a truer indication of how many cases might be happening outside of aircrew flying hours.

The age groups in which syncope most often occurs may also be a factor. The literature reports a bimodal peak in syncope at ages 10 to 30, and at 65 and over.²⁵ The UK has approximately 5000 pilots aged between 18 and 30, 18,000 between 31 and 55, and almost 3000 over the age of 60. The majority of operational pilots fall between these two peaks and the mean age for syncopal events in pilots in this study was 31.9 yr old. Any future discussions of raising the upper age limit for

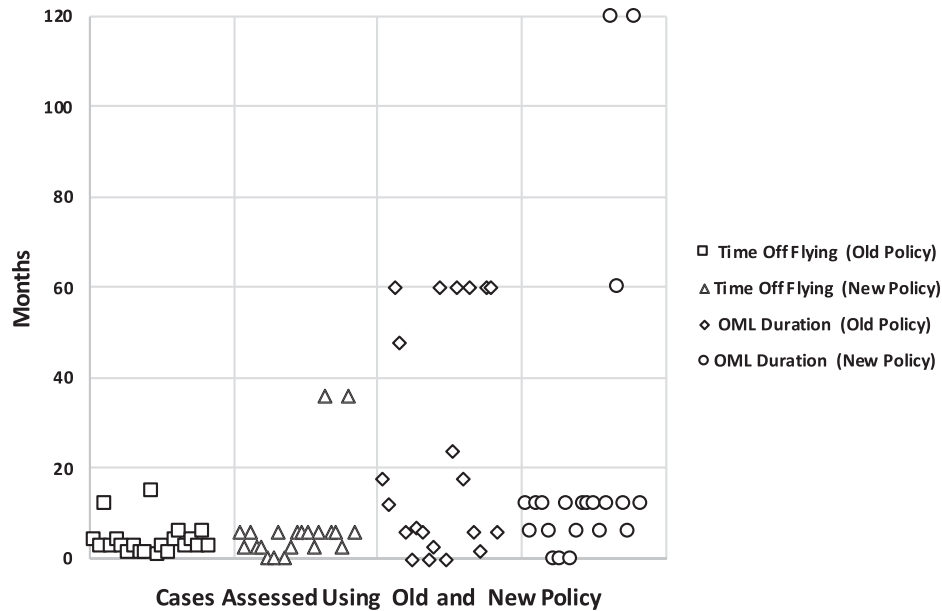


Fig. 3. Comparison of time off flying and Operational Multi-Crew Limitation (OML) duration between the old policy and the new algorithm.

commercial pilot operations from 65 might consider this later peak in incidence.

The causes of syncope are generally divided into reflex (neurally-mediated), cardiac, and orthostatic (hypotension), with the remainder being classified as ‘unknown’. The most common cause of syncope is reflex syncope, which includes vasovagal and situational syncope (such as occurs with micturition or cough).⁵ Of cases in this study, 90% were classified as being ‘probable vasovagal’ in origin. Although there is thought to be no increased risk of cardiovascular morbidity or mortality associated with vasovagal syncope,²³ its incapacitating and unpredictable nature necessitated careful consideration of the period of TOF and any OML duration. Syncope that has an underlying cardiac cause, such as structural heart abnormalities or a brady or tachyarrhythmia, has a higher incidence of mortality including sudden cardiac death,^{7,11} but the new algorithm reassuringly identified all cases where pathology had previously been detected. Orthostatic syncope is seen predominantly in the older population, often in combination with polypharmacy and was, therefore, not expected to be a common finding in the pilot population.¹³

Following the new algorithm, all but unequivocally clear-cut single vasovagal episodes require ‘Level 1’ investigations, including a cardiological clinical examination, supine and standing blood pressures (aimed at detecting orthostatic causes), a resting EKG, and a 24-h Holter monitor (Fig. 2). ‘Level 2’ requires an additional echocardiogram and exercise EKG. If clinically indicated, ‘Level 3’ tests include a tilt-table, cardiac MRI, electrophysiology studies and consideration of an implantable loop recorder. The rationale for most of these investigations relates directly to detecting cardiac pathology in view of the fact that patients experiencing syncope who also have underlying structural abnormalities or inheritable arrhythmia syndromes may have up to a fourfold increased risk

of death.^{2,15} Importantly, there did not appear to be any significant additional burden of investigation imposed by the new algorithm. The importance of adding guidance for the investigation of single episodes of syncope is supported in the finding that two of the four cases of confirmed cardiac pathology in this study were identified after only one episode of syncope. The literature showed that the risk of recurrence in individuals with a confirmed history of syncope is also greater than the incidence of a first episode among those with no prior events.²³

The decision not to include pharmacological intervention in new guidance was based in part on the disappointing results of studies of pharmacological treatment for syncope such as the STAND-trial and the POST studies.^{14,19} Several agents, such as metoprolol (beta-blocker), fludrocortisone (corticosteroid), and midodrine (alpha-adrenergic agonist), were all shown to be ineffective in preventing recurrence. Additionally, almost half of patients that were taking midodrine in the STAND-trial reported side effects such as nausea, headaches and gastro-intestinal discomfort which would not be compatible with flying.^{14,18,20} Newer agents such as the norepinephrine transport inhibitor atomoxetine may offer effective therapeutic options in the future.²²

A nonpharmacological approach to the prevention of vasovagal syncope has been recommended in some studies with effectiveness in up to 70% of patients.² Such measures included adequate hydration, salt intake and physical counterpressure maneuvers,¹ but while increasing fluid intake may help reduce the risk of syncope, an increased need for micturition and bathroom breaks when flying short-haul may reduce compliance. Although research such as the Physical Counterpressure Maneuvers Trial (PC-Trial) provided evidence of a reduction in syncope recurrence (relative risk reduction of 39%),²⁸ the measures required include squeezing hands, arms, and crossing legs for as long as tolerable when a prodrome is detected prior to a

possible syncopal event. This is effectively a basic version of a technique fast-jet crew are trained to use in the form of an anti-G straining maneuver, although in that context it is designed to sustain head level blood pressure in the presence of increased G_z acceleration. Neither of these physical straining techniques are likely to be practical at the controls of a commercial aircraft, and in themselves might be a distraction from the flying task at a critical phase of flight. From a regulatory perspective, aircrew who needed to regularly perform such maneuvers would not be considered fit to fly.

In determining the appropriate TOF and OML duration for the algorithm, the UK DVLA's '3 P's', provocation, posture and prodrome, approach is intuitively attractive.²⁷ The presence of reasonable provocation (dehydration, gastrointestinal illness, nociception), a standing posture, and a reliable prodrome can also be considered mitigators in the assessment of pilots and was therefore incorporated within the new algorithm.

Guidance material for the assessment of aircrew must consider initial applicants as well as existing aircrew. In this study, all 15 initial applicants achieved certification when both the old and new guidance was followed with one reduction in delay to certification achieved with the new algorithm. The relatively low number of delays reflects the fact that most individuals had allowed, either intentionally or unintentionally, a sufficient amount of time to pass between their last syncopal event(s) and the application process, to avoid the required 'unfit' penalty period. Most typically these initial Class 1 applicants had suffered one or more syncopal episodes in their teenage years and were applying one or more years after the last event.

When considering limitations, it is important to acknowledge that not all delays to certification were a purposeful result of aeromedical risk assessment. Other concurrent medical issues may also have influenced decision-making and in some cases, the time taken for clinical reviews, investigations and report submission also contributed to the delay.

In conclusion, this study provides a useful insight into the epidemiology of syncope in commercial aviation and the processes involved in developing regulatory guidance. The importance of educating aircrew on the risks of syncope and encouraging reporting is clear, as is recognition of the individual impact on aircrew of any TOF. All aviation regulations and accompanying interpretive guidance material should be based on the available evidence relevant to the pilot population. Where there is a lack of directly applicable evidence, then pragmatic guidance should be developed that is efficient in terms of investigatory burden, cost and criteria for additional medical surveillance or operational restriction, in order to manage risk. Testing new guidance material, as undertaken in this study, should demonstrate robust but proportionate regulatory oversight which aims for consistent outcomes. By more transparently describing syncope assessment pathways and providing a clearer indication of aeromedical disposition from the outset, we have taken a positive step toward the UK CAA's ambition for a more open and transparent approach to regulatory decision-making.

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REFERENCES

- Benditt DG, Nguyen JT. Syncope: therapeutic approaches. *J Am Coll Cardiol.* 2009; 53(19):1741–1751.
- Brignole M, Moya A, de Lange FJ, Deharo JC, Elliott PM, et al. 2018 ESC Guidelines for the diagnosis and management of syncope. *Eur Heart J.* 2018; 39(21):1883–1948.
- Canada T.Part IV - Personnel Licensing and Training, Canadian Aviation Regulations (CARs) 2019-, Standard 424 - Physical and Mental Requirement. 2007. [Accessed 19 Nov. 2020]. Available from: <https://tc.canada.ca/en/corporate-services/acts-regulations/list-regulations/canadian-aviation-regulations-sor-96-433/standards/part-iv-personnel-licensing-training-1>.
- Civil Aviation Safety Authority Australian Government. Neuro-cardiogenic syncope—aeromedical implications. 2018. [Accessed 19 Nov. 2020]. Available from: <https://www.casa.gov.au/licences-and-certification/aviation-medicine/neuro-cardiogenic-syncope>.
- Colman N, Nahm K, Ganzeboom KS, Shen WK, Reitsma J, et al. Epidemiology of reflex syncope. *Clin Auton Res.* 2004; 14(S1, Suppl 1):9–17.
- Costantino G, Sun BC, Barbic F, Bossi I, Casazza G, et al. Syncope clinical management in the emergency department: a consensus from the First International Workshop on Syncope Risk Stratification in the Emergency Department. *Eur Heart J.* 2016; 37(19):1493–1498.
- Dan GA, Scherr D, Jubele K, Frakowski MM, Iliodromitis K, et al. Contemporary management of patients with syncope in clinical practice: an EHRA physician-based survey. *Europace.* 2020; 22(6):980–987.
- Federal Aviation Administration. Guide for Aviation Medical Examiners, Decision Considerations-Aerospac Medical Dispositions, Item 36. Heart-Syncope. 2014. [Accessed 19 Nov. 2020]. Available from: https://www.faa.gov/about/office_org/headquarters_offices/avs/offices/aam/ame/guide/app_process/exam_tech/item36/amd/syncope/.
- Ganzeboom KS, Mairuhu G, Reitsma JB, Linzer M, Wieling W, van Dijk N. Lifetime cumulative incidence of syncope in the general population: a study of 549 Dutch subjects aged 35–60 years. *J Cardiovasc Electro-physiol.* 2006; 17(11):1172–1176.
- Hayes OW. Evaluation of syncope in the emergency department. *Emerg Med Clin North Am.* 1998; 16(3):601–615.
- Koene RJ, Adkisson WO, Benditt DG. Syncope and the risk of sudden cardiac death: Evaluation, management, and prevention. *J Arrhythm.* 2017; 33(6):533–544.
- McMichael AJ. Standardized mortality ratios and the "healthy worker effect": scratching beneath the surface. *J Occup Med.* 1976; 18(3):165–168.
- O'Brien H, Kenny RA. Syncope in the elderly. *Eur Cardiol.* 2014; 9(1):28–36.
- Romme JJ, van Dijk N, Go-Schon IK, Reitsma JB, Wieling W. Effectiveness of midodrine treatment in patients with recurrent vasovagal syncope not responding to non-pharmacological treatment (STAND-trial). *Europace.* 2011; 13(11):1639–1647.
- Ruwald MH, Okumura K, Kimura T, Aonuma K, Shoda M, et al. Syncope in high-risk cardiomyopathy patients with implantable defibrillators: frequency, risk factors, mechanisms, and association with mortality: results from the multicenter automatic defibrillator implantation trial—reduce inappropriate therapy (MADIT-RIT) study. *Circulation.* 2014; 129(5):545–552.
- Sahota IS, Macey C, Pournazari P, Sheldon RS. Clusters, gaps, and randomness: vasovagal syncope recurrence patterns. *JACC Clin Electro-physiol.* 2017; 3(9):1046–1053.

17. Shah D. Healthy worker effect phenomenon. *Indian J Occup Environ Med.* 2009; 13(2):77–79.
18. Sheldon R, Ayala-Paredes FA, Guzman JC, Marquez M, Raj SR, et al. 015 A randomized clinical trial of midodrine for the prevention of vasovagal syncope by the post4 investigators. Canadian Cardiovascular Society (CCS) Moderated Presentations. October 24, 2019; Montréal, Canada. Montreal (Canada): CCS; 2019.
19. Sheldon R, Connolly S, Rose S, Klingenheben T, Krahn A, et al. Prevention of syncope trial (POST): a randomized, placebo-controlled study of metoprolol in the prevention of vasovagal syncope. *Circulation.* 2006; 113(9):1164–1170
20. Sheldon R, Raj SR, Rose MS, Morillo CA, Krahn AD, et al. Fludrocortisone for the Prevention of Vasovagal Syncope: A Randomized, Placebo-Controlled Trial. *J Am Coll Cardiol.* 2016; 68(1):1–9.
21. Sheldon RS, Grubb 2nd BP, Olshansky B, Shen WK, Calkins H, et al. 2015 heart rhythm society expert consensus statement on the diagnosis and treatment of postural tachycardia syndrome, inappropriate sinus tachycardia, and vasovagal syncope. *Heart Rhythm.* 2015; 12(6):e41–63.
22. Sheldon RS, Lei L, Guzman JC, Kus T, Ayala-Paredes FA, et al. A proof of principle study of atomoxetine for the prevention of vasovagal syncope: the Prevention of Syncope Trial VI. *Europace.* 2019; 21(11):1733–1741.
23. Soteriades ES, Evans JC, Larson MG, Chen MH, Chen L, et al. Incidence and prognosis of syncope. *N Engl J Med.* 2002; 347(12):878–885.
24. Sumner GL, Rose MS, Koshman ML, Ritchie D, Sheldon RS. Prevention of Syncope Trial I. Recent history of vasovagal syncope in a young, referral-based population is a stronger predictor of recurrent syncope than lifetime syncope burden. *J Cardiovasc Electrophysiol.* 2010; 21(12):1375–1380.
25. Task Force for the Diagnosis and Management of Syncope; European Society of Cardiology (ESC); European Heart Rhythm Association (EHRA); Heart Failure Association (HFA); Heart Rhythm Society (HRS); et al. Guidelines for the diagnosis and management of syncope (version 2009). *Eur Heart J.* 2009; 30(21):2631–2671.
26. The Civil Aviation Authority of New Zealand. Medical Certification, Medical Manual, Part 3.1 Cardiovascular system, Part 3.10 Central nervous system. 2016. [Accessed 19 Nov. 2020]. Available from: <https://www.aviation.govt.nz/licensing-and-certification/medical-certification/>.
27. UK Driver and Vehicle Licensing Agency. Transient loss of consciousness ('blackouts') – or lost/altered awareness. 2020. [Accessed 4 March 2020.] Available from: <https://www.gov.uk/guidance/neurological-disorders-assessing-fitness-to-drive#transient-loss-of-consciousness-blackouts-or-lost-altered-awareness>.
28. van Dijk N, Quartieri F, Blanc JJ, Garcia-Civera R, Brignole M, et al. Effectiveness of physical counterpressure maneuvers in preventing vasovagal syncope: the Physical Counterpressure Manoeuvres Trial (PC-Trial). *J Am Coll Cardiol.* 2006; 48(8):1652–1657.