

UNIVERSITY OF  
BIRMINGHAM

**Literature Search On  
The Recurrence Risk In Those Who Have Had An  
Episode Of Cough Syncope**

**Aggressive Research Intelligence Facility  
West Midlands Health Technology Assessment Collaboration**

**May 2006**

For the Drivers Medical Group  
DVLA  
Swansea

***ARIF***



## About ARIF and the West Midlands Health Technology Assessment Collaboration

The West Midlands Health Technology Assessment Collaboration (WMHTAC) is an organisation involving several universities and academic groups who collaboratively produce health technology assessments and systematic reviews. The majority of staff are based in the Department of Public Health and Epidemiology at the University of Birmingham. Other collaborators are drawn from a wide field of expertise including economists and mathematical modellers from the Health Economics Facility at the University of Birmingham, pharmacists and methodologists from the Department of Medicines Management at Keele University and clinicians from hospitals and general practices across the West Midlands and wider.

WMHTAC produces systematic reviews, technology assessment reports and economic evaluations for the UK National Health Service's Health Technology Assessment (HTA) programme, the National Institute for Health and Clinical Excellence (NICE). Regional customers include Strategic Health Authorities, Primary Care Trusts and regional specialist units. WMHTAC also undertakes methodological research on evidence synthesis and provides training in systematic reviewing and health technology assessment.

The two core teams within WMHTAC are the Aggressive Research Intelligence Facility (ARIF) and the Birmingham Technology Assessment Group (BTAG)

ARIF provides a rapid on-demand evidence identification and appraisal service primarily to commissioners of health care. Its mission is to advance the use of evidence on the effects of health care and so improve public health. The rapid response is achieved by primarily relying on existing systematic reviews of research, such as those produced by the Cochrane Collaboration, the National Institute for Health and Clinical Excellence (NICE), the NHS Centre for Reviews and Dissemination, and the NHS Health Technology Assessment (HTA) programme. In some instances, longer answers to questions are required in which case mini rapid reviews of existing systematic reviews and key primary studies are compiled, typically taking 1-2 months to complete.

Occasionally a full systematic review is required and then topics are referred to BTAG who coordinate the production of systematic reviews for several customers under a number of contracts. ARIF is intrinsically involved in the production of these systematic reviews.

Aggressive Research Intelligence Facility (ARIF)  
West Midlands Health Technology Assessment Collaboration (WMHTAC)  
Department of Public Health and Epidemiology  
University of Birmingham  
Birmingham  
B15 2TT

arifservice@bham.ac.uk  
0121 414 3166

### **Warning**

**This is a confidential document.**

**Do not quote without first seeking permission of the DVLA and ARIF.**

The information in this report is primarily designed to give approved readers a starting point to consider research evidence in a particular area. Readers should not use the comments made in isolation and should have read the literature suggested. This report stems from a specific request for information, as such utilisation of the report outside of this context should not be undertaken. Readers should also be aware that more appropriate reviews or information might have become available since this report was compiled.

## 1 Aims

The aims of this report were to address the following questions submitted by the Driver Medical Group:

- What is the per annum recurrence risk in those who have had an episode of cough syncope?
- What treatment and risk factors are associated with cough syncope?
- Does treatment and removal of risk factors improve the recurrence risk?

Further details are given in the request submitted by the Drivers Medical Group (Appendix 1 – Details of Request).

## 2 Background

The Disorders of the Nervous System Driver Medical Group Panel are currently reviewing the licensing guidelines on cough syncope for Group 2 drivers. At present, Group 2 drivers are required to have a period of 5 years free of syncope and presyncope if there is any chronic respiratory condition (including smoking). For individuals identified as having asystole (no cardiac electrical activity) in response to coughing, licensing will only be considered once a pacemaker has been implanted.

Professor Denison, a Respiratory Physician, advised the panel that anecdotal evidence suggests that stopping smoking and reducing BMI to less than 30 leads to the disappearance of symptoms of cough syncope within 1 year.<sup>1</sup> Based on this advice, the Panel are considering whether a 1-year review licence should be issued to people who reduce their BMI to less than 30, stop smoking and have had no previous attacks within the last year.

Further background information is given in the request submitted by the Drivers Medical Group (Appendix 1 – Details of Request).

Syncope is a symptom defined as a transient loss of consciousness and postural tone with rapid and spontaneous recovery. It occurs as a result of transient hypotension and global cerebral hypoperfusion. Cough syncope (also known as tussive syncope, posttussive syncope, tussigenic syncope, cough syndrome, bettolepsy and laryngeal vertigo) is a type of situational syncope triggered by paroxysms of severe coughing. It is thought to occur by two possible mechanisms:

- a neurally-mediated reflex mechanism triggered by irritation of the fibres of the glossopharyngeal and vagus nerves (cranial nerves) or
- a mechanical mechanism triggered by hard coughing or the valsalva maneuver (exhalation against a closed mouth and nose) which results in an increase in intrathoracic pressure and hence a decrease in blood flow to the heart.

Both mechanisms result in vasodilatation and bradycardia which cause systemic hypotension and cerebral hypoperfusion.

### 3 Methods

Outline methods were submitted to the Drivers Medical Group by email and acceptance subsequently confirmed by e-mail (Appendix 2 – Outline methods).

Briefly these were:

- To undertake a search for studies looking at cough syncope.
- To initially search for existing systematic reviews.
- To select all types of studies that report on the relevant outcomes and to comment on the most robust.
- To comment on the methodological quality of such studies.
- Where appropriate and possible, to extract and tabulate data on relevant outcomes.

#### 3.1 Searches

##### 3.1.1 Existing Reviews

Searches to identify existing systematic reviews on this topic were performed utilising the well-established ARIF search protocol (Appendix 3 – Search strategies).

##### 3.1.2 Primary Studies

Searches were undertaken for primary studies in Medline, Embase and the Cochrane Library. A broad search strategy was employed using only terms for cough and syncope. No language restrictions were applied to the searches and databases were searched back to their inception.

The detailed search strategies can be found in Appendix 3 – Search strategies.

Searches were predominantly undertaken by an information specialist with additional searches by a research reviewer. Both interacted to ensure searches were conducted appropriately.

Results of the searches were imported into bibliographic management software (Reference Manager, Vr11; Thomson ISI ResearchSoft) and duplicates were removed. Two research reviewers independently scanned the search results for relevance based on information in the title and abstract. Articles reporting studies that adhered to the following broad criteria were obtained in full for further scrutiny:

<b>Design:</b>	Any
<b>Population:</b>	Adults suffering from cough syncope
<b>Outcomes:</b>	Recurrence risk and any outcome related to the treatment or risk factors associated with cough syncope.
<b>Exclusion:</b>	Studies on children Studies on other forms of syncope Case series with less than 5 participants Case reports

The reference lists of the most relevant articles were also checked in order to identify further relevant papers and attempts were made to contact experts (Professor Denison, Professor Warlow and Professor Chadwick). Contact was made with Professor Denison who provided an invaluable insight into the field.

### **3.1.3 Driving Specific Literature**

In addition to the above searches, *ad hoc* internet searches were conducted to identify relevant driving specific literature on cough syncope using data sources such as the National Transport Laboratory (TRIS), Transport Research Laboratory (TRL) and the Highways Agency.

## **4 Results**

### **4.1 Reviews Identified**

No relevant systematic reviews were identified.

Two narrative reviews on cough syncope were identified,<sup>2,3</sup> which discussed patient characteristics, mechanisms and treatment of the syndrome generally without the provision of supporting data. Furthermore both reviews were published in the 1970s and therefore could not be considered up to date. Several reviews on neurally-mediated syncope (e.g. Melby<sup>4</sup>) were identified, however, again these contained limited information on cough syncope.

### **4.2 Primary Studies Identified**

The literature searches for primary studies identified over 400 articles and from these 18 studies were identified as being potentially relevant. From these, 8 studies were found to meet the predefined inclusion criteria. A further 2 studies were identified by checking articles cited in the relevant studies. The characteristics and results of these 10 studies are outlined in Table 1.<sup>5-14</sup>

All of the studies were of an observational design. One was a case-control study that compared the characteristics of cough syncope patients to patients with syncope not related to coughing or patients with convulsions.<sup>12</sup> The remaining 9 studies were case series. The sample sizes of the studies were small, ranging from 5 to 45 patients. The majority of the studies were published before 1987, with the earliest in 1953, and they were mainly conducted in the United States of America. 1 Chinese study,<sup>15</sup> 1 Polish study<sup>16</sup> and 1 Russian study<sup>17</sup> were identified and relevant data were translated.

None of the studies appear to prospectively and objectively follow a group of cough syncope patients to assess the frequency or recurrence of syncope or the response to changes in patients' characteristics (e.g. smoking cessation or weight loss). One of the studies did seem to provide some information on these parameters from a retrospective analysis.<sup>18</sup>

#### **4.2.1 Risk Factors**

All studies report patient characteristics and they consistently show that cough syncope typically occurs in overweight, short, middle-aged men with a history of smoking, consumption of alcohol and/or chronic

obstructive pulmonary disease. Asthmatics with cough syncope tend not to be typical cough syncope patients.<sup>19</sup>

Anecdotal evidence: Professor Denison added that people with a pre-existing tendency to faint e.g. people with low blood pressure or anaemia, are at an increased risk of cough syncope.

#### **4.2.2 Recurrence Risk and Treatment**

Studies that report on the rate of cough syncopal episodes, suggest a range from 1 attack in 7 years to 10 per day,<sup>6,20</sup> with the length of cough syncope episodes ranging from 30 seconds to 5 minutes,<sup>21,22</sup> and the length of the cough syncope syndrome ranging from 1 week to 22 years.<sup>6,23</sup> The distribution of syncope episodes in an individual is not given in the studies, i.e. if a patient has 5 attacks in a 5 year period the time period between attacks are not given.

None of the studies investigated the effect of removal of risk factors on recurrence risk. Xu<sup>24</sup> associates the severity of the pulmonary symptom with the frequency of attack and conclude that the less severe the pulmonary symptom the less frequent the episodes. However the study does not report the time period during which the attacks occurred so a rate could not be calculated. In addition the Bonekat et al<sup>25</sup> results suggest that smoking cessation is closely associated with a decrease in cough-related symptoms, but the frequency of syncopal episodes were not given.

None of the studies investigated the effect of treatment on recurrence risk. Although they do seem to suggest that treating the cause of cough reduces the frequency of syncope (e.g. Bonekat et al<sup>26</sup>, Blue<sup>27</sup> and Xue<sup>28</sup>).

Three studies report the treatment used in patients with cough syncope.<sup>29-31</sup> Management consists of smoking cessation, prevention of the cause of cough and voluntary suppression of the cough. Whilst these studies seem to indicate that these interventions might reduce cough and cough syncope, the evidence is not very robust due to the retrospective design of the studies, lack of presented data, incomplete follow-up of patients and limited reporting of other information.

Anecdotal evidence: Although not reported in the included studies, weight reduction is also recommended for patients with cough syncope (advised by Professor Denison). Professor Denison provided additional information on the methods used to suppress cough. He stated that the most common cause of cough is post nasal drip syndrome which can lead to chronic nasal infection and can be treated with antibiotics, steroids and decongestant sprays. Over the counter cough suppressants are also used, but these can lead to chest infections due to the accumulation of phlegm. Other causes of cough include chronic obstructive pulmonary disease (e.g. emphysema, bronchitis and asthma), which if possible should be treated.

#### **4.2.3 Driving Literature**

The literature searches identified 3 articles (1 letter<sup>32</sup> which mentions 4 cases, and 2 case reports<sup>33,34</sup>) related to driving and cough syncope. Although these articles indicate that cough syncope affecting drivers has caused serious road traffic accidents, they provide no other relevant information.

Anecdotal evidence: Professor Denison thought that cough syncope would be under reported as drivers would not want to stop driving. It would only be reported in the event of a vehicle accident as an excuse for causing an accident.

## **5 Conclusion**

The evidence surrounding cough syncope is limited and insufficient to determine the per annum recurrence risk in those who have had an episode of cough syncope and whether treatment and/or removal of risk factors improve the recurrence risk. The majority of studies are small case series which are subject to bias (particularly selection bias), chance findings and confounding. Also it should be noted that the majority of studies were published over 20 years ago when smoking habits and clinical management were different to today.

The evidence that is available suggests that cough syncope predominantly affects middle-aged men, who are overweight and/or smoke and who have some form of respiratory problem; either transitory (i.e. infection) or progressive (i.e. chronic obstructive pulmonary disease). There is no published robust evidence on the effectiveness of any treatment or risk factors removal for cough syncope.

### **5.1 Limitations of this report**

This is not a systematic review but a rapid assessment for relevant literature.

Although the search strategies were broad and comprehensive for both systematic reviews and primary studies, other terms for cough syncope (e.g. tussive syncope) were not searched. However it is unlikely that relevant studies were missed as to aid comprehensiveness the reference lists of relevant articles were scanned for further studies.

**Table 1 – Characteristics and results of included studies**

Study	Design	Population	Intervention/Risk Factor	Outcomes	Results	Comments
Bonekat et al <sup>35</sup> 1987	Retrospective case series of 45 patients	Patients with cough syncope without other medical causes for syncope, presenting at the Mayo Clinic from Jan 1978 to Dec 1980	Smoking Medication history	Patient reported outcomes: Presence of cough Presence of cough related symptoms	<p>2.5% of patients evaluated for syncope at the Mayo Clinic had a typical presentation of cough syncope</p> <p><u>Patient characteristics</u>                      43 (96%) male                      Mean age 53 years                      Age range 19 to 77 years                      Mean height 174.9cm                      Mean weight 96.1kg                      43 (96%) patients Caucasian                      73% manual occupation                      36 (80%) patients used alcohol                      29 (64%) patients were smokers                      8 (18%) patients were ex-smokers                      Mean initial age of smoking 19.1 years                      Mean number of years smoking 32                      Most frequent underlying disease chronic obstructive pulmonary disease</p> <p><u>Follow-up results</u> (mean duration of follow-up was 19 months)                      26 patients had no cough-related symptoms, of these:                      18 patients reported no cough                      8 patients reported persistent cough (all 8 patients continued to smoke)</p> <p>19 patients continued to have cough-related symptoms, of these:                      17 felt that cough-related symptoms had improved (1 continued to smoke)                      2 felt cough syncope was unchanged (both continued to smoke)                      Of the 17 patients that felt cough-related symptoms had improved:                      9 reported no syncope                      8 reported persistent syncope</p> <p>Voluntary cough suppression was successful in preventing cough in 8 out of 12 patients                      Medications prescribed included theophylline, oral and inhaled beta-agonists, beclomethasone, dipropionate, codeine, antihistamines, expectorants, non-narcotic cough suppressants and antibiotics                      Smokers were encouraged to stop                      Individual strategies for cough suppression included breath holding, tensing pharyngeal and chest wall muscles, drinking liquids, lessening the vigour of cough and coughing at lower lung volumes</p>	<p><u>Conclusion</u>                      Treatment of cough was 97% effective in relieving or improving cough-related symptoms.                      Smoking cessation was closely associated with decreased symptoms.</p> <p>Small uncontrolled, retrospective, observational study – bias, confounding, chance.</p> <p>No selection bias: all eligible patients responded to questionnaire.</p> <p>Recall bias: retrospective</p> <p>Only patients who reported persistent cough related symptoms were further followed-up by telephone.</p>
Kerr et al <sup>6</sup> 1953	Case series of 40 patients	Patients with cough syncope	Patient characteristics		<p>40 (100%) patients male                      Age range 25-65 years                      Mean age 47 years                      35 (88%) patients Caucasian                      5 (12%) patients African American                      Majority of patients were short and slightly obese                      33 patients questioned on alcohol intake, of which:                      29 patients (88%) consumed alcohol                      35 patients questioned on smoking habits of which:                      35 (100%) were smokers and the majority were heavy smokers</p>	<p>Small observational study – bias, confounding and chance.</p> <p>Selection bias may have been introduced as not clear if patients enrolled consecutively.</p>



**Table 1 – Characteristics and results of included studies**

Study	Design	Population	Intervention/Risk Factor	Outcomes	Results	Comments
					<p>Range of cough syncope syndrome duration 1 week to 22 years                      Range of frequency of attacks 1 in 7 years to 500-1000 in 9 years                      3 (8%) patients experienced convulsions                      6 (15%) patients caused injury to themselves                      1 (3%) patient died during a cough syncope attack                      1 (3%) patient attack whilst driving and caused injury to himself.                      1 (3%) patients stopped driving due to fear of having an attack whilst driving                      Pulmonary disease associated with cough syncope was assessed in 30 patients, of which:                      12 (40%) patients had emphysema                      10 (33%) patients had asthma                      3 (10%) patients had bronchiectasis                      2 (7%) patients had pneumoconiosis                      1 (3%) patient had sarcoidosis                      1 (3%) patient had acute pneumonia                      1 (3%) patient had acute bronchitis</p>	
Khadartsev et al <sup>36</sup> 1991 (Russian)	Case series of 31 patients	Patients with cough syncope with expiratory stenosis of the trachea and bronchi	Patient characteristics	Fibrobronchoscopy results Tracheal x-ray results Esophageal x-ray results External respiration examination results Electrophysiological examination results Disability expert evaluations	<p><u>Patient characteristics</u>                      18 (58%) patients had chronic obstructive pulmonary disease                      9 (29%) patients had asthma                      Number of syncopal episodes ranged from 1-2/year to &gt;10/day                      Length of syncopal spell ranged from 30 secs to 5 mins                      8 (26%) patients had pre-syncope symptoms</p> <p>Fibrobronchoscopy, tracheal x-ray, esophageal x-ray, external respiration examination, electrophysiological examination and disability expert evaluation results are not relevant</p>	<p>Small observational study – bias, confounding and chance.</p> <p>Selection bias may have been introduced as not clear if patients enrolled consecutively.</p>
Blue <sup>37</sup> 1968	Case series of 29 patients	Patients with cough syncope due to asthma	Patient characteristics Treatment		<p><u>Patient characteristics</u>                      18 (62%) patients male                      Age range 5 to 76 years                      Mean age 44 years                      13 (45%) patients diagnosed with asthma alone                      15(52%) patients diagnosed with asthma and emphysema                      1 (3%) patient diagnosed with hayfever alone</p> <p><u>Treatment</u>                      15 (52%) patients were given allergy management of which:                      4 (27%) patients had excellent results to therapy                      5 (33%) patients had good results to therapy                      4 (27%) patients had fair results to therapy                      2 (13%) patients had poor results to therapy                      No information on the treatment for the remaining 14 patients were given</p>	<p>Small observational study – bias, confounding and chance.</p> <p>Selection bias may have been introduced as not clear if patients enrolled consecutively.</p> <p>No explanations of the terms excellent, good, fair and poor results to therapy.</p>
Skolnick et al <sup>38</sup> 1969	Case series of 18 patients	Patients diagnosed with cough syncope at the Mayo Clinic from 1950 to 1967	Patient characteristics	Pulmonary function Diseases of the central nervous system Thorax abnormality Bronchus abnormality Neurological function	<p><u>Patient characteristics</u>                      16 (89%) male                      Mean age 52 years                      Age range 16 to 75 years                      8 (44%) patients had an excessive intake of alcohol                      14 (78%) patients were obese</p>	<p><u>Conclusion</u>                      The typical cough syncope patient is male, has a mild chronic respiratory disorder, obese, a smoker, drinks excessively and has a dry,</p>

**Table 1 – Characteristics and results of included studies**

Study	Design	Population	Intervention/Risk Factor	Outcomes	Results	Comments
				Atherosclerotic changes	<p>12 (67%) patients were smokers who smoked 1-3 packs a day                      6 (33%) patients had no history of smoking                      Cough syncope syndrome duration ranged from 30 days to 4 years                      Syncopal spells lasted from 30 seconds to 3 minutes</p> <p><u>Observations</u>                      4 patients had dilatation of superficial blood vessels                      10 patients had inspiratory wheezes and expiratory slowing                      All smokers had a chronic, productive cough, with the syncopal spells occurring with paroxysms of coughing.</p> <p><u>Bronchoscopy</u>                      1 of the patients who did not smoke had undergone resection for tuberculosis and continued to have a chronic non-productive cough related to empyema                      5 patients who did not smoke had chronic asthmatic bronchitis with paroxysms of coughing associated with wheezing                      1 patient had an bronchial obstruction carcinoma</p> <p><u>Atherosclerotic changes</u>                      3 patients had diffuse atherosclerotic changes, severest in the aortoiliac system.</p> <p><u>Neurological function tests</u>                      17 patients had normal neurological function.</p> <p><u>Roentgenograms of thorax</u>                      3 patients had mediastinal widening of the thorax from lymphoma                      2 patients had thoracic obstructive pneumonitis with a hilar mass                      2 patients had changes compatible with emphysema                      1 patient had empyema                      8 patients had no thoracic abnormalities</p> <p><u>Electroencephalograms</u> (performed on 8 patients)                      No disease of the central nervous system found</p> <p><u>Pulmonary function tests</u> (performed on 7 patients)                      6 patients had an obstructive pattern                      1 patient had a normal pulmonary function</p>	<p>paroxysmal and non-productive cough.</p> <p>Small uncontrolled observational study – bias, confounding, chance.</p> <p>No selection bias – all eligible patients included</p> <p>Observer bias – Electroencephalograms and pulmonary function tests only applied to a subset of patients</p>
Xue <sup>39</sup> 1985 (Chinese)	Case series of 18 patients	Patients with cough syncope	Pulmonary pathological changes Treatment	Frequency of syncopal episodes	<p><u>Patient characteristics</u>                      18 (100%) male                      Mean age 49.8 years                      All patients had severe cough and syncope due to cough                      Causes of cough included (some patients had more than 1 cause of cough):                      Smoking in 6 patients                      Drinking in 2 patients                      Smell in 1 patient                      Choking in 1 patient</p>	<p><u>Conclusion</u>                      The less severe the pulmonary symptom, the less frequent the syncopal episodes.</p> <p>Small observational study – bias, confounding, chance, reverse causality.</p>

**Table 1 – Characteristics and results of included studies**

Study	Design	Population	Intervention/Risk Factor	Outcomes	Results	Comments
					<p>Emotion in 1 patient Cold temperature in 1 patient Feeling suffocated in 1 patient No obvious cause in 8 patients</p> <p><u>Pulmonary pathological changes</u> 10 patients had chronic bronchitis 7 patients had obstructive pulmonary emphysema 1 patient had small airway pathological changes due to smoking</p> <p>4 patients with severe pulmonary pathological changes had 11-17 syncopal episodes and 13 reports of head injuries. No time period reported 4 patients (less severe pulmonary pathological changes) had 6-10 syncopal episodes and 3 reports of head injuries 10 patients (less severe pulmonary pathological changes) had 1-5 syncopal episodes with no reported head injuries</p> <p><u>Treatment</u> 17 patients received treatment for reducing inflammation and relieving cough and phlegm which reduced the frequency of syncopal episodes 1 patient whose syncope was due to smoking, did not have a syncopal episode within 3 years after smoking cessation</p>	Selection bias may have been introduced as not clear if patients enrolled consecutively.
DeMaria et al <sup>40</sup> 1984	Case series of 17 patients	Patients with cough syncope who had electroencephalographic studies performed as part of their evaluation at the Mayo clinic	Diagnosis	Electroencephalogram recordings	<p><u>Patient characteristics</u> 16 (94%) male Age range 29-63 years 4 (24%) patients had no pulmonary disease (2 of which had histories of smoking and 1 had abnormal ECGs) 13 (76%) patients had chronic pulmonary problems (11 of which had histories of smoking and 7 had abnormal ECGs):     9 patients with obstructive pulmonary disease     1 patient with asthma     1 patient with emphysema     1 patient with lung infiltrates     1 patient with granuloma 16 (94%) patients were overweight 3 (18%) patients had histories of alcohol abuse All patients had moderate to severe episodes of coughing which induced transient syncope 8 (47%) patients had repetitive clonic or shaking movements of the limbs during syncope</p> <p><u>EEG results</u> Not relevant</p>	<p><u>Conclusion</u> EEG helps to differentiate syncope from seizures or other transient episodes (not relevant).</p> <p>Small uncontrolled observational study – bias, confounding, chance.</p> <p>Selection bias may have been introduced as not clear if patients enrolled consecutively.</p>
Trim et al <sup>14</sup> 2001 (Abstract)	Case series of 7 patients	Patients with cough syncope	Clinical and investigational profile		<p><u>Clinical characteristics</u> 7 (100%) male Mean age of 53 years Age range 38-68 years Mean weight 85kg</p>	<p><u>Conclusion</u> Tilt table testing is not a sensitive diagnostic test for susceptibility to cough syncope, implying that the</p>

**Table 1 – Characteristics and results of included studies**

Study	Design	Population	Intervention/Risk Factor	Outcomes	Results	Comments
					<p>5 (71%) patients had a smoking history                      6 (86%) patients had chronic airway disease:                      5 due to smoking                      1 due to asthma</p> <p><u>Investigational profile</u>                      7 (100%) patients had normal electrocardiograms                      4 patients had echocardiograms of which:                      2 (50%) patients were normal                      2 (50%) patients showed evidence of diastolic dysfunction                      7 (100%) patients had normal carotid sinus massage                      7 (100%) patients had negative result for tilt table testing for vasodepressor syncope                      3 patients had coughing induced of which:                      2 (67%) patients experienced syncope or presyncope in association with documented hypotension                      5 patients performed the valsalva manoeuvre of which:                      1 (20%) patient had their presyncopal symptoms reproduced in association with hypotension</p>	<p>mechanism of syncope may be other than reflex-mediated.                      Induction of coughing may have some diagnostic value.                      Diagnosis is however primarily based on characteristic history.</p> <p>Small observational study – bias, confounding and chance.                      Selection bias may have been introduced as not clear if patients enrolled consecutively.                      Abstract only so may be reporting bias.</p>
Lindegaard et al <sup>12</sup> 1977	Case-control of 5 patients	<p>Cases: Patients diagnosed with cough syncope between 1961 and 1975 at the National Hospital of Norway                      Controls: aged matched groups of consecutively examined patients with:                      Group 1: syncope not associated with coughing                      Group 2: occasional convulsive episodes.</p>	Hydrocephalus ex vacuo	<p>Pneumoencephalography measurements:                      Septum caudata line                      Maximal anterior Temporal horn width                      3<sup>rd</sup> ventricle width                      Cortical atrophy</p>	<p><u>Patient characteristics of cough syncope group</u>                      5 (100%) male                      Mean age 52 years                      Mean duration of symptoms 1.2 years                      4 (80%) patients had chronic bronchitis and had an average tobacco consumption of 138g/week, of these:                      1 (20%) patient had emphysema                      1 (20%) patient had bronchial asthma and did not smoke</p> <p><u>Results</u>                      The 3<sup>rd</sup> ventricle width is significantly wider in the cough syncope group compared to syncope not associated with coughing group and the convulsions group (p&lt;0.01)                      All other PEG measurements were non-significant</p>	<p><u>Conclusion</u>                      Results suggest an association between cough syncope and a relatively wide 3<sup>rd</sup> ventricle with a ventricular system that has the appearance of hydrocephalus ex vacuo (not low pressure hydrocephalus). Therefore hydrocephalus ex vacuo may be a predisposing factor in cough syncope.</p> <p>Small observational study – bias, confounding, chance, reverse causality.</p>
Jarema et al <sup>41</sup> 1981 (Polish)	Case series of 5 patients	Patients with cough syncope	Patient characteristics		<p>5 (100%) patients male                      Age range 41-54 years                      All pyknic or athletic build or obese (15-40kg overweight)                      All heavy smokers (≥20 cigarettes a day)                      3 (60%) patients had bronchitis                      2 (40%) patients had retrosternal goitre</p>	<p>Small observational study – bias, confounding and chance.</p> <p>Selection bias may have been introduced as not clear if patients enrolled consecutively.</p>

## 6 References

### 6.1 Main References

- (1) Draft Minutes of the Secretary of State's Honorary Medical Advisory Panel on Driving and Disorders of the Nervous System Held on 19th October 2005.  
[http://www.dvla.gov.uk/drivers/medical/minutes\\_2005/meeting\\_minutes\\_19\\_oct\\_05.htm](http://www.dvla.gov.uk/drivers/medical/minutes_2005/meeting_minutes_19_oct_05.htm).  
Accessed on 8/5/06. 19-10-2005.  
Ref Type: Internet Communication
- (2) Corson WA. Cough syncope. *Minnesota Medicine* 1970; 53(1):43.
- (3) Aaronson DW, Rovner RN, Patterson R. Cough syncope: case presentation and review. *Journal of Allergy* 1970; 46(6):359-363.
- (4) Melby DP, Cytron JA, Benditt DG. New approaches to the treatment and prevention of neurally mediated reflex (neurocardiogenic) syncope. [Review] [45 refs]. *Current Cardiology Reports* 2004; 6(5):385-390.
- (5) Bonekat HW, Miles RM, Staats BA. Smoking and cough syncope: follow-up in 45 cases. *International Journal of the Addictions* 1987; 22(5):413-419.
- (6) Kerr A, Derbes VJ. The syndrome of cough syncope. *Annals of Internal Medicine* 1953; 39:1240-1252.
- (7) Khadartsev AA, Morgunova IN. [Cough syncope syndrome in patients with expiratory stenosis of the trachea and bronchi]. [Russian]. *Klinicheskaja Meditsina* 1991; 69(10):54-57.
- (8) Blue JA. Syncope in allergy. *Annals of Allergy* 1968; 26(10):561-568.
- (9) Skolnick JL, Dines DE. Tussive syncope. *Minnesota Medicine* 1969; 52(10):1609-1613.
- (10) Xue LF. [Report of 18 cases of cough syncope]. [Chinese]. *Chinese Journal of Tuberculosis & Respiratory Diseases* 320; 8(5):296-297.
- (11) DeMaria AA, Jr., Westmoreland BF, Sharbrough FW. EEG in cough syncope. *Neurology* 1984; 34(3):371-374.
- (12) Lindegaard KF, Skälpe IO, Sjaastad O. Cough syncope: the possible relation to hydrocephalus ex vacuo. *European Neurology* 1977; 15(6):340-344.
- (13) Jarema M, Osuch Z, Stankowska-Chomicz A. [5 cases of the cough-syncope syndrome]. [Polish]. *Neurologia i Neurochirurgia Polska* 1981; 15(5-6):537-539.
- (14) Trim G, Nicholls S, Saw W, Barlow M, Leitch J. Cough syncope: clinical and investigational profile of seven patients. *Heart, Lung and Circulation* 2001; 10:A95.
- (15) Xue LF. [Report of 18 cases of cough syncope]. [Chinese]. *Chinese Journal of Tuberculosis & Respiratory Diseases* 320; 8(5):296-297.
- (16) Jarema M, Osuch Z, Stankowska-Chomicz A. [5 cases of the cough-syncope syndrome]. [Polish]. *Neurologia i Neurochirurgia Polska* 1981; 15(5-6):537-539.
- (17) Khadartsev AA, Morgunova IN. [Cough syncope syndrome in patients with expiratory stenosis of the trachea and bronchi]. [Russian]. *Klinicheskaja Meditsina* 1991; 69(10):54-57.
- (18) Bonekat HW, Miles RM, Staats BA. Smoking and cough syncope: follow-up in 45 cases. *International Journal of the Addictions* 1987; 22(5):413-419.
- (19) Blue JA. Syncope in allergy. *Annals of Allergy* 1968; 26(10):561-568.

- (20) Khadartsev AA, Morgunova IN. [Cough syncope syndrome in patients with expiratory stenosis of the trachea and bronchi]. [Russian]. *Klinicheskaja Meditsina* 1991; 69(10):54-57.
- (21) Khadartsev AA, Morgunova IN. [Cough syncope syndrome in patients with expiratory stenosis of the trachea and bronchi]. [Russian]. *Klinicheskaja Meditsina* 1991; 69(10):54-57.
- (22) Skolnick JL, Dines DE. Tussive syncope. *Minnesota Medicine* 1969; 52(10):1609-1613.
- (23) Skolnick JL, Dines DE. Tussive syncope. *Minnesota Medicine* 1969; 52(10):1609-1613.
- (24) Xue LF. [Report of 18 cases of cough syncope]. [Chinese]. *Chinese Journal of Tuberculosis & Respiratory Diseases* 320; 8(5):296-297.
- (25) Bonekat HW, Miles RM, Staats BA. Smoking and cough syncope: follow-up in 45 cases. *International Journal of the Addictions* 1987; 22(5):413-419.
- (26) Bonekat HW, Miles RM, Staats BA. Smoking and cough syncope: follow-up in 45 cases. *International Journal of the Addictions* 1987; 22(5):413-419.
- (27) Blue JA. Syncope in allergy. *Annals of Allergy* 1968; 26(10):561-568.
- (28) Xue LF. [Report of 18 cases of cough syncope]. [Chinese]. *Chinese Journal of Tuberculosis & Respiratory Diseases* 320; 8(5):296-297.
- (29) Bonekat HW, Miles RM, Staats BA. Smoking and cough syncope: follow-up in 45 cases. *International Journal of the Addictions* 1987; 22(5):413-419.
- (30) Blue JA. Syncope in allergy. *Annals of Allergy* 1968; 26(10):561-568.
- (31) Xue LF. [Report of 18 cases of cough syncope]. [Chinese]. *Chinese Journal of Tuberculosis & Respiratory Diseases* 320; 8(5):296-297.
- (32) McCorry DJ, Chadwick DW, Barber P, Cooper PM, Wroe S. Cough syncope in Heavy Goods Vehicle drivers. *Qjm* 2004; 97(9):631-632.
- (33) Haffner HT, Graw M. [Cough syncope as a cause of traffic accident]. [German]. *Blutalkohol* 1990; 27(2):110-115.
- (34) Auerbach K. An approach to problem cases in commercial interstate drivers. *Clinics in Occupational & Environmental Medicine* Vol 3(1)(pp 11-26), 2003.
- (35) Bonekat HW, Miles RM, Staats BA. Smoking and cough syncope: follow-up in 45 cases. *International Journal of the Addictions* 1987; 22(5):413-419.
- (36) Khadartsev AA, Morgunova IN. [Cough syncope syndrome in patients with expiratory stenosis of the trachea and bronchi]. [Russian]. *Klinicheskaja Meditsina* 1991; 69(10):54-57.
- (37) Blue JA. Syncope in allergy. *Annals of Allergy* 1968; 26(10):561-568.
- (38) Skolnick JL, Dines DE. Tussive syncope. *Minnesota Medicine* 1969; 52(10):1609-1613.
- (39) Xue LF. [Report of 18 cases of cough syncope]. [Chinese]. *Chinese Journal of Tuberculosis & Respiratory Diseases* 320; 8(5):296-297.
- (40) DeMaria AA, Jr., Westmoreland BF, Sharbrough FW. EEG in cough syncope. *Neurology* 1984; 34(3):371-374.
- (41) Jarema M, Osuch Z, Stankowska-Chomicz A. [5 cases of the cough-syncope syndrome]. [Polish]. *Neurologia i Neurochirurgia Polska* 1981; 15(5-6):537-539.

## 7 Appendices

### 7.1 Appendix 1 – Details of Request

#### ARIF REQUEST FORM

Date of Request

30 / 03 / 2006

Lead Medical Adviser  
Issuing request

Name – Dr Heather Major

Contact details

Drivers Medical Group  
DVLA  
Sandringham Park  
Swansea Vale  
Llansamlet  
Swansea  
SA7 OAA

**1. Without worrying about the structure of the question, state in full the nature and context of the problem.**

The per annum recurrence risk in those who have had an episode of cough syncope.  
Is the condition treatable?  
If so, by what means?  
What factors are contributory to the development of cough syncope? e.g. obesity, chronic respiratory disease, smoking history.  
Does management/removal of risk factors improve recurrence risk? Can this be quantified?

**2. Please give a background to the question. Why has DMG raised this problem?**

Because of a number of fatal accidents and coroners cases, there is a need to balance standards to safeguard the public, but at a level that does not disadvantage those whose recurrence risk may be at an acceptable level (no greater than 2% per annum).

**3. Giving references where appropriate, briefly detail the sources you have used to obtain background information on the *options* and *issues*, which might be important for the problems, you describe.**

a) Minutes of the Secretary of State for Transport's Honorary Medical Advisory Panel on Driving Disorders of the Nervous system held on:

19 October 2005  
23 March 2005  
27 October 2004

b) In-house literature search carried out by S Lloyd 25 April 2005 on "Prognostic features for recurrence in

patients with a first cough syncopal event”.

At A Glance guide to the current Medical Standards of Fitness to Drive February 2006. Chapter 7  
Respiratory and Sleep Disorders.

**4. Please give name and contact details of any expert or clinical contact e.g. relevant Panel Chairman/expert Panel member.**

Prof Charles P Warlow (Chairman)  
Prof of Medical Neurology  
Dept of Clinical Neurosciences  
The University of Edinburgh  
Bramwell Dott Building  
Western General Hospital  
Crewe Road  
Edinburgh EH4 2XU

[REDACTED]

[REDACTED]

Dr Heather Major SMA

[REDACTED]

**What is the nature of the target population of the issue detailed above? E.g. age, profile, vocational drivers, young drivers, other co-morbid features.**

Group 2 drivers.

**6. What are the outcomes you consider particularly important in relation to the question posed? What decisions rest on these outcomes?**

Currently there is limited evidence based on which to base our standards. The outcome will allow us to review the current standards.

**What is the latest date that an ARIF response would be of value**

31 / 05 / 2006

**Please either:**

**Fax this form to: 0121 414 7878 marking FAO ARIF**

**E-mail as a word document or pdf attachment to:** [REDACTED]

**Post to:-**  
**Dr David Moore**  
**Senior Research Reviewer and Analyst**  
**Aggressive Research Intelligence Facility**  
**West Midlands Health Technology Assessment Collaboration**  
**Department of Public Health**  
**University of Birmingham**  
**Edgbaston**  
**Birmingham**  
**B15 2TT**

**Please ring 0121 414 3166 or 6767 if you have any queries, or you want to check the progress with your request.**



## 7.2 Appendix 2 – Outline Methods

Our plan of action is briefly outlined below.

- The report will focus on the recurrence risk in those who have had an episode of cough syncope, the treatment and risk factors associated with the condition, and whether treatment or the removal of risk factors reduce the recurrence risk.
- A scoping search highlighted a limited number of studies on the subject. Therefore MEDLINE (1966-2006), EMBASE (1980-2006) and the Cochrane Library (2006 Issue 2) will be searched using a broad search strategy including only terms for cough and syncope. The identified studies will then be screened by an analyst for relevance.
- Due to the limited information on the subject, all types of studies that report on the relevant outcomes will be selected and the most robust commented upon.
- Methodological quality of these studies will be discussed.
- Data on relevant outcomes will be extracted and reported.

As we have already discussed the information on cough syncope is fairly limited compared to some of the other topics we have addressed for you. So basically this is going to be a 'trawling' exercise to try to find any reasonably robust information to address your questions.

The above search will yield about 300 to 400 articles but we envisage most will be of low relevance or irrelevant so the screening process should not take too long. Secondary screening of the relevant studies to identify the most robust for the subsections of your request and the subsequent analysis and reporting of these will be our main task.

## **7.3 Appendix 3 – Search strategies**

### **7.3.1 ARIF Reviews Protocol**

#### **SEARCH PROTOCOL FOR ARIF ENQUIRIES**

(July 2005)

##### **1. Cochrane Library**

- Cochrane Reviews
- Database of Abstracts of Reviews of Effects (DARE)
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Health Technology Assessment (HTA) database

##### **2. ARIF Database**

An in-house database of reviews compiled by scanning current journals and appropriate WWW sites. Many reviews produced by the organisations listed below are included.

##### **3. NHS CRD**

- DARE
- Health Technology Assessment Database
- Completed and ongoing CRD reviews

##### **4. Health Technology Assessments and Evidence Based guidelines**

- NICE appraisals and work plans for TARs, Interventional Procedures and Guidelines programmes, Public Health excellence
- Office of Technology Assessment
- NHS Coordinating Centre for Health Technology Assessments
- Canadian Co-ordinating Office for Health Technology Assessment
- New Zealand Health Technology Assessment
- Wessex STEER Reports
- Agency for Healthcare Research and Quality (AHRQ)
- National Horizon Scanning Centre
- SIGN (Scottish Intercollegiate Guidelines Network)

##### **5. Clinical Evidence**

##### **6. Bandolier**

##### **7. National Horizon Scanning Centre**

##### **8. TRIP Database**

##### **9. Bibliographic Databases**

- Medline – systematic reviews
- Embase – systematic reviews
- Other specialist databases

## 10. Contacts

- Cochrane Collaboration (via Cochrane Library)
- Regional experts, especially Pharmacy Prescribing Unit, Keele University (& MTRAC) and West Midlands Drug Information Service for any enquiry involving drug products

### 7.3.2 Primary studies protocol

Database: EMBASE <1980 to 2006 Week 14>

Search Strategy:

---

- 1 cough.mp. or exp Coughing/ (26748)
- 2 syncope.mp. or exp SYNCOPÉ/ (10504)
- 3 1 and 2 (249)
- 4 (cough adj2 syncope).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (56)
- 5 3 and 4 (56)
- 6 3 or 4 (249)
- 7 from 3 keep 1-249 (249)

Database: Ovid MEDLINE(R) <1966 to March Week 5 2006>

Search Strategy:

---

- 1 cough.mp. or exp Coughing/ (21681)
- 2 syncope.mp. or exp SYNCOPÉ/ (10039)
- 3 1 and 2 (159)
- 4 (cough adj2 syncope).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (74)
- 5 3 and 4 (74)
- 6 3 or 4 (159)
- 7 from 3 keep 1-159 (159)