NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Clinical Practice – Surveillance Programme

Recommendation for Guidance Executive (post-consultation)

Clinical guideline
CG109: Transient loss of consciousness management in adults and young people

Publication date
August 2010

Surveillance report for GE (post-consultation)
September 2014

Surveillance recommendation
GE is asked to consider the following proposals which were consulted on for two weeks:

- The clinical guideline CG109: Transient loss of consciousness management in adults and young people should not be considered for an update at this time.
- The guideline should be transferred to the static guidance list because it fulfils the following criteria:
  - No evidence was identified that would impact on the current guidance and no major ongoing studies or research has been identified as due to be published in the near future (that is, within the next 3-5 years)

Key findings

			Potential impact on guidance	
			Yes	**No**
Evidence identified from Evidence Update				✓
Evidence identified from literature search				✓
Feedback from Guideline Development Group				✓
Anti-discrimination and equalities considerations				✓
No update	CGUT update	Standard update	**Transfer to static list**	Change review cycle
✓			✓	

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Surveillance review of CG109: Transient loss of consciousness management in adults and young people

Recommendation for Guidance Executive (post consultation)

Background information

Guideline issue date: 2010
4 year review: 2014

NCC: National Clinical Guidelines Centre

Four year surveillance review

1. An Evidence Update was produced for the guideline in 2012 and was used as a source of evidence for the review proposal. The Evidence Update indicated that there was new evidence to potentially generate future change in the guideline in two areas:
   - The clinical history including immediate pre-event symptoms (breathlessness) as this may distinguish between non-cardiac syncope and cardiac syncope. Breathlessness is a red flag symptom for cardiac syncope (recommendation 1.1.4.2) and, as such, the included study supports current recommendations.
   - Psychogenic non-epileptic attacks are a common cause of transient loss of consciousness (TLoC). This fact is already highlighted within the guideline but the study included in the Evidence Update is not a diagnostic accuracy study and hence does not meet the criteria set within the guideline for inclusion within the evidence base.
2. For the 4 year Surveillance Review, a search to identify new evidence was carried out for articles published between 4th October 2011 (the end of the search period for the Evidence Update) and 29th April 2014 and relevant abstracts were assessed. As a diagnostic guideline, the search strategy included observational studies in addition to randomised clinical trials (RCTs) and systematic reviews. Only evidence

that met the criteria for inclusion detailed within the original guideline are included within this surveillance review. Clinical feedback was also obtained from members of the Guideline Development Group (GDG) through a questionnaire survey. Generally the GDG felt that the guideline does not need to be updated.

3. No new evidence was identified through the literature search which would invalidate the guideline recommendations.

Ongoing research

4. None identified.

Anti-discrimination and equalities considerations

5. None identified.

Implications for other NICE programmes

6. A Quality Standard on Transient loss of consciousness in adults is currently in development and is expected to publish in October 2014. The current surveillance review recommendation does not impact on the Quality Standard.

Summary of stakeholder feedback

7. Stakeholders were consulted on the following proposals over a two week consultation period:

The clinical guideline CG109: Transient loss of consciousness management in adults and young people should not be considered for an update at this time.

The guideline should be transferred to the static guidance list because it fulfils the following criteria:

- No evidence was identified that would impact on the current guidance and no major ongoing studies or research has been identified as due to be published in the near future (that is, within the next 3-5 years)

8. In total, 9 stakeholders commented on the surveillance review proposal during the two week consultation period. The table of stakeholder comments can be viewed in Appendix 1.

9. Three stakeholders agreed with the surveillance review proposal to not update the guideline at this time and to place the guidance on the static list, 2 stakeholders disagreed and 4 stakeholders did not state a definitive decision.

10. One stakeholder that disagreed with the decision not to update the guideline and transfer it to the static list felt that the original scope did not include telephone triage as a mode of presentation. As a result, the stakeholder felt that the guideline was difficult to implement for telephone triage systems (111 and 999 services) particulary regarding the recommendation for an ECG during the assessment of the person with TLoC. The original scope included the initial management of people who have experienced TLoC within any setting in which NHS care is received and further diagnostic investigations within secondary care, including specialist blackout clinics. However, there are no specific recommendations realting to telephone triage systems within CG109. No new evidence has been identified relating to telephone triage and how to determine, via this medium, if a patient requires an ECG and, as such, any proposed new recommendations would be consensus based. We have contacted NHS Pathways and understand that they have resolved this issue to their satisfaction for the time being, but they would like us to consider explicitly the application of recommendations in NICE guidelines to the setting of NHS telephone advice services in future iterations of this and other guidelines covering initial assessment of illness outside hospital. This information has been passed on to the commissioning and technical teams within CCP.

11. The same stakeholder identified a number of specific clinical conditions (obstructive cardiac lesions, dysautonomic conditions, recent invasive cardiac intervention) that they wished to see further consideration of within the guideline. The original scope of the guideline covers TLoC as a symptom and, as such, covers a range of conditions that may result in an individual presenting with TLoC. The guideline aims to define the appropriate pathways for the initial assessment of these patients and to suggest a pathway to follow to determine the cause of the person's TLoC, advice on appropriate management until a diagnosis is made and to ensure that the correct referral is made. The current care pathways within CG109 encompass the conditions suggested by the stakeholder and, as no evidence that impacts the recommendations relating to the conditions was identified through the surveillance review, it is doubtful that changes to the guideline are required. Whilst the stakeholder indicated that they wished further guidance it should be noted that the guideline does not override the responsibility of healthcare professionals and others to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer. Similarly, guidance is not designed to be prescriptive, while they assist the practice of healthcare professionals, they do not replace their knowledge and skills.

12. The second stakeholder that disagreed with the no to update and static list proposal wished the guideline to be updated to include the references identified within the surveillance review. Currently NICE does not update guidance if there is no evidence indicating that recommendations for clinical practice require changing.

Conclusion

13. Through the 4 year surveillance review of CG109 and subsequent consultation with stakeholders no new evidence was identified which may potentially change the direction of current guideline recommendations. The proposal is not to update the guideline at this time and to move this guideline onto the static list because it fulfils the following criteria:
    - No evidence was identified that would impact on the current guidance and no major ongoing studies or research has been identified as due to be published in the near future (that is, within the next 3-5 years)

Mark Baker – Centre Director
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Centre for Clinical Practice
October 2014

Appendix 1 Surveillance review consultation

Surveillance review consultation comments table
25 August-5 September 2014

Stakeholder	Do you agree that the guidance should not be updated?	Do you agree that the guidance should be put on the static list?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
College of Emergency Medicine (UK)	Agree	Agree		Comments on proposal not to update the guideline: No evidence was identified that would impact on the current guidance and no major ongoing studies or research has been identified as due to be published in the near future (that is, within the next 3-5 years)	Thank you for your comment.
Royal College of Paediatrics and Child Health				We have not received any responses for this consultation	Thank you.
Resuscitation Council (UK)	Disagree	Disagree	The original scope did not include telephone triage as a mode of presentation.	As written, the guideline makes it virtually impossible for telephone triage systems to be compliant with CG109. This is a common situation that arises via the 111 and 999 services, so this omission is of major relevance to current NHS service delivery. Despite this being raised as a concern in a joint letter from Dr Peter Fox and Dr Fiona Jewkes on behalf of NHS Pathways and from me on behalf of the RC (UK), NICE has not responded adequately, if at all, to suggest how it might address that problem.	Thank you for your comment. The original scope included the initial management of people who have experienced TLoC within any setting in which NHS care is received and further diagnostic investigations within secondary care, including specialist blackout clinics. The guideline makes recommendations to enable emergency and other NHS staff to determine the appropriate management and urgency of treatment required. This initially

Stakeholder	Do you agree that the guidance should not be updated?	Do you agree that the guidance should be put on the static list?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
					includes: using clinical judgment to determine appropriate management and the urgency of treatment if: • the person has sustained an injury • the person has not made a full recovery of consciousness • TLoC is secondary to a condition that requires immediate action After this initial assessment then detailed history taking followed by any relevant clinical examinations are recommended. We appreciate that there are no specific recommendations relating to telephone triage (111 or 999) services within the guideline. We are sorry that you feel this area has not been adequately addressed and as such will look to incorporate changes to this guidance when it is next updated.
			One of our respondents felt that the guideline should have given 1. more consideration to obstructive cardiac lesions (e.g. pulmonary embolism)	These were personal views, based on practical clinical experience rather than on any new published evidence relating to the current scope, structure and wording of CG109.	Thank you for your comments. The orginal scope of the guideline covers any condition that may result in an individual presenting with TLoC. The guideline aims to define the appropriate pathways for the initial

Stakeholder	Do you agree that the guidance should not be updated?	Do you agree that the guidance should be put on the static list?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			presenting with syncope. 2. more guidance to raise awareness of dysautonomic conditions (e.g. postural orthostatic tachycardia syndrome). 3. guidance on the assessment of patients who have undergone recent invasive cardiac intervention (e.g. within the previous month).		assessment of these patients and to suggest a pathway to follow to determine the cause of the person's TLoC, advice on appropriate management until a diagnosis is made and to ensure that the correct referral is made. Obstructive cardiac lesions encompass any narrowing of the pathways to blood flow in the heart or major blood vessels such that a pressure gradient is generated as the blood traverses the circulation. These conditions, if they result in TLoC, are already encompassed by the guideline and no specific evidence relating to these conditions that would imply that the guidance needs to be altered was identified through the surveillance process. With regards to dysautommic conditions, these should be identified during the history assessment of patients with TloC and as such are covered by the guideline. Specific guidance around determining postural orthostaic conditions is already encompassed within the assessment and diagnosis section of the guideline.

Stakeholder	Do you agree that the guidance should not be updated?	Do you agree that the guidance should be put on the static list?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
					With regards to patients who have had a recent cardiac intervention, the initial assessment (history taking and clinical assessment (ECG)) would result in a referral to a cardiac specialist with further tests as deemed appropriate by the clinican and subsequent management.
Royal College of Nursing				The feedback I have received from nurses caring for people with NICE Transient loss of consciousness in adults and young people suggests that there are no additional comments to submit in relation to the Stakeholders' comments response table for the above guidelines.	Thank you.
Department of Health				The Department of Health has no substantive comments to make, regarding this consultation.	Thank you.
Royal College of Physicians of Edinburgh	No	No	No comments.	The College acknowledges that there is presently little substantial new evidence in this area; however the new evidence that exists should be incorporated into the guideline within the standard timeframes. The College would also recommend reviewing the guideline in four years.	Thank you for your comment. Currently NICE does not update Clinical Guidelines if there is no new evidence that would impact on the recommendations. Due to restrictions on time and resources priority is given to updating guidance where new evidence will impact clinical practice. NICE is aware that this means that the evidence base within the guideline may not be up to date. However, placing the guideline on the static

Stakeholder	Do you agree that the guidance should not be updated?	Do you agree that the guidance should be put on the static list?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
					list means that the guideline will be reviewed again in 5 years. As no ongoing research has been identified that is due to publish in the next 3-5years reviewing the guideline at 4 years may be premature. If at the 5 year surveillance review it is found that this topic should be taken off the static list it is the intention that it will fall back within the regular 2 yearly review cycle.
NHS England				NHS England has no substantive comments to make regarding this consultation	Thank you.
Medtronic Limited	Agree	Agree			Thank you.
Dr Sanjiv Petkar - GDG	Agree	Agree			Thank you.

Appendix 2 Decision matrix

The table below provides summaries of the evidence for key questions for which studies were identified.

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
Initial assessment and diagnosis of people who had TLoC			
Q109-1 In people who have experienced a TLoC, what aspects of patient history (including eye-witness accounts) are useful in discriminating between patients with syncope (cardiac, neurally mediated or orthostatic hypotension), epilepsy, psychogenic non-epileptic seizures (PNES) and other causes of TLoC?			
A large retrospective cohort study found that hospital visits for syncope were more frequent in patients taking cholinesterase inhibitors and were associated with increased risk of serious adverse events (that is, syncope, bradycardia, pacemaker insertion and hip fracture) in older patients with dementia [1]. This evidence was also reviewed by the National Prescribing Centre's MeReC Rapid Review 343 [2]. A cross-sectional study assessed the ability of specific pre-event symptoms to predict cardiac and non-cardiac syncope in elderly patients (n=242)[3]. Multivariate regression analysis indicated the most common symptoms	The new evidence highlighted that cholinesterase inhibitors can cause syncope, which is important for clinicians to consider when assessing patients. NICE CG109 emphasises the need to assess and record current medication in the initial assessment algorithm. One study emphasised the importance of a detailed clinical history, and suggested that pre-event symptoms may play a useful role in distinguishing between non-cardiac and cardiac syncope, with breathlessness a potential indicator of cardiac syncope[3]. It should be noted that breathlessness is a red flag symptom (recommendation	A literature-based model for symptoms that were associated with cardiac causes of syncope used a 7 study derivation sample reporting >2 predictors of cardiac syncope that had 10 diagnostic predictors (age, gender, structural heart disease, low number of spells, brief or absent prodrome, supine syncope, effort syncope, and absence of nausea, diaphoresis and blurred vision) was identified[7]. The resulting model was tested in four datasets of patients with syncope. The study found that a model with 5 variables (age, gender, structural heart disease, low	New evidence is unlikely to impact recommendations. A wide range of predictors from patients' clinical history have been identified which aim to discriminate between syncope (and syncope type), epilepsy and other causes of TLoC. These predictors were all identified within the evidence base of NICE CG109 and formed the basis of the recommendations. Information from these studies is unlikely to affect NICE CG109. Clinical feedback indicated that there was a desire to provide evidence based recommendations for the PNES population. However, using the criteria detailed within the guideline no substantial evidence relating to this area was

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
of this group predictive of non-cardiac syncope were awareness of being about to faint, sweating, blurred vision and nausea. Breathlessness was more common in cardiac than non-cardiac syncope) and was the only symptom predictive of cardiac syncope. A retrospective cohort study characterised clinical predictors of primary bradycardia in patients (n=52) undergoing prolonged monitoring for unexplained syncope[4]. Evidence from this study suggested that a history of syncope without prodrome, abnormal ECG and structural heart disease were all predictors of spontaneous primary arrhythmia. A retrospective study reviewed referrals (n=3002) to a tertiary syncope unit and found that the aetiology of syncope changes with age, with the greatest burden of disease in the elderly[5]. A Scottish cohort study of patients referred to a first seizure clinic with suspected PNES and prospectively	1.1.4.2) and as such this study does not impact on the current recommendations within the guideline to consider breathlessness. All of the predictors from patients' clinical history are already covered in NICE CG109 to help decide on the need for cardiovascular assessment. Information from these studies is unlikely to affect NICE CG109. Likewise, evidence from these studies is not expected to alter patient pathways or service commissioning and is unlikely to affect NICE CG109. The new evidence emphasises PNES is a cause of TLoC which is also noted in the current guideline.	number of spells, and lack of prodromal symptoms) was as accurate as the total set. A study of patients with Wolff-Parkinson-White syndrome (n=98) admitted for syncope indicated that syncope associated with WPW syndrome was dependant of age with the electrophysiological malignant form frequent in children/teenagers, rare in adults, and absent in the elderly[8]. Orthodromic atrioventricular re-entrant tachycardia, the main cause of syncope, was as frequent in all age ranges. A study to develop the diagnostic scoring system based on the clinical history allowing to distinguish between cardiac and non-cardiac syncope (n=200) was identified[9]. Multivariate regression analysis identified seven variables: age above 55 years, presence of structural	identified.

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
identified 68 cases of first presentations of PNES, implying an annual incidence of 4.9 per 100,000 in Scotland[6]. The identified patient group had high rates of psychological morbidity, including self-harm and history of abuse, but half were free of attacks at 3 months.		heart disease, syncope in supine position, absence of prodromal symptoms, and chest pain before syncope were predictive of cardiac syncope with a sensitivity of 81%, specificity of 84.8%. Predictors of noncardiac syncope were recovery duration of more than 1 minute and syncope occurring immediately after standing up. One study was identified which investigated the characteristics of syncope to differentiate high-risk syncope episodes from low-risk events in patients with Brugada syndrome (n=84)[10].The results indicated that syncope with prodrome, especially blurred vision, suggests a benign etiology of syncope in patients with Brugada syndrome. **Epilepsy** A systematic review of 2 studies indicated that tongue biting had	

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		a pooled accuracy for determining epileptic seizures with a sensitivity of 33%, specificity of 96%, positive likelihood ratio (LR) of 8.167 and negative LR 0.695 in cases of TLoC[11]. A systematic review of 5 studies determined that urinary incontinence has no value in the differential diagnostic between epileptic seizures and non-epileptic events (including syncope and PNES)[12]. A systematic review of 6 studies which assessed the sensitivity, specificity and LRs of ictal eye closure as a clinical sign supporting the diagnosis of psychogenic non-epileptic events (PNEEs) was identified[13]. Pooled accuracy measures for ictal eye closure for the diagnosis of PNEE were 58% for sensitivity and 80% for specificity however if only studies that had blinded	

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		assessment were included the diagnoses yielded results indicative of a rather lower diagnostic value A systematic review found that tongue biting without further specifications has no value in the differential diagnosis between seizures and PNEEs[14]. **Syncope/near syncope** A retrospective study of patients (n=250) admitted to the geriatric ward utilised a binary logistic regression to predict risk factors for syncope and near-syncope[15]. A multifactorial and cumulative aetiology with frequently overlapping factors was established. Falls, postural hypotension, and/or brain hypoperfusion of different origin seem to be most predictive of the both syncope and near-syncope, however low systemic blood pressure was predictive for the syncope exclusively.	

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		Epidemiology A Danish National cohort study of patients hospitalised with syncope identified 127 508 patients with a first-time diagnosis of syncope. The age distribution of the patients showed three peaks around 20, 60, and 80 years of age[16]. Cardiovascular disease and cardiovascular drug therapy was present in 28% and 48% of the patients, respectively. A significant association between cardiovascular disease and the risk of admission for syncope increased with younger age and age above 80.	
Q109-2 In people who have experienced a TLoC, what aspects of physical examination are useful in discriminating between patients with syncope (cardiac, neurally mediated or orthostatic hypotension), epilepsy, psychogenic non-epileptic seizures and other causes of TLoC?			
A retrospective study which assessed the frequency of syncope in patients with different orthostatic syndromes was identified[17]. Syncope was found to occur more commonly in patients	Evidence from this study is unlikely to affect CG109 TLoC. The new evidence provides support for the NICE CG109	No new evidence identified.	No impact.

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
with postural orthostatic tachycardia syndrome than in patients with orthostatic hypotension. A prospective, study to evaluate the aetiology and diagnostic yield of a standardised diagnostic work-up, in a selected group of patients, in a syncope unit was identified[18]. Patients underwent initial evaluation (history, physical evaluation and a 12-lead echocardiography (ECG) and specific tests based on the suspected aetiology. ECG was used in 55% of people, with a diagnostic yield of only 2%.	recommendation that echocardiography should be used only with clinical or ECG suspicion of structural heart disease.		
Q109-3 In people who have experienced a TLoC, what routine laboratory tests are useful in discriminating between patients with syncope (cardiac, neurally mediated or orthostatic hypotension), epilepsy, psychogenic non-epileptic seizures and other causes of TLoC?			
A cohort study undertaken as a sub-study of the ROSE study aimed to establish whether D-dimer is an independent predictor of 1-month serious outcomes and all-cause death in patients presenting to the A&E with syncope[19]. Receiver-operator characteristic curve analysis showed	Evidence from this study has no impact on NICE CG109.	One observational study of patients (n=40) with diabetes and observed for TLoC indicated that there was an association between episodes of TLoC and low levels of glycaemia in diabetic patients on treatment[20].	No impact on recommendations. Current recommendations within CG109 already state that if during the initial assessment, there is suspicion of an underlying problem causing TLoC relevant examinations and investigations should be carried out. These included checking the

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
no relationship between plasma D-dimer concentration and serious outcome or death at 1 month.			blood glucose levels if diabetic hypoglycaemia is suspected.
Q109-4 Which signs, symptoms and other features of presentation (e.g. patient history) are associated with an increased risk of a serious adverse event?			
A study which examined aetiologies for syncope and risk factors for mortality and re-hospitalisation in patients hospitalised for syncope was identified[21]. 4% of patients were re-hospitalised for syncope and 12% died. Independent risk factors for re-hospitalisation for syncope were diabetes, atrial fibrillation and smoking. Independent risk factors for time to mortality were diabetes, coronary artery bypass graft surgery, history of malignancy, use of narcotics, smoking, atrial fibrillation and volume depletion. Characterisation as high risk by the OESIL risk score or San Francisco Syncope rule was not significantly associated with re-hospitalisation or long-term mortality.	New evidence is unlikely to affect NICE CG109.	Thirteen studies were identified that investigated factors that were found to be associated with adverse serious advents in patients with TLoC/syncope. The studies include the following signs/symptoms: prolonged QTc [22] , QTc interval > 500 ms[22 23] palpitations preceding syncope[24], evidence of bleeding[24] , more than one incidence of syncope in the last 30 days[25-27] , glomerular filtration rate[28], cardiovascular hospitalisation[27] , pacemaker or implantable cardioverter-defibrillator event rate[27]. The following co-morbidities were also associated with an increased serious adverse event rate: diabetes mellitus[23,25] , a history consistent of heart failure[24,25], ischemic heart	New evidence is unlikely impact on recommendations. The guideline currently lists a number of 'red flag symptoms' for when a patient should be referred within 24 hours for specialist assessment. These include: an ECG abnormality, heart failure, TLoC during exertion, a family history of sudden cardiac death in people aged younger than 40 years and/or an inherited cardiac condition, new or unexplained breathlessness, a heart murmur. In addition the recommendation states that the clinician consider referring within 24 hours for cardiovascular assessment, anyone aged older than 65 years who has experienced TLoC without prodromal symptoms. The new evidence on the whole supports the current red flag symptoms. No clinical feedback was received relating

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		disease[24], dementia[25] , stroke[26] , hypertension [28], drug overdose[28] , Brugada syndrome [29] and a history of malignancy[23] . Older age was a predictor of serious adverse events in 3 studies[22,23,30] but not in a fourth[16]. Increasing scores CHADS2 or San Francisco Syncope Score (SFSS) were associated with adverse events in one study respectively [28,31]. In addition, 2 of the studies compared adverse advents between patients with syncope and near syncope. One study indicated that patients with near-syncope were younger than those with syncope and were also more commonly male[32]. Hospitalisations were more common for syncope than for near-syncope. However, multivariable logistic regression revealed that age, heart rate, and renal dysfunction were independent predictors of undesired events, while the type	to this area.

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		of syncope was not. In contrast a second study indicated that emergency department hospitalisation or 30-day adverse outcomes were comparable between near syncope and patients with syncope[33]. However, a similar risk of adverse outcomes for near syncope and syncope. In addition 1 study indicated that exertional syncope was associated with serious adverse events[24].	
Q109-5 Which signs, symptoms and other features of presentation (e.g. patient history) are associated with an increased likelihood of spontaneous remission?			
A prospective cohort study assessed inpatient management of patients (n=540) with syncope admitted to hospital from a UK A&E[34]. The median and mean length of stay were 1 day and 6.3 day respectively. A total of 73% patients were admitted to general or acute medicine, 7% to cardiology, 7% to medicine of the elderly, 6% to surgical specialities and the rest to other specialities. A	Evidence from the inpatient management study is unlikely to affect NICE CG109. Evidence from the psychological profiling study is unlikely to affect NICE CG109. Evidence from the cohort study which evaluated	No new evidence was identified.	No impact. No clinical feedback was received relating to this area.

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
diagnosis was made in 63% patients. The differing levels of diagnosis and variety of diagnostic testing between specialities identified by the study suggest that current inpatient management of syncope may be suboptimal and speciality-dependent. A prospective study which determined the psychological profile of patients (n=116) with recurrent syncope before and after diagnostic HUT, and whether it could be used to predict recurrence of syncope was identified[35]**.** Clinically meaningful levels of distress were observed in 60% of patients at baseline. However, patients with 'unexplained syncope' (negative HUT) had a five-fold greater risk of experiencing depressive or anxiety disorders compared to positive HUT. Recurrence of syncope was predicted by increased levels of baseline psychological distress. A prospective cohort study which evaluated outcomes for high-risk patients diagnosed with benign causes of syncope after standard A&E assessments[36]. Patients classified as	outcomes for high-risk patients diagnosed with benign causes of syncope after standard A&E assessments is unlikely to affect CG109. This study addresses formal clinical recognition of dehydration as a contributing cause of syncope and reinforces the importance of history-taking, and the need to record current medications as recommended by NICE CG109. Current recommendations already encourage early discharge for uncomplicated vasovagal syncope, situational syncope and orthostatic hypotension.		

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
having a benign cause of syncope (vasovagal or dehydration) on the basis of a standard A&E assessment receive no benefit from hospital admission.			
Q109-6 Can clinical decision tools or risk stratification tools be used to discriminate between patients who would benefit from admission and patients who can be safely discharged?			
A prospective study (Risk Stratification of Syncope in the Emergency Department [ROSE] study) in the UK was identified which was designed to develop and validate a clinical decision rule (CDR) to predict 1-month serious outcomes and all-cause death in patients presenting to A&E with syncope[37]. The CDR (the 'ROSE rule') had a sensitivity and specificity of 87.2% and 65.5%, respectively. A systematic review assessed the methodological quality and prognostic accuracy of CDRs in syncope patients in the A&E[38]. Meta-analyses of the San Francisco Syncope rule (SFSR) showed sensitivity of 86% and specificity of 49%; a sensitivity of 95% and specificity of 31% was recorded for the Osservatorio Epidemiologico	The new evidence on CDRs included those looked at during the development of NICE CG109 and acknowledged similar issues as those noted in the NICE process. The evidence on CSSS is important in that it highlights the limitations of this CDR. Awareness-raising is needed to ensure that A&E settings do not use this score in patient triage pathways. The conclusions are unlikely to affect NICE CG109.	A study which aimed to validate the performance of the CSSS in an elderly population (n=180) with suspected VVS (>60 years of age in all patients prior to undergoing head-up tilt test (HUT) was identified [41]. The CSSS has a lower sensitivity (51%) and specificity (73%) in this elderly population compared to previously validated data in young adults. A cross-sectional study of patients (n=216) diagnosed with syncope during emergency department evaluation found 39% were hospitalised[42]. The variables associated with the need of hospital admission were: having health care	New evidence unlikely to impact on guideline recommendations. New evidence was identified that looked at CDRs that were also appraised during the development of NICE CG109. Whilst some of the new evidence indicates that, in practice, they may reduce hospitalisation rates the levels of sensitively and specificity are not different to those reported within CG109 and the limitations of these scores are still valid. Nursing triage was characterised by a low predictive accuracy in identifying high-risk individuals. Hence the conclusions are unlikely to affect the recommendations within CG109.

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
sulla Sincopenel Lazio (OESIL) risk score. A retrospective study which validated the SFSR and indicated a sensitivity of 90% and specificity of 33% was identifed[39]. Implementing the rule in the Canadian setting would increase admission rates from 12.3 to 69.5%. The authors concluded that implementation of the rule would significantly increase admission rates. A prospective cohort evaluating the Calgary Syncope Symptom Score (CSSS) was identified[40].The sensitivity was 87% and specificity 32%. The low sensitivity may lead to misdiagnosis of TLoC and suggests poor utility of the Calgary Score in clinical practice.		insurance, previous known cardiovascular disease, no history of prior stroke, previous syncope and abnormal ECG during the presentation. Patients classified in OESIL score > 2 were significantly more likely to be hospitalised compared to those with a score of 0. A before-and-after cohort study of emergency department patients presenting with syncope assessed the usefulness of the Boston Syncope Criteria. In the "before" phase, 69% patients with syncope were admitted, compared to 58% after the criteria were introduced[43]. A prospective, cohort study was conducted at the emergency department on adult patients (n=231) and over who presented with syncope[44]. Dyspnoea, orthostatic hypotension, precipitating cause of syncope, age over 58 years, congestive heart failure, and ECG	

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		abnormality were found to predict short-term serious outcomes by logistic regression analysis and these were used to compose the Anatolian Syncope Rule (ASR). The sensitivity and specificity of ASR, OESIL, Evaluation of Guidelines in Syncope Study (EGSYS) and SFSR for mortality 100%; 90%, 80% , 100% and 97%,70%,56% and 87% respectively. A systematic review including 12 studies gave a pooled estimate of sensitivity of the SFSR of 0.87, and pooled estimate of specificity of 0.52[45] . A prospective descriptive analysis study in adult patients (n=178) presenting with syncope or near syncope to assess the accuracy of SFSR and OESIL score at predicting short-term serious outcome was identified [46]. The SFSR had 74.7% accuracy, 90.6% sensitivity, 68% specificity, whereas OESIL	

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		score had 80.9% accuracy, 79.4% sensitivity, 81.6% specificity. A retrospective study of patients (n=678) who presented with syncope at the emergency department assessed nursing triage, comorbidities, clinical features and adverse events that occurred both in the emergency department and at 10-day follow-up was identified [47]. 8.1% patients experienced adverse events, 9.4% of which occurred among the patients who were identified as high priority by nursing triage. Sensitivity and specificity of urgent nursing triage in identifying adverse outcomes were 21% and 88% respectively.	
Q109-7 When providing immediate care in the pre-hospital setting to a person who has experienced a TLoC, what aspects of the initial assessment should be performed in the pre-hospital setting?			
No evidence identified.	No impact.	One study evaluated the use of pre-hospital tele-cardiology for emergency medical service	New evidence is unlikely to impact on guideline recommendations. Clinical feedback from one member of the GDG

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		patients (n=2648) referred for syncope[48]. Pre-hospital ECGs were sent to a single tele-cardiology hub, active 24/7 and serving a region of 4-million inhabitants, and promptly read by a cardiologist. Prevalence of significant arrhythmias among patients referred for syncope and evaluated with pre-hospital tele-cardiology ECG was low, and almost absent in subjects below 30 years.	expressed that this study be considered as a potential impact on the guidance. The new evidence indicates that a pre-hospital triage via tele-cardiology for emergency medical service patients may be effective service delivery approach for detecting patients with cardiac arrhythmias. This study did not compare the rate of arrhythmia detection with any other approach. The applicability of this approach from Italy to the UK practice would need to be assessed as it would appear that all patients with TLoC receive an ECG which is not recommended within CG109.
Q109-8 When is transfer to hospital by ambulance appropriate in the immediate care of a person who has experienced a TLoC and what discharge advice should be provided when transfer is not appropriate?			
No evidence identified.	No impact.	No new evidence identified.	No impact.
Q109-9 In people who have experienced TLoC, which diagnostic tests should be performed, both in an unselected population and in specified subgroups (e.g. suspected syncope, epilepsy or psychogenic non-epileptic seizures)?			

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
Computed tomography scans A prospective study assessed the use of computed tomography (CT) scans of the head as routine diagnostic tests for patients presenting with syncope (n=292)[49]. The study identified 3.9% patients with CT abnormalities related to TLoC and 15.3% with abnormalities unrelated to TLoC. The authors concluded that routine use of CT head scans as a diagnostic tool for syncope is unjustifiable. **Structural heart disease** A prospective cohort study which had developed a simple evidence-based point-score to distinguish vasovagal syncope (VVS) from ventricular tachycardia (VT) in patients (n=134) with structural heart disease was identified[50]. The results indicated that the causes of syncope in patients with structural heart disease, and their clinical outcomes can be estimated accurately based on the clinical history, which can be used to rule out VT as the basis for syncope. A prospective, study which assessed	Evidence from the study on CT scans confirms the diagnostic approach taken in NICE CG109, which does not include CT scans. Evidence from one study emphasises the need for taking a good clinical history in patients with syncope, which is already highlighted in NICE CG109. The paper on bundle branch block is unlikely to affect NICE CG109, which identifies complete right or left bundle branch block as a 'red flag' that should result in clinical assessment, ECG, Holter monitoring and echocardiography in these patients, with subsequent investigation and treatment dictated by specialist cardiovascular assessment. The new evidence around tilt-testing is unlikely to affect current guidance. The authors suggested that clomipramine challenge may be better than glyceryl tri-nitrate in identifying patients for pacemaker	**Carotid sinus massage** A study was identified which utilised carotid sinus massage in the supine and standing positions with continuous ECG and blood pressure monitoring on patients (n=1855) aged over 40 years with unexplained syncope after the initial evaluation was used to assess carotid sinus syndrome[53]. Carotid sinus syndrome was identified in 8.8% of patients with 81% having an asystolic reflex and 19% a vasodepressor reflex. Potential multifactorial causes of syncope (orthostatic hypotension, bundle branch block, bradycardia, tachyarrhythmias) were found in 74% of patients. **External loop recorders** A registry based study assessed the diagnostic yield of new external loop recorders (ELRs) in patients (n=307) with history of syncope, pre-syncope, and sustained palpitations with a	New evidence is unlikely to impact on guideline recommendations. New evidence relating to carotid sinus massage, external loop recorders and Holter ECGs supports current recommendations and evidence within CG109. A number of studies relating to tilt testing were identified. These explored a variety of methods for conducting a tilt test in numerous sub groups. The majority of factors were already within the evidence base of the original guideline. The new studies on the whole present contradictory results to that presented in the original guideline. Two studies supported the efficacy of pacing for individuals who had neurally mediated syncope. A secondary analysis of a subset of the patients from the ISSUE-3 trial looked at the applicability of HUT determining who will clinically benefit from pacing produced results that indicated that HUT testing would be more appropriate than ILR in a subset of patients. This is not in line with current

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
outcomes in patients (n=323) with syncope and bundle branch block was identified[51]. A 3-phase diagnostic strategy and aetiological diagnoses were established in 82.7% patients. A pacemaker was implanted in 220 patients, an implantable cardioverter defibrillator in 19 and radiofrequency catheter ablation was undertaken in 3 patients. No comparisons were made with any other possible diagnostic /therapeutic strategies in these patients. **Tilt table testing** A prospective cohort study of patients (n=380) who had previously undergone tilt table testing aimed to determine a possible relationship between clinical triggers of syncope on responses to head-up tilt, using glyceryl trinitrate (nitroglycerin) or clomipramine provocation[52]. In patients with central triggers for	therapy[52]. The data confirmed that neurally mediated syncope can produce convulsive movements, which can be misinterpreted as epilepsy due to the presence of myoclonic jerky movements during syncope, and does not warrant any change to the recommendations in NICE CG109 for suspected epilepsy.	mean monitoring duration of 24.1days[54]. Among patients with syncope, a conclusive diagnosis was obtained in 17% patients. **Holter ECG** A cross-sectional study compared the efficacy of 24-hour Holter ECG with intermittent short ECG recording over four weeks to detect relevant arrhythmias in patients (n=108) with palpitations or dizziness/presyncope[56]. Analysis of Holter registrations showed that intermittent ECG	recommendations within CG109. However, the authors described this result as unexpected and indicated that they believed that this needs to be confirmed by other studies. Clinical feedback from a member of the GDG indicated that the role of TT versus ILR in reflex syncope may need further clarification following the data from the ISSUE-3 trial. However, feedback from the GDG chair indicated that they thought reviewing the use of tilt testing at present may be premature and further studies are required to provide clarity on the use of the tilt test for determining who should have pacing.

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
reflex syncope, clomipramine challenge had greater sensitivity than glyceryl trinitrate. In patients with peripheral triggers, glyceryl trinitrate challenge was more sensitive than clomipramine; mixed and vasodepressor responses were more commonly induced in patients by glyceryl trinitrate (41%) compared with clomipramine (24%). Clomipramine infusion was associated with significantly more adverse events. A retrospective study compared the clinical characteristics of patients with neurally mediated syncope who experience 'seizure-like' symptoms during a head-up tilt test (HUT) with those who do not display such activity[55]. Medical records of patients with a positive HUT (n=226) indicated that 5.75% patients showed 'seizure-like' activities. There were no significant differences in clinical variables and hemodynamic parameters during HUT between patients with and those without 'seizure-like' activity.		during four weeks is more effective in detecting relevant arrhythmias than 24-hour Holter ECG. A prospective 48 month study which evaluated the Holter method of sinoatrial conduction time (SACT) calculation for predicting the future occurrence of sinus node disease and the emergence of indications for permanent pacing in patients with unexplained syncope (n=218) was identified[57]. The results suggest that the Holter method of SACT calculation is useful in predicting sinus node disease and indications for permanent pacing in patients with unexplained syncope. **Tilt-table testing** A meta-analysis which focused on sensitivity and specificity of HUT for diagnosing vasovagal syncope identified 55 articles[58]. The influence of age, test	

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		duration, tilt angle, and nitroglycerine or isoproterenol stimulation on tilt testing outcome was analysed and HUT demonstrated a good overall ability to discriminate between symptomatic patients and asymptomatic controls. Multivariate analysis, advancing age and a 60 degree tilt angle showed a significant effect in reducing sensitivity and increasing specificity of the test. Nitroglycerine significantly raised tilt testing sensitivity by maintaining a similar specificity in comparison to isoproterenol. A study which compared a short pain-provoked head-up tilt (PP-HUT) with the CSSS in a group of patients (n=127) with clinically diagnosed vasovagal syncope and a group of neurological patients without transient loss of consciousness was identified[59] . PP-HUT had a higher diagnostic rate with a sensitivity of 65.9 % and specificity of 89.7 %	

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		whereas the CSSS had sensitivity of 58.5 % and specificity of 46.1 %. A randomized study which compared the diagnostic value of 2 HUT protocols using sublingual nitroglycerin for provocation in patients with recurrent unexplained syncope and normal heart (n=290) was identified[60]. The only difference between two protocols was that nitroglycerin was administered after a five minute resting phase in supine position during one of the protocols. Adding a period of rest and returning to supine position before nitroglycerin administration had no additional diagnostic yield. A study of patients (n=419) referred for the diagnostic evaluation of syncope by HUT indicated that when patients are stratified by between body mass index (BMI) there is a higher proportion of patients with	

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		positive tests among those with BMI <18.5 kg/m2[61]. Multivariate analysis also showed that underweight patients had a 3.9 times higher risk for a positive HUT response A study which compared the sensitivity, specificity, accuracy, of conventional and shortened HUT for a patients with a history of vasovagal syndrome (n=60) was found[62]. The HUT without passive phase was not inferior to the conventional HUT regarding sensitivity, specificity, and accuracy with protocol being better tolerated. A study which investigated the relationship between clinical presentation of VVS and HUT and clinical outcome at long-term follow-up in subjects (n=671) undergoing nitroglycerin-potentiated HUT for suspected VVS was identified[63]. The positivity rate of HUT was 65% and 36% in patients with	

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		established and likely VVS. A study which assessed the role of the HUT in patients previously diagnosed with refractory epilepsy (n=107) to evaluate the ability of this test to correctly diagnose patients with neurocardiogenic syncope[64] . The HUT was positive in 54% of patients with 33% patients misdiagnosed with epilepsy, and 21% patients had a dual diagnosis of neurocardiogenic syncope and epilepsy. A RCT in patients (n=80) with syncope of unknown origin and atrioventricular or sinoatrial block lasting >10 seconds under adenosine 5'-triphosphate administration found that pacing led to fewer recurrences than those who did not receive pacing [65]. **Pacing** A RCT which evaluated the effect of dual-chamber closed-	

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		loop stimulation (on and off) in the prevention of syncope recurrence in patients (n=50) with refractory vasovagal syncope (VVS) and a cardioinhibitory response to head-up HUT during a 36 months follow-up indicated that dual-chamber CLS is an effective algorithm for preventing syncope recurrences[66]. The RCT ISSUE-3 trial included patients (n=511) over 40 years who had experienced at least 3 syncopal episodes in the previous 2 years and all received an ILR[67]. Those participants (n=89) who then had documented syncope with 3s asystole or 6s asystole without syncope within 12 months met criteria for pacemaker implantation. Dual-chamber permanent pacing was shown to be effective in reducing recurrence of syncope in this patient group with severe asystolic neurally mediated	

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		syncope. A second study from the ISSUE-3 which performed an on-treatment analysis, which included additionally those non-randomized patients followed up in the ISSUE registry to evaluate in a better manner the effectiveness of cardiac pacing therapy[68]. During follow-up, cardiac pacing reduced the risk of syncope recurrence with a few complications. A third study from the ISSUE-3 was identified which investigated the role of tilt testing (TT) in predicting recurrences[69]. In 136 patients enrolled in the ISSUE-3, TT was positive in 76 and negative in 60. An asystolic response predicted a similar asystolic form during implantable loop recorder monitoring, with a positive predictive value of 86%. The corresponding values were 48% in patients with non-asystolic TT and 58% in patients with negative TT. Cardiac pacing	

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		was effective in neurally mediated syncope patients with documented asystolic episodes in whom TT was negative; conversely, there was insufficient evidence of efficacy from this data set in patients with a positive TT even when spontaneous asystole was documented.	
Research Recommendations			
109-RR1 Does a serial assessment approach (taking repeated ECGs or repeated observations of vital signs) improve diagnosis of high-risk cardiac arrhythmias when compared with a single assessment approach in people with TLoC in any setting?			
No evidence identified.	No impact.	No evidence identified.	No impact.
109-RR2 In people who are considered on the basis of clinical history and examination to have had an uncomplicated faint, what is the additional clinical effectiveness and cost effectiveness of a 12-lead ECG?			
No evidence identified.	No impact.	No evidence identified.	No impact.
109-RR3 Under what circumstances is the implantable cardiac event recorder the investigation of choice for TLoC in people in whom a cardiac cause is suspected?			
A prospective study which assessed the use of the Reveal IER and its effectiveness in the diagnosis of unexplained syncope was identified[70]. Enrolled patients had syncope or pre-syncope IER was reported to be diagnostic in most patients	The new evidence did not compare different diagnostic strategies for people with unexplained syncope, so is of limited benefit in directing evidence-based clinical guidelines. Nevertheless the data are consistent with the	An RCT which compared conventional testing with prolonged monitoring using an implantable loop recorder (ILR) following the first syncope episode in patients (n=78) with bundle branch block (BBB) and	New evidence unlikely to impact recommendations. A range of studies, which did not always compare the use of ILRs to differing diagnostic strategies in differing populations, indicate that the use of ILRs

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
experiencing recurrent syncope, this occurred more than 30 days after IER implantation and the numbers of people with recurrence increased progressively over 2 years. A prospective, non-randomised single centre study assessed the effectiveness of new IER device with wireless technology, by determining the effect of direct IER transmission to a central ECG monitoring centre on the burden of data reviewed by the physician was identified[71]. Patients (n=40) with unexplained syncope were implanted with a new IER and followed for 8.5 ± 5.1 months. This study found use of the automatic IER with wireless technology to be a feasible option for remote ECG monitoring by IERs; however, there were problems with excessive ECG burden from the recording.	recommendations in NICE CG109. In particular, the results of the studies discourage early use of many investigations and neurology referral for unexplained TLoC, and encourage early use of an IER in those in whom initial clinical assessment and 12-lead ECG fail to identify a likely cause and in whom the frequency of recurrent events is unlikely to allow documentation with an external event recorder.	negative workup found significantly more relevant arrhythmias using ILR and the conventional follow-up[72]. A retrospective study comparing remote monitoring to ILR in patients with syncope and palpations (n=109) indicated that ILR shortened the time to diagnosis and targeted treatment[73]. A cohort study of patients with a range of cardiovascular conditions (n=743) which evaluated the indications and outcomes of the ILR in real clinical practice found that one-third of patients obtained a final diagnosis with the ILR within 1 year, independent of the baseline characteristics[74]. A study which assessed the care pathway and the resulting diagnostic yield in patients with syncope and a potential cardiovascular cause (n=514)	are beneficial in determining a diagnosis. The data on the whole is consistent with the recommendations in NICE CG109 in discouraging early use of many investigations and encouraging early use of an IER in those in whom initial clinical assessment and 12-lead ECG fail to identify a likely cause and in whom the frequency of recurrent events is unlikely to allow documentation with an external event recorder. Clinical input indicates that a new injectable (as opposed to an implantable) loop recorder has been launched in UK and Europe for the investigation of patients with syncope. No studies on this were identified in the current evidence search.

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		who had received an ILR after an "initial phase of the diagnostic work-up" or after a "full evaluation" of unexplained syncope indicated that both approaches resulted in a high diagnostic yield[75]. However, hospitalisation and injury before implant were less common in patients with an "initial work-up" as were visits to specialists. A cohort study of patients with unexplained syncope (n=157) evaluated the diagnostic value of ILR during very prolonged observation[76]. The estimated cumulative diagnostic rates were 30%, 43%, 52%, and 80% at 1, 2, 3, and 4 years, respectively. Prolonging observation up to 4 years increased the diagnostic value of ILR in syncopal patients and was safe. A study to determine the outcome of patients with an ILR (n=97) in terms of syncope recurrence and survival was	

Conclusions from previous review (2 year Evidence Update)	Impact at 2 years	Evidence summary of clinical area at 4 year and GDG/clinical perspective	Impact and comments
		identified[77]. Diagnosis had not been reached in 62% patients when the ILR battery reached end operational life. During a median follow-up of 48 months after ILR explantation, 40% patients had recurrence of syncope. Five patients died with no sudden or cardiac deaths detected during follow-up.	
Areas currently not covered by NICE guidance **Genetic aspects of vasovagal syncope**			
A systematic review of 19 studies which aimed to provide an overview of the current knowledge of the genetics of VVS was identified[78]. The quantity and quality of studies in this area was generally poor, and thus no firm conclusions could be drawn. Included studies also had small sample sizes and heterogeneous phenotype definitions, preventing meta-analysis.	Data from this systematic literature review did not find strong evidence for a genetic basis for vasovagal syncope and has no impact on NICE CG109.	No evidence identified.	No impact.

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