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Centre for Clinical Practice – Surveillance Programme

Clinical guideline

CG92: Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital

Publication date

January 2010

Previous review dates

2-year review: 2012 (no update)

Exceptional review*: 2013 (the section of the guideline on the use of intermittent pneumatic compression in patients with stroke should be updated)

4-year surveillance report for GE

July 2014

Key findings

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

Surveillance recommendation

GE is asked to consider the proposal for a standard update of this guideline.

The discreet update on the use of intermittent pneumatic compression (IPC) in stroke patients already agreed by GE would go ahead as planned through the standing committee.

*exceptional review of the section of the guideline on the use of intermittent pneumatic compression (IPC) to prevent VTE in patients with stroke

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Clinical Practice – Surveillance Programme

4-year surveillance review of CG92: Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital

Background information

Guideline issue date: January 2010

2-year review: 2012 (no update)

Exceptional review*: 2013 (the section of the guideline on the use of pneumatic compression in patients with stroke should be updated)

4-year review: 2014

NCC: National Clinical Guideline Centre

Triage Panel recommendation

1. Through the 4-year surveillance review of CG92, it was concluded that no new evidence had been identified which would impact on the guideline recommendations. This surveillance review proposal was consulted on for 2 weeks with stakeholders, however, general feedback indicated that stakeholders disagreed with the proposal not to update the guideline particularly due to disagreement on the use of aspirin for VTE prevention in total hip and knee replacement and the need for reconsideration of the evidence on the use of pharmacological and mechanical prophylaxis in medical patients.
2. As such, it was felt there would be value in discussing the issues raised during stakeholder consultation at the Triage Panel meeting, focussing particularly on the following areas:
    - *What is the effectiveness of different pharmacological prophylaxis methods in reducing the incidence of VTE in patients undergoing elective hip and knee replacement surgery?*

* exceptional review of the section of the guideline on the use of intermittent pneumatic compression (IPC) to prevent VTE in patients with stroke

- *What is the effectiveness of intermittent pneumatic compression in reducing the incidence of VTE in patients with stroke in whom pharmacological VTE prophylaxis has not been initiated?*
- *What is the effectiveness of different mechanical prophylaxis methods in reducing the incidence of VTE in medical patients in whom pharmacological VTE prophylaxis is contraindicated?*

3. Discussion with topic experts at the triage panel indicated that this guideline had contributed to significant progress for the NHS in reducing the risks of VTE and that it was a guideline that was internationally highly regarded. However, it was noted that there were still large areas of the guideline that are not being implemented because the guideline is seen as out of date at 4 years old particularly in relation to more recent guidelines from the US. The Triage Panel concluded that there would be significant value in conducting a standard update of this guideline particularly bearing in mind the feedback from stakeholders during consultation.

4. In addition to the areas highlighted above, the following areas were suggested by the Triage Panel experts as needing consideration for inclusion in the update: VTE risk assessment, VTE prevention in post-discharge daycase, VTE prevention in pregnancy and postpartum and VTE prevention in psychiatric inpatients.

5. It was agreed that the discreet update on the use of intermittent pneumatic compression (IPC) in stroke patients already agreed by GE would go ahead as planned through the standing committee and the rest of the guideline would be commissioned through the standard process in due course.

Findings of the current (4-year) surveillance review

6. For the 4-year Surveillance Review, a search to identify randomised controlled trials and systematic reviews was carried out for articles published between 18 June 2012 (the end date for the last searches) and 14 January 2014 and relevant abstracts were assessed.

7. Clinical feedback was obtained from members of the GDG through a questionnaire survey; four responses were received.

8. No new evidence was identified for any section of the guideline that may impact on current recommendations.

Main conclusions of the 2-year full review and the 2013 exceptional review

9. CG92 was previously reviewed for update in 2012. No new evidence was identified at the 2-year review point in 2012 that would change the direction of guideline recommendations. However, a new Technology Appraisal was identified - TA245: Apixaban for the prevention of venous thromboembolism after total hip or knee replacement in adults. It was therefore recommended that the guideline should cross refer to this new Technology Appraisal.

10. Following notification of the publication of the CLOTS 3 trial data in 2013, an exceptional review of the section of the guideline on the use of intermittent pneumatic compression (IPC) to prevent venous thromboembolism (VTE) in patients with stroke was also carried out. This review recommended that the section of the guideline on the use of IPC to prevent VTE in patients with stroke (within chapter 24 of the full guideline: Stroke patients) should be updated and was signed-off by Guidance Executive as an update topic in August 2013.

Summary of stakeholder feedback

11. Stakeholders were consulted about the following proposal over a two week consultation period:

The proposal is not to update any further section of the guideline at this time.

12. In total 14 stakeholders commented on the surveillance review proposal during the two-week consultation period (see Appendix 1).

13. Ten stakeholders disagreed with the review proposal to not update the guideline at this time, other stakeholders either did not state a definitive position or had no substatntive comments..

14. Comments from the stakeholders who disagreed related to a number of issues, including:
    - the need for a comprehensive document that has all the latest evidence and relevant technologies incorporated into a single point of reference - currently advice is in multiple documents (original guidelines, 3 single technology assessments and an Evidence update) and difficult therefore to assimilate and digest
    - the evidence on the use of aspirin for VTE prevention in total hip and knee replacement should be reviewed
    - the evidence on the use of pharmacological and mechanical prophylaxis in medical patients should be reviewed
    - the need for guidance for VTE prophylaxis in psychiatric inpatients
    - whether there is evidence to support VTE risk assessment within 24 hours of admission
    - VTE prophylaxis in pregnancy and peripartum needs to be reviewed
    - VTE prophylaxis for day, orthopaedic lower limb fractures/plastercast and outpatient cases needs clearer guidance
    - that the CLOTS 3 trial results should update the use of IPC in stroke patients, although this has previously been agreed by GE to be updated via the standing commmittee

15. No comments were provided by any stakeholder on equality issues or areas excluded from the original scope.

Ongoing trials

16. None identified.

Anti-discrimination and equalities considerations

17. None identified.

Implications for other NICE programmes

18. This guideline relates to a published quality standard on VTE prevention (QS3)
19. An update of CG92 is unlikely to impact on most of the Quality Statements of QS3 as actions from the statements are to be done "in accordance with NICE guidance" with the exception of Statement 4 on re-assessment within 24 hours of admission.

Conclusion

20. Following consultation feedback on the proposal not to update the guideline and discussions at the the panel there would be significant value in conducting a standard update of this guideline.

Surveillance recommendation

21. GE is asked to consider the proposal for a standard update of this guideline.
22. The standing committee update on the use of IPC in stroke patients already agreed by GE should go ahead as planned.

Mark Baker – Centre Director
Sarah Willett – Associate Director
Khalid Ashfaq – Technical Analyst

Centre for Clinical Practice
July 2014

Appendix 1 - Consultation comments and response

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
Anticoagulation & Thrombosis Dudley Group of Hospitals NHS Foundation Trust			On proposed review of nice guidance CG92: VTE reducing the risk – could you review the guidance for the below • SOX trial and usage of class 2 stockings post event. • IPC following clot study 3 and use of IPC • Prophylaxis in pts with plaster casts	Thank you for your comment. Further to consultation and discussions with topic experts it has been agreed that this guideline will undergo a standard update.
Barnsley Hopsital NHS Foundation Trust	Disagree		1. Description - to recommend Intermittent pneumatic compression (IPC) for immobilised stroke patients (Lacet 2013- CLOT 3 trail). 2. To modify the flow diagram (Summary guideline) to include IPC for stroke patients. **Eff ectiveness of intermittent pneumatic compression in reduction of risk of deep vein thrombosis in patients who have had a stroke (CLOTS 3): a multicentre randomised controlled trial** *CLOTS (Clots in Legs Or sTockings after Stroke) Trials Collaboration** ***Lancet* 2013, 382: 516–24** *Published* ***Online*** *May 31, 2013* http://dx.doi.org/10.1016/ *S0140-6736(13)61050-8* ***This publication has been corrected three times. The fi rst corrected version fi rst appeared at thelancet.com on June 5,***	Thank you for your comment. Following notification of the publication of the CLOTS 3 trial data in 2013, an exceptional review of the guideline was carried out. The review recommended that the section of the guideline on the use of IPC to prevent VTE in patients with stroke should be updated and was signed-off by Guidance Executive as an update topic. Your comments will be passed onto the Clinical Guidelines Update Team who will be carrying out the update of this section of the guideline.

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			2013, the second on August 9, 2013, and the third on September 20, 2013	
Lifeblood: The Thrombosis Charity	Disagree		One major issue is that these guidelines will fall into disrepute among health professionals if the content is not updated to include recent RCTs and new oral anticoagulants, even if they do not change practice in a major way, for this guideline is the basis on which thromboprophylaxis for hospitalised patients is administered and there is an extensive infrastructure in all the Trusts to ensure this happens. To have a less than up-to-date guideline is not acceptable. Currently advice on thromboprophylaxis is in multiple documents and difficult therefore to assimilate and digest (original guidelines, 3 single technology assessments and an Evidence update). <u>VTE prophylaxis in Pregnancy and Peripartum</u> The NICE guidelines and the RCOG guidelines on VTE prophylaxis differ in their approach and recommendations. This is an area where there is poor Grade 1 evidence and relies on expert opinion. Why cannot the two organisations produce the same guideline? <u>The use of mechanical thromboprophylaxis in medical and critical care patients.</u> Currently the advice is to use stockings if the patient cannot tolerate pharmacological thromboprophylaxis. But the	Thank you for your comment. Further to consultation and discussions with topic experts it has been agreed that this guideline will undergo a standard update.

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			evidence for this was extrapolated from surgical patients and since the 2010 guidelines the CLOT-2 study has shown stocking were of no efficacy in stroke patients, indeed they were associated with harm. The decision on whether to use stockings in medical patients therefore needs to be reviewed, and the possibility of intermittent pneumatic compression considered in view of their benefit on stroke patients (CLOT-3).	
BOA Patient Liaison Group	Dis-agree – it needs updating	International Orthopaedics (SICOT) (2014) 38:169–175 DOI 10.1007/s00264-013-2134-8 "Antithrombotic prophylaxis in major orthopaedic surgery: an historical overview and update of current recommendations"" Plamen Kinov & Panayot P. Tanchev & Martin Ellis & Gershon Volpin The American College of Chest Physicians (ACCP) have recently commented on VTE – there should be a place in the review for this?	<u>I would like to see this paper included in the orthopaedic section review</u> Aspirin has been somewhat rehabilitated in recent years in line with the ACCP comments. From the patient perspective it will be a show of weakness if NICE DO NOT review their guidelines (especially for TKR & THR) and send out a strong message about the appropriateness of ASA compared with the newer oral prophylaxis drugs. It is not a credible alternative for NICE to sit back and leave the *status quo* in the current orthopaedic climate. Too many patients are at risk from inappropriate VTE management in the absence of clear up to date considered guidelines for not only the orthopaedic surgeons but also for the Trust management and the commissioners who may have little or no experience in this field.	Thank you for your comment. Further to consultation and discussions with topic experts it has been agreed that this guideline will undergo a standard update.

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
The Royal College of Psychiatrists	Disagree	The original guideline does not include any guidance for mental health trusts, and nobody representing mental health trusts was on the advisory panel	This guideline urgently needs updating in order to include guidance for mental health trusts. Psychiatric inpatients may be at increased risk of VTE for a number of reasons, including antipsychotic use, periods of immobility, obesity and smoking. There are also some issues pertinent to VTE prevention that are highly relevant to its practice in the mental health setting that are not covered by the existing guideline; such as patients that lack capacity, and risks of self harm and bleeding within this patient group. There is an increasing awareness of higher rates of morbidity and mortality in people diagnosed with severe mental illness (SMI), and longstanding issues around the quality of physical healthcare for mental health patients, who thought to be likely to suffer healthcare inequalities as a result (Lawrence and Kisely, 2010). There is a growing body of professional literature suggesting that VTE is more common in people with severe mental illness (Van Neste et al, 2010). **I**n particular, treatment with antipsychotic medication (which is commonly prescribed in severe mental illness) is associated with a higher incidence of VTE (Xhang et al 2011; Van Neste et al 2009). A VTE risk prediction tool has been developed that includes the use of antipsychotic medication as an independent risk factor (Hippisley-Cox and Coupland, 2011). Patients with severe mental illness may also suffer from many known risk factors for VTE, including being smokers, being overweight and having decreased mobility, either due to their underlying illness, sedation due to medication or concurrent physical illness or frailty, the latter which is particularly of relevance in the elderly population (Van Neste et al, 2010).	Thank you for your comment. Further to consultation and discussions with topic experts it has been agreed that this guideline will undergo a standard update.

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			The Royal College of Psychiatrists have acknowledged the issue of VTE in psychiatric inpatients in its recent publication 'Whole Person Care –From Rhetoric to Reality (RCPsych, 2013) which makes the recommendation that NICE consider reviewing it's guideline to incorporate mental health patients. Hippisley-Cox, J. and Coupland, C. (2011) 'Development and validation of risk prediction algorithm (QThrombosis) to estimate future risk of venous thromboembolism: prospective cohort study' *British Medical Journal* Vol 343:d4656 p343 Lawrence, D. & Kisely, S. (2010) 'Review: Inequalities in healthcare provision for people with severe mental illness' *Journal of Psychopharmacology* Vol 24(11) Supplement 4 pp 61–68 Royal College of Psychiatrists (2013) Occasional Paper 88 - Whole Person Care: From Rhetoric to Reality, Achieving Parity in Physical and Mental Health' RCPsych, London Van Neste E.G., Verbruggen, W., and Leysen, M. (2009) 'Deep vein thrombosis and pulmonary embolism in psychiatric settings' *European Journal of Psychiatry* Vol 23:No 1 pp19-30 Xhang,, R., Dong, L., Shao, F., Tan, X. and Ying, K. (2011) Antipsychotics and venous thromboembolism risk – a metaanalysis *Pharmacopsychiatry* 44(5):183-8.	

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
British Thoracic Society	Disagree		In the General Medical Patients (4 studies) section, one systematic review and meta-analysis (ref 50) of pharmacological prophylaxis to prevent VTE in medical patients found no significant differences in overall mortality, symptomatic VTE or major bleeding between pharmacological prophylaxis and no intervention. We are concerned that “No clinical feedback was provided” by the GDG and this evidence may potentially impact CG92. Please could the evidence supporting a VTE risk re-assessment within 24 hours of admission and/or how this recommendation has improved patient outcomes since the release of CG92 be provided? In the latest version there is no mention of the link between iron deficiency and risk of DVT/PE, although this was in a population with hereditary haemorrhagic telangiectasia (Livesey J *et al*. Thorax 2012;67:328e333	Thank you for your comment. Further to consultation and discussions with topic experts it has been agreed that this guideline will undergo a standard update.
ArjoHuntleigh			**Comments in email**: As a stakeholder organisation, ArjoHuntleigh are very interested in gaining further information during the guideline update process for the use of IPC in Stroke patients. We would be very happy to provide input during the review and during consultation of the final draft before publication. **Comments in proforma**: Thank you for providing ArjoHuntleigh with the opportunity to review the VTE consultation document CG 92. ArjoHuntleigh agree that with the exception of the section on IPC in Stroke patients the rest of the guideline should not be updated at this time. There are	Thank you for your comment and for your interest in our work - we encourage stakeholders to get involved in the development of our guidance at all stages. Our consultation processes enable stakeholders and others with an interest in our guidance to comment on guidance development at

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			however a couple of comments that ArjoHuntleigh would like NICE to consider during the review of the section on Intermittent Pneumatic Compression (IPC) in stroke patients, as follows: We note with interest the recommendation to update the guidance in light of evidence from the publication of the CLOTS 3 trial and the use of IPC devices in stroke patients. As a manufacturer of mechanical IPC devices, we are able to provide a significant level of expertise and clinical evidence to support its use in high risk patient populations. The term IPC has been described generically in the literature and in a growing number of peer reviewed guidelines. Whilst there has been some debate about the relative merits of 'uniform' versus 'sequential' compression, studies have consistently shown little difference in terms of VTE outcome, haemodynamics, type of garment or compression cycle. Furthermore independent technical reports (ECRI Institute 2007, 2009) and literature reviews (Morris & Woodcock 2004, Morris 2008) have concluded that the characteristics of sleeve type and compression cycle are not as important as safety features, ease of use and patient comfort. We would request that ArjoHuntleigh are involved in the review and consultation process during the update to the section on VTE prophylaxis in Stroke patients. **References:** ECRI Institute (2007). Intermittent Compression Device evaluation. Health Devices, USA; 36(6): 177-204	specific stages and feed back into the decision-making process. Your comments will be passed onto the Clinical Guidelines Update Team who will be carrying out the update of this section of the guideline.

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			ECRI Institute (2009) Intermittent Pneumatic Compression Therapy. Health Devices, April:120-123 Morris RJ, Woodcock JP (2004) Evidence based compression. Prevention of stasis and deep vein thrombosis. Annals of Surgery; 239(2):162-171 Morris RJ (2008) Intermittent pneumatic compression – systems and applications. Journal of Medical Engineering and Technology; 32(3):179-188. Intermittent pneumatic compression or graduated compression stockings for deep vein thrombosis prophylaxis? A systematic review of direct clinical comparisons	
COVIDIEN	Disagree		Covidien agrees that the section of the guideline on the use of intermittent pneumatic compression needs to be reviewed as mentioned above. This is mainly supported by the study CLOT 3 published in the Lancet in 2013: *Dennis MS, et al. Effectiveness of intermittent pneumatic compression in reduction of risk of deep vein thrombosis in patients who have had a stroke (CLOTS 3): a multicentre randomised controlled trial; Lancet 2013, 382: 516–24* **Covidien would like to pinpoint the fact that Kendall SCD™ Sequential Compression System with Vascular Refill Detection is the only intermittent pneumatic compression device studied in the CLOTS 3 Trial. Kendall is the only device with a Vascular Refill Detection system. Therefore, the guideline should highlight this in the guideline specifying the name of**	Thank you for your comment. Your concerns will be passed onto the Clinical Guidelines Update Team who will be carrying out the update of this section of the guideline.

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			Kendall SCD™ Sequential Compression System with Vascular Refill Detection and it cannot be generic to intermittent pneumatic compression (IPC). Prevention for stroke patients is discussed in the following two chapters that needs to be updated accordingly : - chapter 4.2 VTE prophylaxis for medical patients - chapter 4.4 VTE prophylaxis for patients after stroke In chapter 4.2, the following paragraph needs specifically to be reviewed: “The evidence concerning mechanical VTE prophylaxis in medical patients is sparse. There have been a few small trials of patients with coronary syndrome but the only large, randomised controlled trial was of patients with stroke. This trial showed that routine care plus thigh-length anti-embolism stockings did not confer significantly more protection against VTE than routine care alone and was associated with significantly more harm.” **In the long version of the guideline “ METHODS, EVIDENCE & GUIDANCE”,** Covidien recommends its update with the CLOT 3 study Page 39 chapter 4.2 VTE prophylaxis for medical patients: “The evidence concerning mechanical VTE prophylaxis in medical patients is sparse. There have been a few small trials of patients with coronary syndrome but the only large, randomised controlled trial was of patients with stroke. This trial showed that routine care plus thigh-length anti-embolism stockings did not confer significantly more protection against VTE than routine care alone and was associated with significantly more harm.”	

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Papworth Hospital	Disagree		In the General Medical Patients (4 studies) section, one systematic review and meta-analysis (ref 50) of pharmacological prophylaxis to prevent VTE in medical patients found no significant differences in overall mortality, symptomatic VTE or major bleeding between pharmacological prophylaxis and no intervention. We are concerned that “No clinical feedback was provided” by the GDG and this evidence may impact CG92. We would like to be advised of the evidence to support a VTE risk re-assessmnet within 24 hours of admission and how this recommendation has improved patient outcomes since the release of CG92	Thank you for your comment. Further to consultation and discussions with topic experts it has been agreed that this guideline will undergo a standard update.
British Orthopaedic Association	Disagree		*Introduction* The BOA would assert that NICE should undertake a review of CG92 and that the draft decision not to do so should be reviewed. In this response, we draw attention to relevant evidence on this topic as we believe a number of articles have not been considered in the review and others have not been considered appropriately. These are covered under the subheadings below. In addition, we should like to highlight the previous correspondence between the BOA and NICE on this issue, and our earlier critique of the NICE guideline CG92 – this is provided as a PDF attachment with this response (at Annex A). We would also like to draw to your attention that your extensive and well-researched evidence are often used as a good data source when cases come to court as regards VTE	Thank you for your comment. Further to consultation and discussions with topic experts it has been agreed that this guideline will undergo a standard update.

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			events. However, because of the complexity of the data presentation as to relative reduction, many experts say that had the patient had prophylaxis with 'x' (i.e. any modality not used for that patient) as recommended in the NICE guidelines, then this event would not have happened. At present there are a number of coroners who have been vilified in the press and online for interpreting the data correctly and therefore not supporting the case for "negligence". For negligence to be proven there must be a clear breach in the duty of care owed to the patient, i.e. no reasonable and responsible practitioner would have followed the path taken by the treating doctor in the case in question. That breach of duty must also have led to injury or damage to the patient. Your data in the appendices clearly shows that at best the reduction in incidence is around 15% using all prophylactic modalities. The legal test is "on the balance of probabilities" which is at least 50% and therefore at present your guidelines as written are being over interpreted in common use leading to a number of unhappy relatives and legal cases. Yet again no evidence has been led for those unfortunate patients with a previous DVT or PE or thrombophilia. As there is no evidence and NICE cannot therefore make any evidence based recommendation would it not be appropriate for NICE to recommend research be undertaken urgently in this area? We strongly support risk assessment for *all* patients and multimodal prophylaxis tailored to the needs of the patient. There is growing evidence of a significant reduction in the	

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			rates of DVT /PE following surgery from registry data. This should not be overinterpreted however there can be little doubt that early mobilisation has had an effect. *Evidence analysis* **Risk factor stratification** Parvizi J Huang R Raphael IJ Arnold WV Rothman RH Clin Orth Relat Res 2014 472(3) 903-12 This article includes a considerable number of orthopaedic patients. It does not include new categories but gives an absolute risk factor for different conditions. **Assessing the risk of DVT** Kulshresa V; Kumar S J Arthoplasty 2013 28(10) 1868-73 (though clearly underpowered because of the low incidence of DVT\PE in arthoplasty patients) show that the incidence of DVT was the same whether the patients were routinely anticoagulated or selectively anticoagulated based on individual risk assessment however the bleeding risk was higher when routine prophylaxis was given. This suggests that we are overtreating some patients and causing problems. **Reducing the risk of VTE** The paper quoted (Stewart / Freshour Annals of Pharmacology where the first author is an industry paid speaker) is a review of much bigger AAOS and ACCP guidelines and reviews the same evidence as you have done before, perhaps with a different view rather than new data. In the past you have agreed that the evidence (used in the most recent AAOS and ACCP guidelines) remains the same	

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			as you have assessed and that you formally agreed to differ from the recommendations made by the ACCP and AAOS based on interpretation of the data rather than the evidence from the data itself. Indeed in your own excellent appendix there are detailed graphs showing the increased bleeding risk from LMWH compared with aspirin and the reduced rate of VTE events on aspirin. This is contradicted by the paper quoted here on no new evidence and inferior methodology to your own. You may wish to consider that as of January 2014 either aspirin or a compression device will be considered as acceptable measures for THR, TKR and hip fracture VTE prophylaxis as well as the other drug modalities under the American Surgical Care Improvement Programme used to audit medicare hospitals. It does seem odd that there is such a difference between major western healthcare providers given the solid evidence base and effort put into guidelines (and in contra-distinction to the Stewart paper). **Using VTE prophylaxis** This section perhaps should include the more recent trend towards multimodal prophylaxis including early mobilisation and the combined effect of drug prophylaxis (including aspirin) and stockings. Morris JK; Fincham BM; Orthopaedics 2012 35(12) 1716-21 looked at prevention using aspirin and pneumatic compression though the treatment was multimodal. Raphael IJ; Tishler EH; Huang R; RothmanRH; Hozack WJ; Parvizi J: Clin Orth Rel Res 2014 472(2) 482-8 Reports two case series at one institution warfarin (26123	

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			cases) Vs aspirin(28923 cases) using propensity score analysis matching for age and comorbid conditions. Overall the incidence of PE was lower in the aspirin group as was the incidence of DVT and wound related problems with shorter length of stay in the aspirin group. **Novel Anticoagulants Rivaroxaban Dabigatran Apixaban** Adams SS; McDuffie JR; Lachiewicz PF; Ortel TL; Williams JW; Ann Intern Med 2013 159(4) 275-84 is a systematic review of comparative effectiveness of various drug regimens using newer oral anticoagulants which agrees with your summation that they are as effective at preventing VTE events but ***the bleeding risks are higher***. This study was funded by the US Veterans administration (unlike some of the other analysis quoted) and probably the most comprehensive review to date however there is now a problem with overlapping meta-analysis in the literature using the same studies but slightly different techniques to reach differing conclusions perhaps reflecting author bias rather than data analysis (bit like guidelines and the Stewart paper!). You quote a similar paper with no mention of difference in bleeding. Bleeding on the newer oral anticoagulants remains an issue with a number of case series reported This is a poorly recorded complication in most industry sponsored trials which generally downplay complication. Buddhev P; Basu D; Davies N; Waters T; from West Hertfordshire Hospital at the British Hip Society meeting Manchester 2012 reported the results of introducing	

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			Rivaroxaban as a part of multimodal prophylaxis in 495 patients with a significant increase in wound complication rate. Bayley E; Brown S; Howard P; Royal Derby Hospital again at British Hip society Manchester 2012 reported on 6528 cases using multimodal prophylaxis. 1478 received warfarin 1722 LMWH and 3328 aspirin. The 90 day mortality was 0.33% for warfarin 0.93 for LMWH and 0,42% on aspirin. There were 6 fatal PE's 5 on LMWH and one on warfarin. Russel RD; Hotchkiss WR; Knight JR; Huo MH: Thrombosis 2013 762310 Highlighted that Rivaroxaban had a higher risk of bleeding than enoxaparin. Li J; Jing JH; Shi ZJ; Zhou Y: Zhongguo Gu Shang 2014 27(1) 34-7 A small randomised series of hip replacements comparing Rivaroxaban versus placebo resulting in a significant increase in blood loss and transfusion in the Rivaroxaban group. Bloch BV; Patel V; Best AJ; Bone Joint J 2014 96B 122-6 Compared the introduction of dabigatran (following your guidelines) with multimodal prophylaxis using LMWH and extended aspirin and found increased wound leakage on Dabigatran and reverted back to multimodal with LMWH and aspirin as extended prophylaxis. The rate of thrombo-embolic events was higher in the dabigatran group however the study was not big enough (1728 cases) to make this significant because of the low incidence of VTE events.	

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			Jameson SS[1], Rymaszewska M, Hui AC, James P, Serrano-Pedraza I, Muller SD. J Bone Joint Surg Am. 2012 Sep 5;94(17):1554-8 This retrospective review looked at 2762 patients given rivaroxaban and 10361 patients case matched on rivaroxaban. There was no difference in VTE events or death however there was a significant increase in wound complications in the rivaroxaban group. Zou Y; Tian S; Wang Y; Sun K: Blood Coag Fibrinolysis 2014 epub ahead of pub This is a prospective randomised trial comparing aspirin LMWH and Rivaroxaban for prophylaxis in knee surgery. This showed that Rivaroxaban reduced the incidence of VTE events but increased bleeding significantly. Aspirin and LMWH were equally efficacious in preventing DVT and no difference in bleeding. This is a small study and probably underpowered for the VTE issues however bleeding was statistically increased for Rivaroxaban. A multimodal regimen was used and recommended either with aspirin or LMWH. **Combined mechanical and drug prophylaxis and duration** Jorgensen C; Jacobsen MK; Soeballe K ;Hansen TB; Husted H; Kjaersgaard-Andersen P; Hansen LT; Laursen MB; Kehlet H; BMJ Open 2013 3 e003965 Looked at multimodal prophylaxis using in hospital LMWH and very rapid mobilisation showing very low numbers of VTE events with a thorough follow up of all their patients (4964 cases). Vulcano E; Gesell M; Esposito A; Ma Y; Memtsoudis SG;	

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			Gonzalez Della Valle A :Int Orthop 2012 36(10) 1995-2002 report a multimodal prophylaxis regime in which aspirin was administered in 1115 patients (other patients were given warfarin and LMWH but case mix selection not clear) with rates given for DVT PE which were as low as most other series. All of this suggests that early mobilisation and shorter length of stays combined with other modalities which have marginal effects (according to your own data) have significantly reduced the incidence of DVT the actual drug use brings with it problems of bleeding interaction and applicability for the elderly patients treated but not included in large industry funded trials. We have tried to obtain funds for proper randomised studies to answer these questions however the low effect size of drug prophylaxis (around 10% reduction in your data) on a condition which occurs rarely meant that costs were too great leaving industry to sponsor and control studies. What attempts to randomise have been made are relatively underpowered on VTE prophylaxis as a result yet they uniformly identify the issue of wound ooze and bleeding. **Major orthopaedic surgery (cost-effectiveness)** Shousboe JT; Brown GA: J Bone Joint Surg Am 2013 95(14) 1256-64 looked at the cost effectiveness of various drugs and risk stratify for age and joint replacement using incidence data. For all groups except knee replacement under 80 aspirin was the cost effective choice based on the actual incidence of DVT/PE and bleeding. For patients under 80 having a knee	

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			replacement there was no clear benefit to either. As ever these figures are mired in technique and incidence levels however as with the multiple meta-analysis on the same data suggests more about methodology rather than the actuality. In your own economic model enclosed in CG92 there is a table which looks at risk and benefit for various rates of DVT/ PE. If the much larger real time population figures now available for hip and knee and the detailed studies on bleeding complications may shift the analysis on your table towards less use of LMWH. We would like the actual rates now published nationally used to interpret this table. **Elective hip replacement** In the reference 103 (Jameson SS[1], Baker PN, Charman SC, Deehan DJ, Reed MR, Gregg PJ, Van der Meulen JH. J Bone Joint Surg Br. 2012 Jul;94(7):914-8) we suspect your point is overstated and enclose the abstract here: “Aspirin had a higher likelihood of return to theatre but similar rates of death DVT and PE We compared thromboembolic events, major haemorrhage and death after knee replacement in patients receiving either aspirin or low-molecular-weight heparin (LMWH). Data from the National Joint Registry for England and Wales were linked to an administrative database of hospital admissions in the English National Health Service. A total of 156,798 patients between April 2003 and September 2008 were included and followed for 90 days. Multivariable risk modelling was used to estimate odds ratios adjusted for	

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			baseline risk factors (AOR). An AOR < 1 indicates that risk rates are lower with LMWH than with aspirin. In all, 36,159 patients (23.1%) were prescribed aspirin and 120,639 patients (76.9%) were prescribed LMWH. We found no statistically significant differences between the aspirin and LMWH groups in the rate of pulmonary embolism (0.49% vs 0.45%, AOR 0.88 (95% confidence interval (CI) 0.74 to 1.05); p = 0.16), 90-day mortality (0.39% vs 0.45%, AOR 1.13 (95% CI 0.94 to 1.37); p = 0.19) or major haemorrhage (0.37% vs 0.39%, AOR 1.01 (95% CI 0.83 to 1.22); p = 0.94). There was a significantly greater likelihood of needing to return to theatre in the aspirin group (0.26% vs 0.19%, AOR 0.73 (95% CI 0.58 to 0.94); p = 0.01). Between patients receiving LMWH or aspirin there was only a small difference in the risk of pulmonary embolism, 90-day mortality and major haemorrhage. These results should be considered when the existing guidelines for thromboprophylaxis after knee replacement are reviewed." **J Arthroplasty. 2014 Feb 12. pii: S0883-5403(14)00078-3. doi:** 10.1016/j.arth.2014.02.002. [Epub ahead of print] **Early Death Following Primary Total Hip Arthroplasty.** Jones MD, Parry MC, Whitehouse MR, Blom AW. "This study aims to describe the timing, cause of death, and excess surgical mortality associated with primary total hip arthroplasty when compared to a population awaiting primary total hip arthroplasty. Mortality rates were calculated at cutoffs of 30 and 90days post-operation or following the addition to the waiting list. Cause of death was recorded from the death certificate. An excess surgical mortality of 0.256%	

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			at 30days (P=0.002) and 0.025% at 90days post-operation (P=0.892), unaffected by age or gender, was seen with myocardial infarction and pneumonia the cause of death in the majority of cases. By using a more appropriate control population, an excess surgical mortality at 30days post-operation is demonstrated; the effect diminishes at 90days post-operation." **Lancet. 2013 Sep 28;382(9898):1097-104. doi: 10.1016/S0140-6736(13)61749-3.** 90-day mortality after 409,096 total hip replacements for osteoarthritis, from the National Joint Registry for England and Wales: a retrospective analysis. Hunt LP1, Ben-Shlomo Y, Clark EM, Dieppe P, Judge A, MacGregor AJ, Tobias JH, Vernon K, Blom AW; National Joint Registry for England, Wales and Northern Ireland. **"BACKGROUND:** Death within 90 days after total hip replacement is rare but might be avoidable dependent on patient and treatment factors. We assessed whether a secular decrease in death caused by hip replacement has occurred in England and Wales and whether modifiable perioperative factors exist that could reduce deaths. **METHODS:** We took data about hip replacements done in England and Wales between April, 2003, and December, 2011, from the National Joint Registry for England and Wales. Patient identifiers were used to link these data to the national mortality database and the Hospital Episode Statistics database to obtain details of death, sociodemographics, and	

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			comorbidity. We assessed mortality within 90 days of operation by Kaplan-Meier analysis and assessed the role of patient and treatment factors by Cox proportional hazards model. **FINDINGS:** 409,096 primary hip replacements were done to treat osteoarthritis. 1743 patients died within 90 days of surgery during 8 years, with a substantial secular decrease in mortality, from 0·56% in 2003 to 0·29% in 2011, even after adjustment for age, sex, and comorbidity. Several modifiable clinical factors were associated with decreased mortality according to an adjusted model: posterior surgical approach (hazard ratio [HR] 0·82, 95% CI 0·73-0·92; p=0·001), mechanical thromboprophylaxis (0·85, 0·74-0·99; p=0·036), chemical thromboprophylaxis with heparin with or without aspirin (0·79, 0·66-0·93; p=0·005), and spinal versus general anaesthetic (0·85, 0·74-0·97; p=0·019). Type of prosthesis was unrelated to mortality. Being overweight was associated with lower mortality (0·76, 0·62-0·92; p=0·006). **INTERPRETATION:** Postoperative mortality after hip joint replacement has fallen substantially. Widespread adoption of four simple clinical management strategies (posterior surgical approach, mechanical and chemical prophylaxis, and spinal anaesthesia) could, if causally related, reduce mortality further." **Elective Knee replacement** section has a section on increased bleeding due to Rivaroxaban which should be included in the novel anticoagulation section as well. Ref 110	

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			We believe there is a paper By Blom et al from the national joint register about to be published as regards the deaths following Knee replacement (similar to the paper published on hip replacement in the Lancet) It is disappointing that yet again no evidence has been led for patients with thrombophilia or a previous or family history of DVT or pulmonary embolus. The very patients who would (or should) benefit most from prophylactic measures. This despite enormous expenditure on the subject. It is surprising that patient support groups have not commented on this.	
Department of Health	I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.			Thank you.
Royal College of Physicians (RCP)	Disagree		The RCP is grateful for the opportunity to respond to this consultation. We strongly support a review of the guidance with respect to medical patients and wish to endorse the comments made by the British Thoracic Society.	Thank you for your comment. Further to consultation and discussions with topic experts it has been agreed that this guideline will undergo a standard update.

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
UK Thromboprophylaxis Forum	Disagree		This guideline is a key and fundamental document for patient safety, and has supported transformation of VTE prevention practice across the UK It is used widely by multidisciplinary staff, not necessarily expert in the field of VTE prevention. VTE remains a core safety issue, with defined standards which Trusts must aim to fully meet. With the change in CQUIN funding and dependence upon NICE VTE Quality Standards to maintain and ensure best practice is current and embedded in hospital care we need to have timely and relevant data on the assessment of technologies and approaches to VTE prevention processes and practice. In a field that changes, the guidance clinical staff will expect to be working from will be an assessment based on all data currently available. Currently opinion and guidance on technologies is scattered in a number of documents and not easily accessible for those who are not necessarily knowledgeable in the area. To ensure maximal utilization of the NICE assessments and guidance, there needs to be a comprehensive document that has all the relevant technologies incorporated into a single point of reference. From a user perspective, this ensures that it is simple, useable and that items are not overlooked. As this is such an important document and an effective patient safety initiative, it needs to remain visibly up to date	Thank you for your comment. Further to consultation and discussions with topic experts it has been agreed that this guideline will undergo a standard update.

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			and relevant - many readers will look at the publication date and assume that, at 4yrs old, it is less relevant and no longer up to date. This does not necessarily mean that CG92 guidance needs to change, just that it must reflect the most recent data to remain relevant. This will be especially so given that the American College of Chest Physicians (ACCP) guidance on Antithrombotic Therapy and Prevention of Thrombosis contains divergent opinions on some aspects. We appreciate that ACCP guidance does not necessarily reflect UK practice, opinion or cost effectiveness assessment, but it is frequently referred to and equally considered a key summary of the practice and guidance of thrombosis prevention. Although the NICE position may validly remain unchanged, the age of the document CG92 without either current revision or an explicit statement regarding the evaluation of the current literature up to 2014, may lead to a downgrading of users opinion of the relevance and even perception of validity of the NICE CG92 guidance. Such an alteration in perception will potentially have knock on effects on the appropriate implementation and practice of best care for VTE prevention and risk reduction. Members of the UK TP forum commented: The issue of whether to use mechanical thromboprophylaxis in medical patients needs review and has huge implcations re cost savings in the NHS. Budget for stockings in London alone is £5 million	

Stakeholder	Do you agree that the guidance should not be updated?	Comments on equality issues or areas excluded from the original scope	Comments If you disagree please explain why	Response
			VTE Prophylaxis for day, orthopaedic lower limb fractures/Plastercast and outpatient cases needs clearer guidance- further support for a comprehensive document It should be noted that although the NICE guidelines do not hold quite as much weight in Scotland, they are still an important source of guidance that is frequently used. In Wales, positive momentum has been gained in the recognition of VTE prevention and this has certainly been helped by having the NICE CG92 in place and having the support of both Lifeblood and the UK Thromboprophylaxis Forum have been key to raising this onto the Welsh Government's priority health agenda	
Royal College of Nursing			The document has highlighted the need for the guidance in prevention of hospital acquired thrombosis, therefore emphasising on patient safety as number one priority. Prevention of VTE has been mandated in organisations in the UK. However it requires further work to order to ensure steps are taken to reduce the risk of VTE, keep the momentum and key messages about the importance of preventative measures. Agree that the guideline needs to be updated to incorporate the latest evidence.	Thank you for your comment. Further to consultation and discussions with topic experts it has been agreed that this guideline will undergo a standard update.

Appendix 2 - Decision matrix

Surveillance and identification of triggers for updating CG92. The table below provides summaries of the evidence/intelligence that were identified.

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
Assessing the risks of VTE and bleeding			
Risk assessment models			
2-year review (2012) One study based on the CLOTS trials cohorts[1] concluded that models based on clinical factors alone discriminate poorly between immobile patients with stroke at high and low risk, and would not facilitate individual tailoring of DVT prophylaxis strategies. One retrospective chart review[2] examined whether the Davison-Caprini risk-assessment model could stratify patients undergoing excisional body contouring surgery. Results showed that the highest risk patients had a significantly increased rate of VTE when compared with lower risk patients; body mass index greater than 30 and hormone therapy use were associated with a significantly increased VTE rate.	VTE risk assessment models (6 studies) Six studies[3-8] on risk assessment models to identify patients at risk of VTE were identified. A systematic review[3] of published risk assessment models concluded that published risk assessment models for VTE lack generalisability and adequate validation. One study[9] presented a weighted risk index to identify patients at increased risk of 30-day VTE events after surgery. The authors concluded that further research is necessary to create a comprehensive VTE risk model. One study[5] assessed the accuracy of the Padua Prediction Score (PPS) to predict VTE in patient with sepsis admitted to internal medicine departments and concluded that PPS	A GDG member commented that there remains significant uncertainty about the appropriate balance between the risks of bleeding and VTE events and the way that these are managed. One GDG member also commented that there is uncertainty regarding risk assessment for vascular procedures and the use of the oral contraceptive pill	The new evidence continues to indicate a lack of a VTE risk assessment tool that has been robustly validated in a broad range of patients and that been shown to improve patient outcomes.

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
<u>Exception review – IPC in stroke patients (2013)</u> This section of the guideline was not considered in the exceptional review.	lacks granularity in detecting patients at risk of VTE. Three studies [6-8] aimed to validate the Caprini Risk Assessment Model (RAM) in different patient populations, including plastic and reconstructive surgery[6], otolaryngology[7] and in surgical intensive care unit (SICU) patients[8]. The Pannucci 2014 study[8] concluded that physicians under-risk stratify SICU patients when using the 2005 Caprini RAM, while the other two studies, using a similar retrospective cohort study design, concluded that the Caprini RAM effectively risk-stratifies plastic and reconstructive surgery patients[6] and otolaryngology patients[7] for VTE risk.		
Which surgical procedures carry a high risk of deep vein thrombosis (DVT)/Pulmonary Embolism (PE)?			
<u>2-year review (2012)</u> A meta-analysis and univariate logistic regression[10] to determine the prevalence of and risk factors for VTE following elective spine surgery concluded that the risk of VTE is relatively low following elective spine surgery, particularly for patients who receive pharmacologic prophylaxis,	No.		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
which however, exposes patients to a greater risk of epidural hematoma. One systematic review[11] of upper extremity deep vein thrombosis (DVT) in orthopaedic and trauma surgery showed that the incidence of upper extremity DVT and pulmonary embolism was greatest in cases following shoulder surgery; there did not appear to be any greater risk in patients with diabetes or obesity. The authors concluded that although a relatively uncommon complication, upper extremity DVT can lead to pulmonary embolism. Exception review – IPC in stroke patients (2013) This section of the guideline was not considered in the exceptional review.			
Which medical conditions carry a high risk of DVT/PE?			
2-year review (2012) One study using data from the International Medical Prevention Registry on Venous Thromboembolism (IMPROVE)[12] showed that active gastroduodenal ulcer, prior bleeding and low platelet	VTE risk factors – medical conditions (11 studies) Eleven studies[13-23] on medical conditions as risk factors for VTE were identified. Medical conditions associated with a high risk of VTE included cancer[13],		The new evidence on medical and individual risk factors for VTE is essentially in line with the guideline recommendations. The new evidence would therefore not change current guidance on risk factors for VTE or the use of the

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
count were the strongest independent risk factors at admission for bleeding. Other bleeding risk factors were increased age, hepatic or renal failure, ICU stay, central venous catheter, rheumatic disease, cancer, and male sex. Exception review – IPC in stroke patients (2013) This section of the guideline was not considered in the exceptional review.	acute stroke[14], chronic liver disease[15], chronic kidney disease[16], nephrotic syndrome[17], infections and inflammatory diseases[18], inflammatory bowel disease[24] and rheumatoid arthritis[20-22]. The authors of the Gunderson (2013) study[23] concluded that the risk of DVT in cellulitis and erysipelas is low.		national tool for assessment of VTE and bleeding risk.
Which individual patient factors (for both surgical and medical patients) are risk factors for developing DVT/PE?			
2-year review (2012) A systematic review and meta-analysis of epidemiological studies[25] concluded that immobilisation increases the risk of VTE among medical patients, although a specific role of underlying conditions cannot be excluded. Exception review – IPC in stroke patients (2013) This section of the guideline was not considered in the exceptional review.	VTE risk factors – individual patient factors (28 studies) Twenty eight studies[26-53] on individual patient factors as risk factors for VTE were identified. Individual risk factors associated with a risk of VTE were known thrombophilias[26,27], advanced cancer – lymph node metastatsis[38], cancer treatment[40], varicose veins[43], use of oestrogen-containing contraceptive therapy[44,45] or hormone replacement therapy[46,47], reduced mobility[48], increasing age[51], obesity[50], operative time exceeding 260 minutes[49] and family		The new evidence on medical and individual risk factors for VTE is essentially in line with the guideline recommendations. The new evidence would therefore not change current guidance on risk factors for VTE or the use of the national tool for assessment of VTE and bleeding risk.

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
	history of VTE[53]. Menopause[32], use of non-steroidal anti-inflammatory drugs (NSAIDS)[31], white blood cell (WBC) count[33], smoking[34-36] and heart healthy diet[41] were not associated with a risk of VTE. There was unclear association with VTE risk for the following factors - antipsychotic drugs[28-30], alcohol intake[39], increased levels of free thyroxine [37], elevated levels of fibrinogen [42], being a farmer, blue-collar worker or unemployed[52], with further research recommended.		
Reducing the risk of VTE			
2-year review (2012) No new evidence was identified Exception review – IPC in stroke patients (2013) This section of the guideline was not considered in the exceptional review.	One systematic review[54] evaluated the appropriateness of aspirin to prevent VTE in high-risk orthopaedic surgery patients and concluded that data do not support the hypothesis that aspirin is less likely to cause adverse bleeding events than more potent anticoagulants.	One GDG member commented the concern remains that the all-cause mortality may be greater with the current guideline recommendations	The identified evidence is consistent with the guideline recommendation not to regard aspirin or other antiplatelet agents as adequate prophylaxis for VTE.
Using VTE prophylaxis			
2-year review (2012) Mechanical prophylaxis (11 studies)	Mechanical VTE prophylaxis (2 studies) *Anti-embolism stockings (1 study)*	One GDG member commented the concern remains that the all-cause mortality may be greater	No new evidence was found that would change the direction of current guideline recommendations;

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
Graduated compression stockings (GCS) (2 studies) One Cochrane review[55] on elastic compression stockings for prevention of deep vein thrombosis concluded that graduated compression stockings (GCS) are effective in diminishing the risk of DVT in hospitalised patients and that GCS combined with another method of prophylaxis is more effective than GCS alone. One Cochrane review[56] on knee-length versus thigh- length GCS for prevention of DVT in postoperative surgical patients concluded that there is insufficient high quality evidence to determine whether or not knee-length or thigh- length GCS differ in their effectiveness in terms of reducing the incidence of DVT in hospitalised patients. *Intermittent pneumatic compression (IPCD) devices (5 studies)* One RCT[57] of a portable calf compression device for prevention of VTE in high-risk neurosurgical patients concluded that the device was	A meta-analysis[68] of thigh-length versus knee-length compression stockings found no significant difference between the two types of compression stockings in regard to the development of DVT in the inpatient setting. *Intermittent pneumatic compression devices (1 study)* A meta-analysis[69] of intermittent pneumatic compression (IPC) of the lower limbs to prevent VTE in hospitalised patients concluded that IPC was effective in reducing VTE, and that combining pharmacological thromboprophylaxis with IPC was more effective than using IPC alone. <u>Pharmacological VTE prophylaxis (1 study)</u> One systematic review and meta-analysis of observational sudies[70] concluded that given their low risk of bleeding, statins have the potential to serve as a safe pharmacological therapy in VTE prevention, however further investigations in the form of well-designed trials are needed.	with the current guideline recommendations. Another GDG member commented that there is now a growing body of opinion which regards smaller VTE as insignificant and the detection of such clots has led to treatment which may be harmful; the current guidance did not have the remit to comment on this and the hard data is still lacking to make a definitive statement A GDG member commented that the CLOTS 3 data strongly suggests that pneumatic compression should be used after stroke.	feedback from the GDG is also unlikely to impact on the guideline recommendations at this time as no evidence was provided to back up their concerns. Regarding CLOTS 3 data, the section on the use of intermittent pneumatic compression to prevent VTE in patients with stroke which has already been identified to undergo an update following notification of publication of the trial and a subsequent exception review in 2013.

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
effective in preventing VTE in high-risk neurosurgical patients. One RCT[58] comparing a mobile compression device with low molecular weight heparin (LMWH) for prevention of VTE in total hip arthroplasty showed no significant difference in VTE between the groups; major bleeding however, was significantly less in the device group than the LMWH group. One preliminary RCT[59] randomized patients undergoing total knee or total hip arthroplasty to a portable, continuous enhanced circulation therapy compression device with LMWH or LMWH. Results showed a significant reduction in DVT after total knee arthroplasty when the device was combined with LMWH. One RCT[60] comparing the efficacy and safety of different modes of thromboembolic prophylaxis (GCS, IPC, and LMWH) for elective total knee arthroplasty in Asian patients showed that DVT point prevalence was significantly higher than in patients receiving IPC or LMWH. And			

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
concluded that IPC is the preferred method of thromboprophylaxis for total knee arthroplasty in Asian patients. One systematic review[61] of VTE prophylaxis in gynaecologic surgery concluded that IPC provides sufficient prophylaxis for the majority of gynaecology patients undergoing benign surgery and that additional risk factors warrant the use of combined mechanical and pharmacologic prophylaxis. *Other mechanical (1 study)* One Cochrane review[62] on continuous passive motion for preventing VTE after total knee arthroplasty concluded that there is not enough evidence from the available RCTs to conclude that the intervention reduces VTE in these patients. *Combined modalities (3 studies)* One systemic review and meta-analysis[63] of IPC and pharmacological prophylaxis versus single modalities alone in preventing VTE in high-risk patients showed that combined prophylactic modalities significantly			

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
decrease the incidence of VTE but not fatal pulmonary embolism, compared to single modalities. One RCT[64] evaluated the incidence of VTE in Japanese patients who had pharmacological anticoagulation in addition to mechanical prophylaxis following primary unilateral cementless total hip replacement. The authors concluded that routine pharmacological thromboprophylaxis is not necessary in these patients as mechanical thromboprophylaxis without the use of anticoagulant drugs were effectiveness and safe. One RCT[65] of an arteriovenous impulse system combined with LMWH versus LMWH alone, for prophylaxis of DVT following total knee arthroplasty showed a significant difference in DVT in favour of the combined modality. <u>Vena caval filters (2 studies)</u> One Cochrane review[66] on vena caval filters for the prevention of pulmonary embolism concluded that no recommendations can be drawn and that further trials are needed to assess			

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
vena caval filter safety and effectiveness. One systematic review and meta-analysis of observational studies[67] of inferior vena cava filters for pulmonary embolism prophylaxis in trauma patients could not draw firm conclusions either for or against the routine use of prophylactic inferior vena cava filters. <u>Exception review – IPC in stroke patients (2013)</u> This section of the guideline was not considered in the exceptional review.			
Medical patients			
What is the effectiveness of different prophylaxis methods in reducing the incidence of VTE?			
<u>2-year review (2012)</u> <u>General medical patients (12 studies)</u> One Cochrane review[71] on the efficacy of statins in the primary prevention of VTE found one RCT which showed that rosuvastatin was associated with a reduced incidence of VTE. The authors concluded that randomised trials of statins (including rosuvastatin) are needed to evaluate the efficacy of	<u>General medical patients (4 studies)</u> One systematic review and meta-analysis[97] of pharmacological prophylaxis to prevent VTE in medical patients found no significant differences in overall mortality, symptomatic VTE or major bleeding between pharmacological prophylaxis and no intervention.	No clinical feedback was provided for this section of the guideline.	No new evidence was found that would change the direction of current guideline recommendations

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
statins in the prevention of VTE. One meta-analysis of observational studies[72] on the effect of statins on VTE concluded that further well-designed trials are needed to evaluate the risks and benefits of statins in preventing VTE in adults, identify high-risk subgroups, and analyze cost-effectiveness of statin use for this indication. One Cochrane review[73] of heparin for the prevention of VTE in general medical patients was found. Results showed a reduction in risk of VTE with heparin compared with placebo or no treatment, but there was also an increase in major and minor haemorrhage. There was no statistically significant difference in efficacy between LMWH and UFH; however, there was a significantly reduced risk of bleeding in favour of LMWH. An individual patient data meta-analysis[74] evaluated the relative efficacy and safety of enoxaparin and UFH in preventing VTE in hospitalized medical patients. The authors	One multicentre RCT[98] of rivaroxaban versus enoxaparin for thromboprophylaxis in acutely ill medical patients concluded that extended-duration rivaroxaban reduced the risk of VTE but was associated with an increased risk of bleeding. One systematic review and network meta-analysis[99] concluded that commonly available LMWHs are similar in relative efficacy for the prevention of VTE in hospitalised medical patients. One systematic review[100] of extended thromboprophylaxis for medically ill patients with decreased mobility concluded that routine administration of post-discharge prophylaxis is not beneficial to patients admitted for medical illness. <u>Patients with stroke (1 study)</u> A sub-analysis of the EXCLAIM trial[101] concluded that extended-duration thromboprophylaxis with enoxaparin was associated with reduced VTE risk but increased major bleeding in patients with ischemic stroke.		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
concluded that enoxaparin significantly reduces VTE in these patients, compared with UFH, without increasing the risk for major bleeding, and was associated with a trend towards reduced all-cause mortality. A meta-analysis [75] on the evidence for thromboembolism prophylaxis in general medicine patients was found. RCTs comparing UFH or LMWH to control, as well as head-to-head comparisons of UFH to LMWH were included. The authors concluded that among medical patients, prophylaxis with LMWH or UFH reduced the risk of thromboembolism without increasing risk of major bleeding and that the current literature does not demonstrate superior efficacy of UFH or LMWH. One RCT[76] of certoparin versus UFH to prevent VTE in acutely ill, non-surgical, elderly patients (the CERTIFY trial) concluded that thromboprophylaxis with certoparin was not inferior to UFH and had a favourable safety profile. One open-label, active-controlled,	<u>Patients with cancer (9 studies)</u> One systematic review of RCTs[102] of anticoagulant therapy compared with placebo in hospitalised patients with cancer found no significant difference in risk of VTE events between the two groups of patients. Two systematic reviews[103,104] on primary prophylaxis for VTE in ambulatory cancer patients receiving chemotherapy concluded that further investigation is needed to guide and narrow recommendations for prophylaxis in this group of patients. One multicenter trial[105] of the ultra-low-molecular-weight heparin semuloparin concluded that the drug reduces the incidence of VTE events in patients receiving chemotherapy for cancer, with no apparent increase in major bleeding. One RCT[106] of gemcitabine versus the same drug plus dalteparin in advanced pancreatic cancer patients concluded that weight-adjusted dalteparin used as primary prophylaxis is safe and produces a highly significant reduction of all-type VTE.		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
multicenter trial[77] of certoparin with unfractionated heparin for the prevention of thromboembolic complications concluded that in acutely ill medical patients of at least 40 years of age, thromboprophylaxis with certoparin is effective and safe in comparison with UFH. A subgroup analysis of the CERTIFY trial[78] assessed the benefits and risks of certoparin in comparison to unfractionated heparin (UFH) in patients with severe renal insufficiency. The authors concluded that certoparin was as efficacious as UFH in patients with severe renal insufficiency but with a reduced risk of bleeding. One RCT[79] of apixaban versus enoxaparin for thromboprophylaxis in medically ill patients was found. The authors concluded that an extended course of thromboprophylaxis with apixaban was not superior to a shorter course with enoxaparin and that apixaban was associated with significantly more major bleeding events than was enoxaparin.	One report of two RCTs[107] of LMWH versus placebo for the prevention of VTE in metastatic breast cancer (TOPIC-1) and stage III/IV lung cancer (TOPIC-2) concluded that thrombosis risk and prophylactic benefit was highest in stage IV lung carcinoma. A systematic review[108] to evaluate the efficacy and safety of aspirin, warfarin and LMWH thromboprophylaxis in multiple myeloma patients on thalidomide found no clear advantage of any particular thromboprophylaxis strategy. One RCT[109] of aspirin or enoxaparin thromboprophylaxis for patients with newly diagnosed multiple myeloma treated with lenalidomide found no significant difference in the proportion of VTE between the two groups. The MELISSE multicentre study[110] in patients with multiple myeloma treated with immunomodulatory drugs found that VTE occurred in 7% on aspirin prophylaxis vs 3% on LMWH prophylaxis, and none on vitamin K antagonists.		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
One RCT[80] evaluated the efficacy and safety of extended-duration enoxaparin thromboprophylaxis in acutely ill medical patients. The authors' conclusion was that the use of extended-duration enoxaparin reduces VTE more than it increases major bleeding events in acutely ill medical patients with level 1 immobility, those older than 75 years, and women. One multi-centre RCT[81] reported on mortality among hospitalised, acutely ill medical patients using elastic stockings with graduated compression, who received enoxaparin or placebo. The authors concluded that the use of enoxaparin in these patients was not associated with a reduction in the rate of death from any cause. One systematic review[82] of economic analyses of VTE prevention in hospitalised patients concluded that low-molecular-weight heparins and fondaparinux are the most economically attractive drugs for VTE prevention in hospitalised patients.	<u>Patients with central venous catheters (4 studies)</u> One RCT[111] comparing different prophylactic strategies for catheter-related DVT in cancer patients found that anticoagulation significantly reduced the incidence of DVT. Two systematic reviews[112,113] of peripherally inserted central catheters (PICCs) compared to other central venous catheters (CVCs) found that PICCs have a tendency towards increased risk for DVT but not PE, and a decreased risk for catheter occlusion. One systematic review[114] of non-pharmacologic interventions for prevention of catheter-related thrombosis concluded that PICCs and femoral insertion of CVCs should be avoided if possible.		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
Stroke (5 studies) One Cochrane review[83] assessed the effectiveness and safety of physical methods of reducing the risk of VTE and death in patients with recent stroke. Results showed that overall, physical methods (graduated compression stockings or intermittent pneumatic compression) were not associated with a significant reduction in DVTs during the treatment period or death at the end of follow up. A critical appraisal of a quasi-RCT[84] of low-molecular weight heparin for VTE prophylaxis compared with mechanical methods in patients with acute intracerebral haemorrhage concluded that initiation of low-dose LMWH for the purpose of VTE prophylaxis in these patients is likely to be safe but that a well-designed RCT is needed to answer the clinical question. One RCT[85] on LMWH for DVT prophylaxis in patients with intracerebral haemorrhage (ICH) concluded that Low dose heparin treatment after 48 hours of stroke is			

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
not associated with an increased hematoma growth and should be used for VTE prophylaxis. One meta-analysis[86] on the efficacy and safety of anticoagulants for the prevention of VTE in patients with acute hemorrhagic stroke concluded that that in these patients, early anticoagulation is associated with a significant reduction in PE and a non-significant reduction in mortality, with the trade-off of a non-significant increase in hematoma enlargement. One RCT[87] compared the effectiveness of thigh-length stockings with that of below-knee stockings for preventing proximal DVT in immobile, hospitalised patients with stroke. The authors' conclusion was that proximal DVT occurs more often in patients with stroke who wear below-knee stockings than in those who wear thigh-length stockings. <u>Cancer (6 studies)</u> One Cochrane review[88] evaluating the efficacy and safety of anticoagulation in patients with cancer and a central			

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
venous catheter showed no statistically significant effect of heparin or vitamin K antagonists on the outcomes of interest to the authors. A subgroup analysis of the CERTIFY trial[89] assessing heparin-based prophylaxis to prevent VTE and death in patients with cancer concluded that certoparin and UFH were equally effective and safe with respect to bleeding complications in patients with cancer. One randomised phase II trial[90] of apixaban for the prevention of thromboembolism in patients with metastatic cancer was identified. The author concluded that apixaban was well tolerated in their study population an that the results support further study of apixaban in phase III trials to prevent VTE in cancer patients receiving chemotherapy. One RCT[91] comparing aspirin or fixed low-dose warfarin versus LMWH for preventing thromboembolism in patients with multiple myeloma treated with thalidomide-based regimens concluded that in the two drugs			

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
showed similar efficacy in reducing serious thromboembolic events, acute cardiovascular events, and sudden deaths in these patients compared with LMWH, except in elderly patients where warfarin showed less efficacy than LMWH. One RCT[92] of warfarin thromboprophylaxis in cancer patients with central venous catheters showed that prophylactic warfarin compared with no warfarin is not associated with a reduction in symptomatic catheter-related or other thromboses in patients with cancer. The authors concluded that newer treatments should therefore be considered A cost-effectiveness analysis[93] of dalteparin versus unfractionated heparin as VTE prophylaxis in malignant gynaecologic surgery demonstrated cost savings if dalteparin was routinely utilised as VTE prophylaxis. However, the authors caution that the findings should be viewed as preliminary, and that institutions should perform their own cost-effectiveness studies in this			

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
patient population. Critical care (3 studies) One systematic review[94] of LMWH in critically ill patients concluded that LMWH cannot be recommended routinely in these patients as no trials have compared LMWH against an alternative active strategy. One RCT[95] of LMWH and UFH prophylaxis against DVT in critically ill patients undergoing major surgery concluded that both the drugs were highly effective and well tolerated. However, considering the advantage of once-daily dosing, the authors suggested that, a wider adoption of prophylaxis with LMWH may be justified on the basis of patient acceptability and saving of nursing time. One RCT[96] of dalteparin versus unfractionated heparin in critically ill patients was found. Patients received subcutaneous dalteparin plus placebo or unfractionated heparin while they were in the intensive care unit. Results showed that among critically ill			

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
patients, dalteparin was not superior to unfractionated heparin in decreasing the incidence of proximal deep-vein thrombosis. Exception review – IPC in stroke patients (2013) One study relating to the clinical question was identified. The study was a report of the findings of a UK multicentre RCT (94 centres, n = 2876) that assessed intermittent pneumatic compression (IPC) in immobile patients with acute stroke - the CLOTS 3 trial. Participants were randomised to receive either IPC or no IPC; compression duplex ultrasound (CDU) of both legs was carried out by technicians blinded to treatment allocation and followed up for 6 months to determine survival and later symptomatic VTE. Intention-to-treat analysis was carried out. Results showed that DVT in the proximal veins occurred in 8.5% of participants allocated IPC and 12.1% of participants allocated no IPC; an			

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
absolute reduction in risk of 3.6% (95% CI 1.4% to 5.8%); the adjusted Odds Ratio (OR) for the comparison of was 0.65 (95% CI 0.51 to 0.84). Other results for intervention vs control were as follows: death - 11% vs 13% (p=0.057); skin breaks on the legs - 3% vs 1% (p=0.002); falls with injury 2% vs 2% (p=0.221) The authors concluded that IPC is an effective method of reducing the risk of DVT and possibly improving survival in a wide variety of patients who are immobile after stroke.			
Surgical patients			
What is the effectiveness of different prophylaxis methods in reducing the incidence of VTE?			
2-year review (2012) Gastrointestinal surgery (1 study) One Cochrane review[115] of prolonged thromboprophylaxis with low molecular weight heparin for abdominal or pelvic surgery was found. The authors concluded that prolonged thromboprophylaxis with LMWH for at least 1 month after surgery significantly reduces the risk of VTE	All surgery (1 study) A pooled analysis of 3 RCTs[143] of patients that underwent major orthopaedic surgery under general, regional or combination anaesthesia revealed a slightly higher rate of major VTE and VTE-related mortality with general versus regional anaesthesia. Gastrointestinal, gynaecological,	One GDG member commented that many orthopaedic surgeons have questioned the guidelines and generated data from registries to state that the risk of VTE is overstated and that aspirin is a suitable thrombprophylactic agent. One GDG member commented that extended prophylaxis was	New evidence was identified for VTE prophylaxis in surgical patients admitted in hospital. However, the identified new evidence would not change the direction of current guideline recommendations. One systematic review[54] evaluated the appropriateness of aspirin to prevent VTE in high-risk orthopaedic surgery patients and

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
compared to thromboprophylaxis during hospital admittance only, without increasing bleeding complications after major abdominal or pelvic surgery. Gynaecological surgery (1 study) One RCT[116] of DVT prophylaxis in high risk gynaecological surgery patients was found. Intervention patients received IPC or LMWH and the control group received no prevention strategy. Results showed significantly reduced lower limb DVT in the intervention group compared to the control group, with no bleeding. Laparoscopic surgery (1 study) One systematic review and meta-analysis[117] assessed the clinical burden of VTE after laparoscopic bariatric surgery. The authors concluded that the rate of VTE after the procedure is relatively low with standard regimens for antithrombotic prophylaxis and the incidence of major bleeding seems to increase using weight-adjusted doses of heparin with no advantage in terms of VTE reduction.	thoracic and urological (8 studies) *Gastrointestinal surgery (5 studies)* One systematic review and meta-analysis[144] of pharmacologic and mechanical strategies for preventing VTE after bariatric surgery found that LMWH is more efficacious than UFH in preventing VTE, that prolonged therapy after discharge with enoxaparin may prevent VTE better than inpatient treatment only and that filters are associated with higher mortality and DVT rates. No studies randomised patients to receive different interventions. One RCT[145] of VTE prophylaxis given for 1 week or 4 weeks in patients undergoing laparoscopic surgery for colorectal cancer concluded that extended antithrombotic prophylaxis for 4 weeks is safe and reduces the risk for VTE as compared with 1-week prophylaxis. One prospective cohort study[146] comparing the efficacy and safety of fondaparinux combined with IPC with IPC alone for VTE prophylaxis after resection for colorectal cancer	only cursorily discussed and this is becoming a bigger component due to facilitated discharging of patients earlier than previously and there is uncertainty about extended prophylaxis for cancer surgery in the abdomen and pelvic procedures. One GDG member commented that there is increasing evidence that the risk of VTE is very high after surgery for inflammatory bowel disease and these patients should be offered extended thrombprophylaxis. The GDG member also commented that there is now NICE single technology approval for the use of dabigatran, rivaroxaban and apixaban in the prevention of VTE after hip replacement and that this is not incorporated in the guideline.	concluded that data do not support the hypothesis that aspirin is less likely to cause adverse bleeding events than more potent anticoagulants. This is consistent with the guideline recommendation not to regard aspirin or other antiplatelet agents as adequate prophylaxis for VTE Regarding the concern of the GDG member about extended prophylaxis for cancer and pelvic procedures, one RCT[145] of VTE prophylaxis given for 1 week or 4 weeks in patients undergoing laparoscopic surgery for colorectal cancer was identified. It concluded that extended antithrombotic prophylaxis for 4 weeks is safe and reduces the risk for VTE as compared with 1-week prophylaxis. Another cost-effectiveness study[150] of prolonged VTE prophylaxis with enoxaparin in high-risk surgical patients with ovarian cancer found that prolonged prophylaxis improves patient outcomes and is also a cost saving strategy when modelled over

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
<u>Cranial surgery (1 study)</u> One systematic review and meta-analysis[118] of VTE prophylaxis in patients undergoing cranial neurosurgery showed that heparin prophylaxis reduced the risk of VTE but may also increase bleeding risks. <u>Cardiac surgery (1 study)</u> One RCT[119] evaluating the safety and efficacy of combined low dose aspirin and warfarin therapy following mechanical heart valve replacement concluded that the combined therapy was associated with a greater reduction in thromboembolism than warfarin therapy alone, with no associated increase in the rate of major bleeding or mortality. <u>Vascular surgery (1 study)</u> One Cochrane review[120] on interventions for preventing VTE following abdominal aortic surgery concluded that there was not enough evidence to make a definitive conclusion about the use of anticoagulant drugs (with or without mechanical devices) for DVT	concluded that the combined modality was highly effective, well tolerated and safe. One prospective cohort study[147] of LMWH in DVT prophylaxis in general surgical patients found that LMWHs are more effective than no prophylaxis in the prevention of DVT and PE in highest-risk general surgical patients. One systematic review and meta-analysis[148] of VTE after laparoscopic cholecystectomy found no statistically significant reduction in VTE in patients receiving heparin prophylaxis after laparoscopic cholecystectomy. *Gynaecological surgery (2 studies)* One clinical trial[149] of graduated compression stockings (GCS) or combined with IPC, for VTE prophylaxis after gynaecological pelvic surgery found that the combination of GCS and IPC was more effective than GCS alone for thrombosis prevention in this group of patients. One cost-effectiveness study[150] of prolonged VTE prophylaxis with enoxaparin in high-risk surgical patients		five years This is in line with the guideline recommendation to extend pharmacological VTE prophylaxis to 28 days postoperatively for patients who have had major cancer surgery in the abdomen or pelvis. Dabigatran and rivaroxaban are already mentioned in the guideline as a treatment options for VTE prevention after total hip or total knee replacement in adults. The last surveillance review of this guideline (2-year review) in 2012 identified the new Technology Appraisal on Apixaban and it has been recommended that the section of the guideline on elective hip and knee replacement should cross refer to this new Technology Appraisal (TA245).

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
prophylaxis in these patients. Orthopaedic surgery *Major orthopaedic surgery (6 studies)* Aspirin (2 studies) A pooled-analysis of 14 RCTs[121] cited by the American College of Chest Physicians in their guidelines on VTE prophylaxis showed that VTE rates with aspirin were not significantly different than the rates for vitamin K antagonists, low molecular weight heparins (LMWH), and pentasaccharides. The authors of one study[122] critically reappraised RCTs of aspirin in VTE prevention. They concluded that aspirin is efficacious in preventing VTE compared to placebo or no treatment, but less efficacious than LMWH in small trials and that there was little data for aspirin in comparison with UFH and warfarin. They contended that a large RCT is required to clarify the role of aspirin compared to contemporary anticoagulant strategies for the prevention of VTE.	with ovarian cancer found that prolonged prophylaxis improves patient outcomes and is also a cost saving strategy when modelled over five years. *Thoracic surgery (1 study)* One systematic review [151] of VTE risk in patients undergoing operations for lung cancer found that the evidence for using thromboprophylaxis after lung cancer operations is relatively sparse and the use is based predominantly on clinical consensus. Neurological (cranial or spinal) (1 study) One systematic review [152] of perioperative thromboprophylaxis in patients with craniotomy for brain tumours showed a trend of reduction of VTE in patients treated with mechanical methods (IPC or GCS) and that the addition of enoxaparin starting the day after surgery, significantly reduces clinically manifest VTE, despite an increase in major bleeding events. Orthopaedic surgery (37 studies) *Major orthopaedic surgery (clinical) – (19 studies)*		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
Fondaparinux (1 study) One meta-analysis22 of VTE prevention investigated the effect of fondaparinux on mortality in patients that underwent major orthopaedic or abdominal surgery. Results showed a non-significant reduction in mortality with fondaparinux compared to LMWH or placebo. Low molecular weight heparin (1 study) One systematic review[123] of LMWH for VTE prophylaxis in orthopaedic surgery concluded that there is clear supporting evidence for the application of LMWH for DVT prophylaxis in orthopaedic surgery. Other drugs (2 studies) One meta-analysis of cause of death following total joint replacement[124] was found. Results showed that the proportion of deaths due to pulmonary embolism was not significantly affected by the thromboprophylaxis regimen One systematic review[125] of drugs for VTE prophylaxis in major orthopaedic	Aspirin (2 studies) One systematic review[54] evaluated the appropriateness of aspirin to prevent VTE in high-risk orthopaedic surgery patients and concluded that data do not support the hypothesis that aspirin is less likely to cause adverse bleeding events than more potent anticoagulants. One systematic review[153] on optimal perioperative VTE prophylaxis in patients with cardiac diseases undergoing joint replacement surgeries found that for patients already on aspirin, the dosage should be adjusted or additional LMWH administered. Warfarin (1 study) A report of the Michigan Anticoagulation Quality Improvement Initiative (MAQI2)[154] on the use of warfarin for VTE prophylaxis following knee and hip arthroplasty concluded that there were questions about the efficacy of warfarin therapy in the first 1-2 post-operative weeks. Low molecular weight heparin (1 study) One systematic review[155] of comparative effectiveness of LMWHs versus other		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
surgeries showed that fondaparinux was more favourable than enoxaparin (but had a higher bleeding rate) but consistent conclusions as to the superiority of rivaroxaban could not be made because of significant heterogeneity. Fondaparinux, rivaroxaban, dabigatran, apixaban and bemiparin were non-inferior to enoxaparin. *Elective hip or knee replacement (15 studies)* Apixaban (3 studies) A pooled-analysis of 2 RCTs[126] of apixaban versus enoxaparin for thromboprophylaxis after hip or knee replacement concluded that apixaban is more effective than enoxaparin, with no risk of increased bleeding. One RCT[127] of apixaban versus enoxaparin for thromboprophylaxis after hip replacement concluded that apixaban was associated with lower rates of venous thromboembolism, without increased bleeding. One RCT[128] of apixaban versus enoxaparin for thromboprophylaxis	anticoagulants in major orthopaedic surgery found that LMWH prophylaxis provides additional benefits with less harm compared with unfractionated heparin (UFH), the balance of benefits to harms for factor Xa inhibitors or direct thrombin inhibitors compared with LMWHs seems favourable, while the known benefits in total DVT and distal DVT with LMWHs versus VKAs may not be sufficient to counteract the increased risk of bleeding. New anticoagulants - Dabigatran, Rivaroxaban and Apixaban (11 studies) ○ All combined - A pooled analysis of RCTs[156] comparing dabigatran, rivaroxaban and apixaban versus enoxaparin for thromboprophylaxis after total hip or knee replacement (THR or TKR) concluded that overall, new anticoagulants showed more efficacy and same safety when compared to enoxaparin. One meta-analysis[157] comparing Factor Xa inhibitors to enoxaparin for the prevention of VTE after THR or TKR concluded that Factor Xa inhibitors were superior to enoxaparin		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
after knee replacement (ADVANCE-2) was found. The authors concluded that apixaban offers a convenient and more effective orally administered alternative to enoxaparin, without increased bleeding. *Dabigatrin (3 studies)* A pooled-analysis of 3 RCTs[129] of dabigatran versus enoxaparin for prevention of VTE after hip or knee arthroplasty concluded that oral dabigatran was as effective as subcutaneous enoxaparin in reducing the risk of major VTE and VTE-related mortality in these patients and has a similar bleeding profile. One RCT[130] comparing the efficacy and safety of dabigatran in patients undergoing total hip arthroplasty (RE-NOVATE II) showed that extended prophylaxis with dabigatran was as effective as enoxaparin in reducing the risk of VTE after total hip arthroplasty, and superior to enoxaparin for reducing the risk of major VTE. The risk of bleeding and safety profiles was similar. One Cochrane review[131] of direct	in preventing DVT and there was no difference in the rate of PE, death and major bleeding. One systematic review and network meta-analysis[158] of pharmacological prophylaxis of VTE following THR or TKR concluded that the novel anticoagulants demonstrated similar or improved efficacy and similar safety compared with current therapies. Three systematic reviews[159-161] of new anticoagulants for VTE prophylaxis in major orthopaedic surgeries compared with LMWH concluded that new anticoagulants are effective for thromboprophylaxis in patients having THR or TKR. One systematic review[162] of thromboprophylaxis with newer anticoagulants compared to enoxaparin for patients undergoing major orthopaedic surgery concluded that variations in the definitions of major bleeding may change the benefit-to-harm ratio and subsequently affect its interpretation. ○ Dabigatran - One study[163] using data from the orthopaedic clinical		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
thrombin inhibitors versus vitamin K antagonists or LMWH for prevention of VTE following total hip or knee replacement concluded that although direct thrombin inhibitors are as effective in the prevention of major VTE as LMWH and vitamin K antagonists in these patients, they are associated with a higher mortality and more bleeding than LMWH. Fondaparinux (2 studies) One publication of two RCTs[132] of fondaparinux versus placebo for prevention of VTE in Japanese patients undergoing total knee replacement or total hip replacement was found. The authors concluded that fondaparinux is a potent anticoagulant with a favourable benefit-to-risk ratio in the prevention of VTE in these patients. One RCT[133] on the effect of fondaparinux sodium for prevention of VTE after hip fracture surgery in Japanese patients was found concluded that the drug demonstrated positive effects on the prevention of VTE after hip fracture surgery but that	development programme of dabigatran concluded that dabigatran is as effective as enoxaparin in high risk patients undergoing THR or TKR and is associated with a favourable bleeding rate. A pooled analysis[164] of the RE-MODELTM and RE-NOVATE trials on the efficacy of thromboprophylaxis with dabigatran concluded that no loss of efficacy occurred if initiation of dabigatran etexilate is delayed beyond 1 to 4 hours after major orthopaedic surgery. ○ Rivaroxaban - A systematic review and meta-analysis[165] of rivaroxaban versus LMWHs for VTE prophylaxis after major THR or TKR concluded that rivaroxaban is more effective than enoxaparin and as safe as LMWHs. ○ Apixaban - A meta-analysis[166] of apixaban versus enoxaparin for thromboprophylaxis after total hip or knee arthroplasty concluded that apixaban was more effective than the recommended dose of enoxaparin and had a similar safety profile. Combined (mechanical and		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
careful postoperative observation is warranted to prevent serious side effects after its administration. Low molecular weight heparin (3 studies) One meta-analysis[134] of LMWH versus placebo in patients undergoing total hip replacement concluded that as clinically relevant VTEs are a rare complication in those undergoing the procedure, the use of potent pharmacological thromboprophylaxis in these patients should be restricted to those with additional thromboembolic risk factors. One publication of two RCTs[135] of enoxaparin versus placebo for prevention of post-operative VTE in Japanese patients undergoing total hip or knee arthroplasty was found. The authors concluded that their findings support the use of enoxaparin in these patients. One historical cohort study[136] on the effectiveness of LMWH for prevention of DVT after total hip arthroplasty concluded that the incidence of DVT in	pharmacological) modalities (2 studies) Two systematic reviews[167,168] of combined pharmacologic and mechanical thromboprophylaxis versus either method alone in major orthopaedic surgery concluded that that the addition of mechanical leg compression augments the efficacy of anticoagulation in preventing DVT in patients undergoing THR or TKR. Duration of prophylaxis (2 studies) One systematic review[169] of prolonged versus standard-duration venous thromboprophylaxis in major orthopaedic surgery concluded that prolonged prophylaxis decreases the risk VTE while increasing the risk for minor bleeding in patients undergoing THR. A retrospective cohort study[170] of extended versus short term thromboprophylaxis in THR or TKR in the Indian population concluded that extended thromboprophylaxis was more effective than short term thromboprophylaxis in minimizing the risk of postoperative VTE.		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
these patients is high, and that LMWH can reduce the incidence of DVT and has good safety. Rivaroxaban (4 studies) A meta-analysis of RCTs[137] compared the efficacy and safety of rivaroxaban versus enoxaparin for thromboprophylaxis after total hip or knee arthroplasty. The authors concluded that rivaroxaban was more effective than enoxaparin and had a similar safety profile for thromboprophylaxis after hip and knee arthroplasty. A systematic review[138] of rivaroxaban versus enoxaparin in the prevention of VTE after hip or knee replacement was found. The authors concluded that rivaroxaban is superior to enoxaparin in venous thromboembolism prophylaxis after hip- or knee-joint replacement and that extended therapy - longer than 30 days - is recommended. A pooled-analysis of 3 RCTs[139] of rivaroxaban versus enoxaparin for prevention of VTE in patients	*Major orthopaedic surgery (cost-effectiveness) – (7 studies)* Six cost-effectiveness analyses[171-176] comparing rivaroxaban [171-173,175,176]and apixaban [174] with existing prophylaxis, from the US[171,172], Canadian [173,174] and European [175,176] payer's perspective, concluded that these rivaroxaban and apixaban may be an economically dominant strategy for VTE prophylaxis in patients undergoing THR or TKR. One study[177] of rivaroxaban and dabigatran compared to enoxaparin for the prevention of VTE after THR and TKR concluded that rivaroxaban and dabigatran have similar efficacy and safety outcomes compared to enoxaparin, but there was uncertainty regarding cost-effectiveness. *Elective hip replacement (3 studies)* A non-randomised comparative study[178] of aspirin and LMWH on VTE after hip replacement using data from the National Joint Registry for England and Wales found that there was increased mortality with aspirin compared to LMWH.		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
undergoing elective hip and knee replacement concluded that rivaroxaban started six to eight hours after surgery was more effective than enoxaparin started the previous evening in preventing symptomatic VTE and all-cause mortality, without increasing major bleeding. One RCT[140] of rivaroxaban versus enoxaparin for thromboprophylaxis after total knee arthroplasty (RECORD4) was found. The authors concluded that oral rivaroxaban was significantly superior to subcutaneous enoxaparin for the prevention of VTE after total knee arthroplasty. *Pelvic or acetabular fractures (1 study)* One systematic review[141] on effectiveness of thromboprophylactic strategies to prevent VTE after pelvic or acetabular fractures concluded that there is limited data to guide clinical prophylaxis decisions in these patients. The authors suggested that well-designed clinical trials to prevent and detect VTE in pelvic and acetabular trauma are needed.	One randomised study[179] on the use of vitamin E for VTE prevention in total hip arthroplasty concluded that the combining vitamin E with rivaroxaban can be more effective than rivaroxaban alone in preventing venous thromboembolism events, without an extra risk of bleeding. One RCT[180] of aspirin versus dalteparin found that extended prophylaxis for 28 days with aspirin was noninferior to and as safe as dalteparin for the prevention of VTE after THR in patients who initially received dalteparin for 10 days. *Elective knee replacement (5 studies)* A non-randomised comparative study[181] of aspirin and LMWH on VTE after knee replacement using data from the National Joint Registry for England and Wales found that there was a significantly greater likelihood of needing to return to theatre in the aspirin group compared to LMWH. One randomised study[182] comparing routine anticoagulation with the risk screening approach found that symptomatic DVT rates after TKR were similar using either strategy, however,		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
Knee arthroscopy (1 study) One Cochrane review[142] of interventions for preventing VTE in adults undergoing knee arthroscopy was found. The authors concluded that the meta-analysis suggests that LMWH reduces the incidence of distal DVT diagnosed by ultrasound but that the clinical benefit of this is uncertain. They posited that no strong evidence was found to conclude thromboprophylaxis is effective to prevent thromboembolic events and safe, in people with unknown risk factors for thrombosis, undergoing knee arthroscopy. <u>Exception review – IPC in stroke patients (2013)</u> This section of the guideline was not considered in the exceptional review.	there was a significantly higher incidence of wound complications after routine anticoagulation. One systematic review[183] of direct factor Xa inhibitors and LMWH in the prevention of DVT after TKR found that compared with LMWH, direct factor Xa inhibitor can significantly reduce the incidence of symptomatic DVT without increasing bleeding risk, with no significant differences in mortality and PE period between the two groups. One meta-analysis[184] aimed to determine the trend and incidence of VTE in TKA in Asians when no prophylaxis is used. The authors found a low incidence of symptomatic PE and DVT in these patients which has not changed over time, despite Westernizing lifestyles and an aging populace. One study[185] evaluated the impact of rivaroxaban following the introduction of NICE guidelines and compared prospectively done TKRs with TKRs done prior to adoption of the guidelines. Results showed that the number of symptomatic radiologically confirmed PE		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
	events declined but the return to theatre rate due to wound complications increased. *Hip fracture (1 study)* One RCT[186] of extended VTE prophylaxis with the ultra-low molecular-weight heparin semuloparin in patients undergoing hip fracture surgery (SAVE-HIP3) found that extended thromboprophylaxis with semuloparin reduced the rate of any VTE or all-cause death compared with placebo. *Other orthopaedic surgery (2 studies)* Two systematic reviews[187,188] on prophylaxis for VTE in people undergoing major amputation of the lower extremity[187] or shoulder arthroplasty [188] concluded that the ideal method of prophylaxis for this population of patients remains unknown and should be investigated in future high-quality clinical studies. <u>Vascular (2 studies)</u> One RCT[189] of LMWH for prevention of VTE after varicose vein surgery in moderate-risk patients showed no		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
	superiority of a short-term regimen of LMWH and early ambulation plus compression therapy compared with early ambulation and compression therapy alone. One RCT[190] comparing the impact of supine and leg elevation positions during coronary artery bypass graft on DVT occurrence was found, with the authors concluding that there was no effect of position on the presence of DVT. <u>Day surgery (1 study)</u> One study[191] on the prevention of VTE in day surgery (the SMART study) was found. The authors concluded that it is effective and tolerable to use a risk stratified dose of enoxaparin in patients undergoing day surgery. <u>Other surgical patients (3 studies)</u> One RCT[192] of enoxaparin versus semuloparin thromboprophylaxis in major abdominal surgery concluded that semuloparin commenced postoperatively did not demonstrate non-inferiority to enoxaparin initiated preoperatively for thromboprophylaxis		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
	after major abdominal surgery. One RCT[193] on the efficacy and safety of rivaroxaban versus placebo for the prevention of VTE after abdominoplasty in patients considered to be at risk was identified. The study was stopped early due to large haematomas requiring drainage in the study group. A database analysis[194] of the American College of Surgeons National Surgery Quality Improvement Program dataset of VTE after abdominal aortic aneurysm (AAA) repair found that patients with the identified risk factors may benefit from pharmacologic thromboprophylaxis after AAA repair but that pharmacologic thromboprophylaxis may be unnecessary after endoluminal repair.		
What is the effectiveness of regional anaesthesia vs general anaesthesia in reducing the incidence of postoperative VTE?			
2-year review (2012) No new evidence was identified Exception review – IPC in stroke patients (2013) This section of the guideline was not considered in the exceptional review.	A pooled analysis of 3 RCTs[143] of patients that underwent major orthopaedic surgery under general, regional or combination anaesthesia revealed a slightly higher rate of major VTE and VTE-related mortality with general versus regional anaesthesia.		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
Does adding a regional to a general anaesthetic reduce the risk of postoperative VTE?			
No new evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
Other patient groups			
What is the effectiveness of different prophylaxis methods in reducing the incidence of VTE?			
2-year review (2012) <u>Spinal injury (1 study)</u> A systematic review of thromboprophylaxis in patients with acute spinal injuries[195] concluded that LMWH is more effective for the prevention of DVT in these patients, with fewer bleeding complications, than UFH. <u>Lower limb plaster casts (1 study)</u> One Cochrane review[196] on low molecular weight heparin for prevention of VTE in adult patients with lower-leg injuries immobilized in plaster casts or braces concluded that the use of LMWH significantly reduces VTE in these patients. <u>Major trauma (2 studies)</u> A decision analysis[197] of prophylactic anticoagulation to prevent VTE in	<u>Major trauma (4 studies)</u> One systematic review[200] on the safety and efficacy of pharmacological thromboprophylaxis in traumatic brain injury concluded that early administration (<72 h) reduces the risk of VTE without affecting progression of intracranial haemorrhage One pilot RCT[201] of enoxaparin versus placebo (DEEP I) in low-risk traumatic brain injury found that progression rates after starting enoxaparin in small, stable injuries 24 hours after injury are similar to those of placebo and are subclinical. One Cochrane review[202] on thromboprophylaxis for trauma patients found evidence for DVT but not PE or mortality as follows: pharmacological prophylaxis is more effective than mechanical methods, LMWH more than UH and people who received both	A GDG member commented that there remained uncertainty regarding recommendations for gynaecological admissions and another commented that NICE are at variance with the Royal College of Obstetricians and Gynaecologists guidelines regarding pregnancy and risk of VTE, without elaborating any further.	The identified new evidence would not change the direction of current guideline recommendations. Feedback from the GDG is unlikely to impact on the guideline at this time.

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
traumatic intracranial haemorrhage showed no clear advantage to providing or withholding low molecular weight heparin (LMWH) anticoagulant prophylaxis for VTE prevention at 24 hours after traumatic brain injury associated with ICH. A systematic review and meta-analysis[198] of mechanical compression and heparin therapy in post-operative and post-trauma patients concluded that in terms of VTE prophylaxis, the benefits were similar between the two groups but the overall bleeding risk profile favours the use of compression over heparin. <u>Pregnancy and post partum (1 study)</u> One Cochrane review[199] on prophylaxis for VTE in pregnancy and the early postnatal period concluded that there is insufficient evidence on which to base recommendations for thromboprophylaxis during pregnancy and the early postnatal period. <u>Exception review – IPC in stroke patients (2013)</u> This section of the guideline was not	mechanical and pharmacological prophylaxis had a lower risk of DVT. One systematic review[203] on the safety and efficacy of pharmacologic thromboprophylaxis following blunt head injury concluded that there is currently insufficient evidence to guide thromboprophylaxis in this group of patients. <u>Spinal injury (1 study)</u> One systematic review and meta-analysis [204] of heparins for VTE prophylaxis in patients with acute spinal cord injury found that low-dose UFH has no thromboprophylaxis effect compared with placebo or untreated while LMWH reduced bleeding but not VTE compared with LDUH. <u>Lower limb plaster casts (1 study)</u> One small RCT[205] of IPC beneath the plaster cast in patients who underwent repair of acute Achillis tendon rupture revealed a high incidence of DVT in both the IPC and control groups, with no significant differences in incidence at two or six weeks post-operatively.		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
considered in the exceptional review.	<u>Pregnancy and up to 6 weeks postpartum (1 study)</u> One study[206] assessed the mobility of postpartum mothers to identify those at greatest risk of VTE. The study found that those who underwent any form of vaginal delivery were mobile soonest and almost twice as mobile as those who underwent caesarean section (CS) while women who underwent emergency CS were more mobile than those who had elective CS. <u>Critical care (3 studies)</u> One RCT[207] of IPC plus GCS or GCS alone to prevent VTE in intensive care unit (ICU) patients with high risk of bleeding (CIREA1 trial) found no difference in the VTE rates between the two groups. A post-hoc analysis of a prospective cohort study[208] evaluating statin therapy for VTE prophylaxis during ICU stay showed that statin therapy was not associated with a reduction of VTE incidence or in hospital mortality. One systematic review[209] of thromboprophylaxis in critically ill		

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
	patients showed that any type of heparin thromboprophylaxis decreases DVT and PE and LMWH compared with UFH decreases symptomatic PE, while major bleeding and mortality rates do not appear to be significantly influenced by heparin thromboprophylaxis in the ICU setting. <u>Other (1 study)</u> One RCT[210] of fondaparinux versus LMWH for VTE prevention in patients requiring rigid or semi-rigid immobilisation for isolated non-surgical below-knee injury concluded that fondaparinux may be a valuable therapeutic option over nadroparin for preventing VTE in this group of patients.		
Patient information and planning for discharge			
What specific information about the prophylaxis methods or VTE should be provided to patients who require VTE prophylaxis?			
No new evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
What is the effectiveness of regional anaesthesia vs general anaesthesia in reducing the incidence of postoperative VTE?			
No new evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.
Does adding a regional to a general anaesthetic reduce the risk of postoperative VTE?			

Conclusion from the previous surveillance reviews	Is there any new evidence/intelligence identified during this 4-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG at the 4-year point	Conclusion of this 4-year surveillance review (2014)
No new evidence was found for this section.	No studies identified.	None identified.	No relevant evidence identified.

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