APPENDIX A. SEARCH STRATEGIES

Database: MEDLINE (via PubMed)

Search date: 10/30/14

Set #	Search Terms	Results
#1	Search "venous thrombosis"[MeSH Terms] OR venous thrombo*[tiab] OR deep-venous thrombo*[tiab] OR deep vein thrombo*[tiab] OR deep-vein thrombo*[tiab] OR phlebothrombo*[tiab] OR "Thromboembolism"[Mesh:NoExp] OR "thrombophlebitis"[tiab] OR thromboemboli*[tiab] OR "Venous Thromboembolism"[Mesh] OR venothrombolic event*[tiab] OR "VTEs"[tiab] OR "VTE"[tiab] OR "Thrombosis"[Mesh:NoExp] OR "Thrombosis"[tiab]	187,263
#2	Search "intermittent pneumatic compression devices"[MeSH Terms] OR compression device*[tiab] OR "intermittent compression"[tiab] OR "intermittent pneumatic"[tiab] OR foot pump*[tiab] OR foot-pump*[tiab] OR "Gravity Suits"[Mesh] OR "compression garment"[tiab] OR "inflatable garment"[tiab] OR "pneumatic pump"[tiab] OR "gradient pressure"[tiab] OR "Pneumatic compressor"[tiab] OR "pneumatic appliance"[tiab] OR "WizAIR"[tiab] OR "Flowtron"[tiab] OR "Phlebo"[tiab] OR "Kendall"[tiab] OR air massage*[tiab] OR "A-V impulse system"[tiab] OR "VenaFlow"[tiab] OR "Jobst"[tiab] OR "ArtAssist"[tiab] OR "Plexipulse"[tiab] OR "SC-2004 Sequential Circulator PCD"[tiab] OR "Walkcare"[tiab] OR "Venodyne"[tiab] OR "IPC"[tiab] OR "PIC"[tiab] OR "EPIC"[tiab] OR	28,466
#3	Search #1 AND #2	1923
#4	Search #3 NOT (animals[mh] NOT humans[mh])	1879
#5	#4 NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp]) Sort by: Author Filters: Publication date from 1995/01/01; English	963

Database: Embase

Search date: 10/30/14

Set #	Search Terms	Results
#1	'vein thrombosis'/exp OR 'thrombosis'/de OR thrombo*:ab,ti OR phlebothrombo*:ab,ti OR "venothrombolic event":ab,ti OR "VTE":ab,ti OR "VTEs":ab,ti	460,903
#2	'intermittent pneumatic compression device'/exp OR "A-V Impulse System":ab,ti OR "ArtAssist":ab,ti OR "Flexitouch system":ab,ti OR "FLOWTRON":ab,ti OR "intermittent pneumatic compression devices":ab,ti OR "Plexipulse":ab,ti OR "pneumatic intermittent impulse device":ab,ti OR "SC-2004 Sequential Circulator PCD":ab,ti OR "Walkcare":ab,ti OR 'assisted circulation'/de OR 'bandage'/de OR 'mast suit'/exp OR 'compression instrument'/de OR "compression device":ti,ab OR "intermittent compression":ti,ab OR "intermittent pneumatic":ti,ab OR "foot- pumps":ti,ab OR "foot-pump":ti,ab OR "compression garment":ti,ab OR "inflatable garment":ti,ab OR "pneumatic pump":ti,ab OR "gradient pressure":ti,ab OR "Pneumatic compressor":ti,ab OR "pneumatic appliance":ti,ab OR "WizAIR":ti,ab OR "Phelebo":ti,ab OR "Kendall":ti,ab OR "air massage":ti,ab OR "air massages":ti,ab OR "VenaFlow":ti,ab OR "Jobst":ti,ab OR "Venodyne":ti,ab	25,460
#3	#1 AND #2	2519
#4	#3 AND ([embase]/lim OR [embase classic]/lim) NOT [medline]/lim	807
#5	#4 NOT ('case report'/exp OR 'editorial'/exp OR 'letter'/exp OR 'note'/exp)	735
#6	#5 AND [humans]/lim AND [english]/lim	437
#7	#6 AND [1995-2014]/py	425

Database: CINAHL (Key Question 4 only)

Search date: 10/30/14

Set #	Search Terms	Results
S1	(MH "Compression Garments")	1634
S2	(MH "Compression Therapy")	1673
S3	(MH "Bandages and Dressings")	7649
S4	TI ("intermittent pneumatic compression device" or "A-V Impulse System" or "ArtAssist" or "Flexitouch system" or "FLOWTRON" or "intermittent pneumatic compression devices" or "Plexipulse" or "pneumatic intermittent impulse device" or "SC-2004 Sequential Circulator PCD" or "Walkcare" or "assisted circulation" or "bandage" or "compression instrument" or "compression device" or "intermittent compression" or "intermittent pneumatic" or "foot pump" or "foot-pumps" or "foot-pump" or "compression garment" or "inflatable garment" or "pneumatic pump" or "gradient pressure" or "Pneumatic compressor" or "pneumatic appliance" or "WizAIR" or "Phlebo" or "Kendall" or "air massage" or "air massages" or "VenaFlow" or "Jobst" or "Venodyne") OR AB ("intermittent pneumatic compression device" or "A-V Impulse System" or "ArtAssist" or "Flexitouch system" or "FLOWTRON" or "intermittent pneumatic compression device" or "SC-2004 Sequential Circulator PCD" or "Walkcare" or "assisted circulation" or "bandage" or "Pneumatic compression device" or "Jobst" or "Venodyne") OR AB ("intermittent pneumatic compression device" or "A-V Impulse System" or "ArtAssist" or "Flexitouch system" or "FLOWTRON" or "intermittent pneumatic compression devices" or "SC-2004 Sequential Circulator PCD" or "Walkcare" or "assisted circulation" or "bandage" or "compression instrument" or "compression device" or "A-V Impulse System" or "ArtAssist" or "Flexitouch system" or "FLOWTRON" or "intermittent pneumatic compression devices" or "SC-2004 Sequential Circulator PCD" or "Walkcare" or "assisted circulation" or "bandage" or "compression instrument" or "compression device" or "SC-2004 Sequential Circulator PCD" or "Walkcare" or "assisted circulation" or "bandage" or "compression instrument" or "compression device" or "Intermittent compression garment" or "inflatable garment" or "pneumatic pump" or "gradient pressure" or "Pneumatic compression garment" or "inflatable garment" or "pneumatic pump" or "gradient pressure" or "Pneumatic compressor" or "pneumatic appli	1187
S5	S1 OR S2 OR S3 OR S4	10,761
S6	TI (thrombo* or phlebothrombo* or "venothrombolic event" or "VTE" or "VTEs") OR AB (thrombo* or phlebothrombo* or "venothrombolic event" or "VTE" or "VTEs")	25,614
S7	(MH "Venous Thrombosis+") OR (MH "Thromboembolism+") OR (MH "Thrombosis+")	21,952
S8	S6 OR S7	36,538
S9	S5 AND S8	841
S10	S9 Limiters - English Language; Published Date: 19950101-20141231; Exclude MEDLINE records; Language: English; Search modes - Find all my search terms	309
S11	(MH "Prospective Studies+") OR (MH "Cross Sectional Studies") OR (MH "Quasi- Experimental Studies+") OR (MH "Retrospective Design")	433,714
S12	S10 AND S11	18

Database: Cochrane CENTRAL

Search date: 10/30/14

Set #	Search Terms	Results
#1	deep vein thrombosis:ti,ab,kw (Word variations have been searched)	2205
#2	deep vein thromboses:ti,ab,kw (Word variations have been searched)	40
#3	thrombo* or phlebothrombo* or "venothrombolic event" or "VTE" or "VTEs":ti,ab,kw (Word variations have been searched)	22,495
#4	[or #1-#3]	22,495



Set #	Search Terms	Results
#5	"intermittent pneumatic compression device" or "A-V Impulse System" or "ArtAssist" or "Flexitouch system" or "FLOWTRON" or "intermittent pneumatic compression devices" or "Plexipulse" or "pneumatic intermittent impulse device" or "SC-2004 Sequential Circulator PCD" or "Walkcare" or "assisted circulation" or "bandage" or "compression instrument" or "compression device" or "intermittent compression" or "intermittent pneumatic" or "foot pump" or "foot-pumps" or "foot-pump" or "compression garment" or "inflatable garment" or "pneumatic pump" or "gradient pressure" or "Pneumatic compressor" or "pneumatic appliance" or "WizAIR" or "Phlebo" or "Kendall" or "air massage" or "air massages" or "VenaFlow" or "Jobst" or "Venodyne":ti,ab	1984
#6	[and #4-#5] Publication Year from 1995 to 2014, in Cochrane Reviews (Reviews and Protocols) and Trials	205

APPENDIX B. QUALITY (RISK OF BIAS) ASSESSMENT OF RCTS—CRITERIA USED AND DETAILED RATINGS

General Instructions: Rate each risk of bias item listed below as **Low risk/High risk/Unclear risk** (see Cochrane guidance to inform judgements). Add comments to justify ratings. After considering each of the quality items, give the study an overall rating of "**Low risk**," "**Moderate risk**," or "**High risk**" (see below).

Rating of individual items:

1. Selection bias:

- *a.* <u>*Randomization adequate</u> (Adequate methods include: random number table, computergenerated randomization, minimization w/o a random element) **Low risk/High risk/Unclear risk**
- *b.* <u>*Allocation concealment</u> (Adequate methods include: pharmacy-controlled randomization, numbered sealed envelopes, central allocation) **Low risk/High risk/Unclear risk**
- c. <u>Baseline characteristics</u> (Consider whether there were systematic differences observed in baseline characteristics and prognostic factors between groups, and if important differences were observed, if the analyses controlled for these differences) Low risk/High risk/Unclear risk

2. Performance bias:

- *a.* *<u>Concurrent interventions or unintended exposures</u>: (Consider concurrent intervention or an unintended exposure [eg, crossovers; contamination some control group gets the intervention] that might bias results) **Low risk/High risk/Unclear risk**
- *b.* <u>*Protocol variation:*</u> (Consider whether variation from the protocol compromised the conclusions of the study) **Low risk/High risk/Unclear risk**

3. Detection bias:

- *a.* <u>*Subjects Blinded?</u>: (Consider measures used to blind subjects to treatment assignment and any data presented on effectiveness of these measures) Low risk/High risk/Unclear risk
- *b. <u>*Outcome assessors blinded (hard outcomes)</u>: (Outcome assessors blind to treatment assignment for "hard outcomes" such as mortality) Low risk/High risk/Unclear risk*
- *c.* <u>*Outcome assessors blinded (soft outcomes)</u>: (Outcome assessors blind to treatment assignment for "soft outcomes" such as symptoms) **Low risk/High risk/Unclear risk**
- *d.* <u>*Measurement bias:*</u> (Reliability and validity of measures used-VTE) Low risk/High risk/Unclear risk



e. <u>Measurement bias</u>: (Reliability and validity of measures used- **Ease of use/Acceptability Low risk/High risk/Unclear risk**

4. Attrition bias:

a. <u>*Incomplete outcome data</u>: (Consider whether incomplete outcome data were adequately addressed, including: systematic differences in attrition between groups [differential attrition]; overall loss to follow-up [overall attrition]; and whether an "intention-to-treat" [ITT; all eligible patients that were randomized are included in analysis] analysis was performed) (Note – mixed models and survival analyses are in general ITT) Low risk/High risk/Unclear risk

5. Reporting bias:

a. <u>*Selective outcomes reporting</u>: (Consider whether there is any suggestion of selective outcome reporting (eg, systematic differences between planned and reported findings)? Low risk/High risk/Unclear risk

*Items contained in Cochrane Risk of Bias Tool

Overall study rating:

Please assign each study an overall quality rating of "Low risk," "High risk," or "Unclear risk" based on the following definitions:

A "**Low risk**" study has the least bias, and results are considered valid. A low risk study uses a valid approach to allocate patients to alternative treatments; has a low dropout rate; and uses appropriate means to prevent bias, measure outcomes, and analyze and report results. [Items 1a and 1c; 2a; 3b and 3c; and 4a are all rated low risk]

A "**Moderate risk**" study is susceptible to some bias but probably not enough to invalidate the results. The study may be missing information, making it difficult to assess limitations and potential problems (unclear risk). As the moderate risk category is broad, studies with this rating vary in their strengths and weaknesses. [Most, but not all of the following items are rated low risk: Items 1a and 1c; 2a; 3b and 3c; and 4a]

A "**High risk**" rating indicates significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; have large amounts of missing information; or have discrepancies in reporting. The results of a high risk study are at least as likely to reflect flaws in the study design as to indicate true differences between the compared interventions. [At least one-half of the individual quality items are rated high risk or unclear risk]

<u>Conflict of interest:</u> (Record but not used as part of Risk of Bias Assessment)

a. <u>*Was there the absence of potential important conflict of interest?:* The focus here is financial conflict of interest. If no financial conflict of interest (eg, if funded by government or foundation and authors do not have financial relationships with drug/device manufacturer), then answer "Yes." **Yes/No/Unclear**</u>



Otrada			l	ndividu	al Quali	ty Asse	ssment	Criteria	Rating	S			Overall	COI
Study	1a	1b	1c	2a	2b	3a	3b	3c	3d	3e	4	5	Rating	Absent?
Blanchard, 1999 ⁵²	UR	LR	UR	LR	LR	LR	UR	UR	LR	UR	LR	LR	High	Yes
Colwell, 2010 ¹⁷	LR	HR	LR	UR	LR	HR	LR	UR	LR	UR	LR	LR	Moderate	No
Edwards, 2008 ⁵⁸	UR	UR	LR	UR	HR	HR	UR	UR	LR	UR	UR	LR	High	No
Ginzburg, 2003 ⁵⁵	LR	UR	LR	LR	HR	LR	LR	UR	LR	UR	HR	LR	Moderate	Unclear
Greenfield, 1997 ⁶¹	UR	UR	UR	LR	LR	LR	UR	UR	LR	UR	UR	UR	High	Unclear
Lachiewicz, 2004 ⁴⁶	UR	LR	LR	LR	LR	LR	LR	UR	LR	UR	LR	LR	Moderate	Yes
Murakami, 2003 ²³	LR	HR	LR	LR	LR	HR	UR	UR	LR	LR	LR	LR	Moderate	Yes
Pagella, 200747	LR	LR	LR	LR	LR	HR	UR	HR	UR	UR	LR	LR	Moderate	Unclear
Pambianco, 1995 ⁵⁹	LR	LR	LR	LR	LR	LR	UR	UR	LR	UR	HR	LR	Moderate	Yes
Pitto, 2004 ¹⁸	LR	UR	LR	LR	UR	LR	LR	HR	LR	UR	HR	LR	Moderate	No
Rokito, 1996 ⁴⁹	UR	UR	LR	UR	LR	HR	LR	UR	UR	UR	LR	LR	Moderate	No
Silbersack, 2004 ⁵⁷	UR	UR	LR	UR	HR	LR	LR	UR	LR	UR	LR	LR	Moderate	No
Stannard, 2001 ⁵⁰	LR	UR	LR	UR	UR	UR	LR	UR	LR	UR	HR	LR	Moderate	No
Stone, 1996 ⁵⁶	UR	UR	LR	LR	UR	LR	UR	UR	LR	UR	UR	LR	Moderate	Unclear
Warwick,2002 ¹⁹	LR	UR	LR	UR	UR	LR	LR	HR	LR	UR	UR	LR	Moderate	No
Warwick, 1998 ⁵³	LR	UR	LR	LR	HR	HR	LR	HR	LR	LR	LR	LR	Moderate	No
Windisch, 2011 ⁵⁴	UR	UR	UR	LR	LR	HR	LR	UR	LR	UR	LR	LR	Moderate	Unclear
Wood, 1997 ⁵¹	UR	UR	HR	UR	UR	HR	LR	HR	LR	UR	UR	LR	High	Unclear

*The quality rating criteria described above were not used for the 3 included observational studies.^{48,60,62} They were evaluated using the 5 domains of basic design, selection bias, performance bias, attrition bias, and detection bias, and only the overall score is reported in the body of the report.

Abbreviations: COI=conflict of interest; HR=high risk; LR=low risk; RCTs=randomized controlled trials; UR=unclear risk

References to Appendix B:

- 1. Blanchard J, Meuwly JY, Leyvraz PF, et al. Prevention of deep-vein thrombosis after total knee replacement. Randomised comparison between a low-molecular-weight heparin (nadroparin) and mechanical prophylaxis with a foot-pump system. *J Bone Joint Surg Br.* 1999;81(4):654-659.
- 2. Colwell CW, Jr., Froimson MI, Mont MA, et al. Thrombosis prevention after total hip arthroplasty: a prospective, randomized trial comparing a mobile compression device with low-molecular-weight heparin. *J Bone Joint Surg Am.* 2010;92(3):527-535.
- **3.** Edwards JZ, Pulido PA, Ezzet KA, Copp SN, Walker RH, Colwell CW, Jr. Portable compression device and low-molecular-weight heparin compared with low-molecular-weight heparin for thromboprophylaxis after total joint arthroplasty. *J Arthroplasty*. 2008;23(8):1122-1127.
- **4.** Ginzburg E, Cohn SM, Lopez J, Jackowski J, Brown M, Hameed SM. Randomized clinical trial of intermittent pneumatic compression and low molecular weight heparin in trauma. *Br J Surg.* 2003;90(11):1338-1344.
- **5.** Greenfield LJ, Proctor MC, Rodriguez JL, Luchette FA, Cipolle MD, Cho J. Posttrauma thromboembolism prophylaxis. *J Trauma*. 1997;42(1):100-103.
- 6. Lachiewicz PF, Kelley SS, Haden LR. Two mechanical devices for prophylaxis of thromboembolism after total knee arthroplasty. A prospective, randomised study. *J Bone Joint Surg Br.* 2004;86(8):1137-1141.
- 7. Murakami M, McDill TL, Cindrick-Pounds L, et al. Deep venous thrombosis prophylaxis in trauma: improved compliance with a novel miniaturized pneumatic compression device. *J Vasc Surg.* 2003;38(5):923-927.
- **8.** Pagella P, Cipolle M, Sacco E, Matula P, Karoly E, Bokovoy J. A randomized trial to evaluate compliance in terms of patient comfort and satisfaction of two pneumatic compression devices. *Orthop Nurs.* 2007;26(3):169-174.
- **9.** Pambianco G, Orchard T, Landau P. Deep vein thrombosis: prevention in stroke patients during rehabilitation. *Arch Phys Med Rehabil*. 1995;76(4):324-330.
- **10.** Pitto RP, Hamer H, Heiss-Dunlop W, Kuehle J. Mechanical prophylaxis of deep-vein thrombosis after total hip replacement a randomised clinical trial. *J Bone Joint Surg Br*. 2004;86(5):639-642.
- **11.** Rokito SE, Schwartz MC, Neuwirth MG. Deep vein thrombosis after major reconstructive spinal surgery. *Spine (Phila Pa 1976)*. 1996;21(7):853-858; discussion 859.



- **12.** Silbersack Y, Taute BM, Hein W, Podhaisky H. Prevention of deep-vein thrombosis after total hip and knee replacement. Low-molecular-weight heparin in combination with intermittent pneumatic compression. *J Bone Joint Surg Br.* 2004;86(6):809-812.
- **13.** Stannard JP, Riley RS, McClenney MD, Lopez-Ben RR, Volgas DA, Alonso JE. Mechanical prophylaxis against deep-vein thrombosis after pelvic and acetabular fractures. *J Bone Joint Surg Am.* 2001;83-a(7):1047-1051.
- **14.** Stone MH, Limb D, Campbell P, Stead D, Culleton G. A comparison of intermittent calf compression and enoxaparin for thromboprophylaxis in total hip replacement. A pilot study. *Int Orthop.* 1996;20(6):367-369.
- **15.** Warwick D, Harrison J, Whitehouse S, Mitchelmore A, Thornton M. A randomised comparison of a foot pump and low-molecular-weight heparin in the prevention of deep-vein thrombosis after total knee replacement. *J Bone Joint Surg Br.* 2002;84(3):344-350.
- **16.** Warwick D, Harrison J, Glew D, Mitchelmore A, Peters TJ, Donovan J. Comparison of the use of a foot pump with the use of low-molecular-weight heparin for the prevention of deep-vein thrombosis after total hip replacement. A prospective, randomized trial. *J Bone Joint Surg Am.* 1998;80(8):1158-1166.
- **17.** Windisch C, Kolb W, Kolb K, Grutzner P, Venbrocks R, Anders J. Pneumatic compression with foot pumps facilitates early postoperative mobilisation in total knee arthroplasty. *Int Orthop.* 2011;35(7):995-1000.
- **18.** Wood KB, Kos PB, Abnet JK, Ista C. Prevention of deep-vein thrombosis after major spinal surgery: a comparison study of external devices. *J Spinal Disord*. 1997;10(3):209-214.
- **19.** Bockheim HM, McAllen KJ, Baker R, Barletta JF. Mechanical prophylaxis to prevent venous thromboembolism in surgical patients: a prospective trial evaluating compliance. *J Crit Care*. 2009;24(2):192-196.
- **20.** Proctor MC, Greenfield LJ, Wakefield TW, Zajkowski PJ. A clinical comparison of pneumatic compression devices: the basis for selection. *J Vasc Surg.* 2001;34(3):459-463; discussion 463-454.
- **21.** Robertson KA, Bertot AJ, Wolfe MW, Barrack RL. Patient compliance and satisfaction with mechanical devices for preventing deep venous thrombosis after joint replacement. *J South Orthop Assoc.* 2000;9(3):182-186.

APPENDIX C. PEER REVIEW COMMENTS/AUTHOR RESPONSES

Reviewer	Comment	Response					
Question 1. Are the objectives, scope, and methods for this review clearly described?							
1	Yes	Acknowledged					
2	Yes	Acknowledged					
3	Yes	Acknowledged					
4	Yes	Acknowledged					
6	Yes	Acknowledged					
Question 2.	Is there any indication of bias in our synthesis of the evidenc	e?					
1	No	Acknowledged					
2	No	Acknowledged					
3	No	Acknowledged					
4	No	Acknowledged					
6	No	Acknowledged					
Question 3.	Are there any <u>published</u> or <u>unpublished</u> studies that we may	have overlooked?					
1	No	Acknowledged					
2	No	Acknowledged					
3	No	Acknowledged					
4	No	Acknowledged					
6	Yes - Colwell report from 2014 JBJS of large cohort trial with IPCD	This article was identified in our search, but did not meet inclusion criteria at the comparator level. This Colwell study is a non-randomized registry trial that compares VTE events of an IPCD with published symptomatic rates for anticoagulants. This study, however, does not directly compare IPCDs with pharmacological prophylaxis, which is required for inclusion. Furthermore, this study did not report on outcomes of interest (such as ease of use or adherence) required for inclusion of non- randomized trials in our review.					

Reviewer	Comment	Response
	Please write additional suggestions or comments below. If ap	plicable, please indicate the page and line numbers from the
draft report. 1	The purpose of the study that I had in mind when I asked for your assistance in evaluating pneumatic compression devices used to prevent DVT and PE in post-op surgical patients was for you to evaluate and critically compare the various devices used to provide compression. Since there were several different devices available using different modes of compression, my hope was that if one method was superior to the others we could identify it and direct the VA to use it preferentially. Your study was most helpful in that it shows, within the limits of the evaluation, that all of the devices provide similar prophylaxis for DVT and similar levels of comfort for the patient during their use. This was most helpful as it means that we should primarily select a device or	Thank you. While the existing data do not allow any strong conclusions about differential effectiveness or ease of use, we noted other factors to consider: 1) Clinical guidelines from ACCP and AAOS, and 2) safety features, ease-of-use features, and most frequently studied devices. We have added a new table providing more details about the characteristics of the devices examined in the included studies (Appendix E).
2	pneumatic compression system on value which equals quality divided by cost. Word missing from line 14. "The committee is interested developing policy"	Thank you. This error has been corrected.
3	[No comments submitted]	_
4	Overall well done review and the reports in concise and transparent with appropriate methodology.	Thank you.
	Search date (consider an update)	An updated search is not part of the standard processes for the Evidence Synthesis Program.
4	English language restriction is problematic. At a minimum there should be a rationale provided for doing so.	We restricted eligible studies to those published in English because we did not have the resources to translate non-English publications. Although this restriction introduces the chance of publication bias, we were reassured that the risk was low after reviewing a recent study without this restriction (Ho 2013) and finding that it had not identified any eligible non-English language studies.
4	Agreement among reviewers is not reported or described (I apologize if I missed it).	Inter-rater agreement is not reported. However, in the methods section we specify, "All data abstractions were confirmed by a second investigator. Disagreements were resolved by consensus or by obtaining a third investigator's opinion."

Reviewer	Comment	Response
4	Figure 1 (and other figures) that reference to the questions (KQ1, KQ2, etc) are hard to read. I suggest you add the question in a shortened format to remind readers. For example, you can say "KQ1-surgical patients", etc.	Acknowledged. We modified the labels to reference the KQs in Figure 1, and we have clarified that the other figures reference surgical patients.
4	Major bleeding in KQ1 is clearly not precise: RD=25 fewer (34 fewer to 19 more) and such direct evidence is clearly not moderate, but rather of low quality. Nonetheless, indirect evidence (from people treated with anticoagulation in other settings and conditions) tells us that bleeding risk increases with anticoagulation. So, in this case, the indirect evidence is probably better to use for the outcome of bleeding (you can list both in the evidence profile as two subsequent lines).	The denominator for this calculation was missing from the draft table and has been corrected to show a risk difference of 25 fewer per 1000 patients (34 fewer to 19 more). However, this RD was based on few events and we agree that this is an imprecise result. We have re-rated the SOE as "Low". Although it is well established that long-term anticoagulation does increase the risk of bleeding, the SOE in Table 3 is based only on studies included in the current review.
6	The report concludes that IPCD prophylaxis is equivalent to anticoagulation in prevention of VTE and that the risk of bleeding from using chemoprophylaxis is higher. Because ACCP guidelines recommend that IPCD devices be portable, battery powered and record compliance and because the ACCP guidelines have always been the gold standard for VTE prophylaxis recommendations in orthopaedics, a comparison of various IPCD devices can be done by just comparing characteristics of each of the devices as to whether they all conform to these recommendations (only one device is portable, battery-powered and records compliance). Also, this device has documented efficacy in prevention of symptomatic VTE in a very large (>3000 total hip and knee patients) multicenter study that is similar (non-inferior) to that of LMWH. Also, several studies have been published indicating a higher rate of readmission in patients treated with chemoprophylaxis compared to IPCD, this fact should be presented in the study.	Our conclusions states, "Although IPCDs differ in practical features and in effects on physiology, current evidence does not show a clear difference in effects on clinically important outcomes." In the discussion, we cite the ACCP guidelines and note that "for orthopedic procedures, portable battery powered IPCDs and devices capable of recording wear time are recommended as an option for patients at low risk of bleeding, but pharmacological prophylaxis with or without IPCD is preferred." We give characteristics of devices evaluated in the studies included in this review (Table 2 and Appendix E)) but note that this is not a comprehensive listing of all the devices on the market. We believe the multicenter study cited by the reviewer is Colwell et al, Journal of Bone and Joint Surgery, 2014;96: 177-83. This study was identified by our search and excluded because it is a non-randomized trial reporting VTE outcomes. It also does not report any outcomes required for inclusion of non-randomized studies. Readmission was not an outcome identified by our content

Reviewer	Comment	Response
	Extra comments	
1	Extra comments from an email from Reviewer 1 on 05/18/15 (he turned in comments via the form on 05/27/15, so the comments below precede those):	Acknowledged. Thank you.
	"I have read and re-read the results of your research into the effectiveness of the various types of pneumatic compression devices for DVT/PE prophylaxis in high risk surgical and medical patients. It is a truly excellent document - clearly written with easily comprehendable study objectives and outcomes. I was amazed to see how few studies out of the 1500+ total actually provided meaningful information. You have out done yourselves in providing me (and other clinicians, I suspect) with very useful information. It will help our team understand that most of the pneumatic compression devices perform well and with the exceptions you identify, we can recommend that the VA use competitive price for the basis for acquisition of these devices. My sincere thanks for all you effort and dedication. I will send any thoughts for improvement in the publication as I find them - if I can note any."	

APPENDIX D. STUDY CHARACTERISTICS

Study Information	Population	Intervention (IPCD)	Comparator	Adjunctive Therapy*
Author, year	Country	Device	Name	ASA
Number randomized	Procedure	Location	Dosage or location	GCS
Risk of bias	Sex (mean % men)	Initiation	Initiation	Other
KQ(s)	Age (mean [range])	Duration	Duration	
Blanchard, 1999 ⁵²	Switzerland	A-V Impulse System™	LMWH (nadroparin)	NR
130	ТКА	Foot	2850-5700 IU daily	No
High	23.8%	12 hours pre-op	12 hours pre-op	Acenocoumarol after 8-
KQ 1	73 (49-88)	8-12 days	10-12 days	12 days over 6-8 weeks
Bockheim, 2009 ⁶⁰	United States	SCD	Venous pump	NR
150	Trauma	Calf	Foot	NR
High	51%	NR	NR	NR
KQ 4	62 (NR)	NR	NR	
Colwell, 2010 ¹⁷	United States	ActiveCare+S.F.T.®	LMWH (enoxaparin)	81 mg/day allowed
386 or 392	ТНА	Calf	30 mg per 12 hours to	No
Moderate	45%	Intra-op	discharge, then 40 mg	NR
KQ 1	63 (20-88)	10 days post-op	daily	
			1 day post-op	
			10 days post-op	
Edwards, 2008 ⁵⁸	United States	ActiveCare DVT®	LMWH (enoxaparin)	NR
277	TKA, THA	Calf	30 mg per 12 hours	No
High	42.5%	Intra-op	1 day post-op	Intervention: Enoxaparin
KQ 1	68 (32-88)	To discharge	8 days post-op	30 mg per 12 hours until
		_		8 days post-op
Ginzburg, 2003 ⁵⁵	United States	Flowtron®	LMWH (enoxaparin)	NR
442	Trauma	Calf	30 mg per 12 hours	No
Moderate	74.0%	Post-op within 24 hours	Post-op within 24 hours	NR
KQ 2	41.5 (NR)	30 days, discharge, or	30 days, discharge, or	
		death	death	
Greenfield, 1997 ⁶¹	United States	IPCD	Low dose unfractionated	NR
53	Trauma	Calf	heparin	NR
High	60.4%	Post-admission	5000 U SC twice daily	Intervention: AV foot
KQ 2	44 (NR)	Up to 4 weeks	Post-admission	pump
			Up to 4 weeks	Comparator: LMWH

Study Information	Population	Intervention (IPCD)	Comparator	Adjunctive Therapy*		
Author, year	Country	Device	Name	ASA		
Number randomized	Procedure	Location	Dosage or location	GCS		
Risk of bias	Sex (mean % men)	Initiation	Initiation	Other		
KQ(s)	Age (mean [range])	Duration	Duration			
Lachiewicz, 2004 ⁴⁶	United States	VenaFlow®	Kendall SCD™	325 mg pre-op; 650 mg		
423	TKA	Calf	Calf	twice daily, post-op		
Moderate	35.5%	During surgery	During surgery	Yes		
KQ 3	66.8 (23-94)	NR, probably discharge	NR, probably discharge	Continuous passive		
				movement machine, 1		
				hour, 3 times daily		
Murakami, 2003 ²³	United States	WizAir DVT™ CECT	Kendall SCD	NR		
33	Trauma	Calf	Calf	NR		
Moderate	60.6%	Immediately post-	Immediately post-	Addition of heparin at		
KQ 4	48.4 (NR)	randomization	randomization	the discretion of the MD		
		NR	NR			
Pagella, 2007 ⁴⁷	United States	Kendall SCD	Flowtron	NR		
65	THA or TKA	Calf	Calf	Allowed		
Moderate	41.5%	NR	NR	Warfarin, LMWH,		
KQ 4	57.6 (NR)	NR	NR	unfractionated heparin,		
				and IVC filters also		
				allowed		
Pambianco, 1995 ⁵⁹	United States	Anthrombic pump	Adjusted dose heparin;	NR		
360	Stroke patients	(Jobst)	5000-10,000 U SC	Yes		
Moderate	41.5%	Calf	every 8 hours	NR		
KQ 2	71.4 (NR)	Post-admission	Post-admission			
10		Discharge or day 28	Discharge or day 28			
Pitto, 2004 ¹⁸	New Zealand	A-V Impulse System	LMWH (nadroparin)	NR		
216	THA	Foot	NR	Yes		
Moderate	31%	Post-op, in recovery	Post-op, in recovery	LMWH given to both		
KQ 1	57.7 (NR)	room	room	groups at 12 hours pre-		
D		NR	Until discharge	op		
Proctor, 2001 ⁶²	United States	NR	NR	NR		
1350	Surgical & medical	Foot, calf, or calf-thigh	Foot, calf, or calf-thigh	Allowed		
High	NR 54.0 (NB)	Admission	Admission	Heparin allowed		
KQ 4	54.3 (NR)	Discharge or 30 days	Discharge or 30 days			

Study Information Population		Intervention (IPCD)	Comparator	Adjunctive Therapy*		
Author, year	Country	Device	Name	ASA		
Number randomized	Procedure	Location	Dosage or location	GCS		
Risk of bias	Sex (mean % men)	Initiation	Initiation	Other		
KQ(s)	Age (mean [range])	Duration	Duration			
Robertson, 2000 ⁴⁸	United States	Kendall SCD	PlexiPulse®	NR		
224	THA or TKA	Calf-thigh	Foot	Yes with Intervention,		
High	NR	NR	NR	NR with Comparator		
KQ 4	NR	NR	NR	Enoxaparin and warfarin allowed per MD		
Rokito, 1996 ⁴⁹	United States	Kendall SCD	Warfarin	NR		
110	Spinal surgery	Calf-thigh	10 mg	Yes		
Moderate	39.5%	Intra-op ("at surgery")	Day before surgery	No		
KQ 1	44.5 (22-77)	5-7 days post-op	5-7 days post-op			
Silbersack, 2004 ⁵⁷	Germany	VenaFlow	LMWH (enoxaparin)	Allowed		
131	THA or TKA	Calf	40 mg daily	Yes (Comparator only)		
Moderate	35.7%	Immediately post-op	Evening prior to surgery	Intervention: Enoxaparin		
KQ 1	64 (29-90)	NR	30 days	40 mg daily until 30		
				days		
Stannard, 2001 ⁵⁰	United States	Kendall SCD	PlexiPulse	No		
107	Trauma	Calf-thigh	Calf-foot	NR		
Moderate	NR	<72 hours from injury	<72 hours from injury	NR		
KQs 3 and 4	NR	NR	NR			
Stone, 1996 ⁵⁶	United Kingdom	Flowtron	LMWH (enoxaparin)	No		
50	THA	Calf	40 mg daily	NR		
Moderate	NR	Immediately post-op	Evening prior to surgery	NR		
KQ 1	NR	NR	Until discharge			
Warwick, 2002 ¹⁹	United Kingdom	A-V Impulse System	LMWH (enoxaparin)	Allowed		
229	TKA	Foot	40 mg daily	Yes		
Moderate	40%	In recovery room	12 hours pre-op	NR		
KQ 1	72 (NR)	Until discharge	Until discharge			
Warwick, 1998 ⁵³	United Kingdom	A-V Impulse System	LMWH (enoxaparin)	Allowed		
290	THA	Foot	40 mg daily	Yes		
Moderate	62.5%	In recovery room	12 hours pre-op	NR		
KQ 1	68 (NR)	7 days post-op	7 days post-op			

Study Information	Population	Intervention (IPCD)	Comparator	Adjunctive Therapy*
Author, year	Country	Device	Name	ASA
Number randomized	Procedure	Location	Dosage or location	GCS
Risk of bias	Sex (mean % men)	Initiation	Initiation	Other
KQ(s)	Age (mean [range])	Duration	Duration	
Windisch, 2011 ⁵⁴	Germany	A-V Impulse System	LMWH (enoxaparin)	Yes
80	TKA	Foot	40 mg daily	NR
Moderate	NR	Immediately post-op	24 hours pre-op	Intervention: Enoxaparin
KQ 1	68.9	8 days post-op	8 days post-op	40 mg daily until 8 days
				post-op
Wood, 1997 ⁵¹	United States	PlexiPulse	Kendall SCD	NR
136	Spinal surgery	Foot	Calf-thigh	Yes
High	59%	Intra-op or at surgery	Post-op	No
KQs 3 and 4	39.5 (NR)	Until discharge	Until discharge	

*Adjunctive therapies (ASA, GCS, or Other) apply to both Intervention and Comparator groups unless otherwise noted.

Abbreviations: ASA=acetylsalicylic acid (aspirin); AV=arteriovenous; CECT=Continuous Enhanced Circulation Therapy; GCS=graduated compression stockings; IPCD=intermittent pneumatic compression device; IVC=inferior vena cava; KQ(s)=key question(s); LMWH=low molecular weight heparin; NR=not reported; PCD=pneumatic compression device; SC=subcutaneously; SCD=sequential compression device; S.F.T.=Synchronized Flow Technology; THA=total hip arthroplasty; TKA=total knee arthroplasty

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APPENDIX E. TECHNICAL FEATURES OF NAMED DEVICES EVALUATED IN INCLUDED STUDIES

Manufacturer	Device Name	Sleeve Location	Single vs Multiple (Bladder Position)	Average Cycle Duration	Average Compression Duration	Pressure Pattern (Constant vs Sequential) and Amount	Inflation Rise Time (Rapid vs Slow)	Portable?	Hour Meter?
Aircast	VenaFlow [®]	Calf*	Multiple	60 sec	6 sec	Sequential; 52 mm Hg (distal), 45 mm Hg (proximal)	Rapid	No	Yes
Huntleigh	Flowtron [®]	Calf*	Single	60 sec	12 sec	Constant; 30-60 mm Hg	Slow	No†	No
Jobst	Anthrombic Pump (System 2500)‡	Calf§	Multiple	60 sec	7-8 sec	Sequential; 30-50 mm Hg	Slow	No	No
NuTech	PlexiPulse®	Foot, foot-calfl	Multiple	Varies: 20-60 sec	2.5 sec	Constant; 160 mm Hg	Rapid	No	Yes (1 study) No (2 studies)
Kendall	Kendall SCD™	Calf, calf- thigh#	Multiple	Varies; 20-60 sec	11 sec	Sequential; 30-45 mm Hg	Slow	No†	No
Medical Compression Systems	ActiveCare DVT [®] or ActiveCare+S.F.T. [®] CECTs	Calf*	Multiple	Varies; 30-60 sec	10 sec	Sequential; Average maximum 50 mm Hg	Slow	Yes	Yes
-	WizAir DVT™ CECT	Calf	Multiple	60 sec	8 sec	Sequential; average maximum 50 mm Hg	Slow	Yes	Yes
Novamedix	A-V Impulse System™	Foot	Single (sole of foot)	Varies: 20-50 sec	3 sec	Constant; 60-200 mm Hg	Rapid	No	Yes

*Sleeves also available for foot and calf-thigh locations.

†Device available in both portable and non-portable options; answer given here is for the specific devices evaluated in the included studies.

\$Specific information on this device was not provided in the published study included in our report, but rather by Huntleigh, the company that most recently bought out Jobst.

§Sleeve also available for calf-thigh location.

Sleeve also available for calf location.

#Sleeve also available for foot location.

Abbreviations: CECT(s)=continuous enhanced circulation therapy device(s); DVT=deep vein thrombosis; SCD=sequential compression device; S.F.T.=Synchronized Flow Technology