



**TITLE: Acetylsalicylic Acid for Venous Thromboembolism Prophylaxis: an Update of Clinical Evidence**

**DATE:** 15 August 2014

## **RESEARCH QUESTION**

What is the clinical evidence for the use of acetylsalicylic acid for venous thromboembolism prophylaxis in patients undergoing total hip or total knee replacement?

## **KEY FINDINGS**

Two systematic reviews, two randomized controlled trials, and two non-randomized studies were identified regarding the use of acetylsalicylic acid (ASA) for venous thromboembolism (VTE) prophylaxis in patients undergoing total hip or total knee replacement.

## **METHODS**

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 8), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2011 and August 7, 2014. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

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**SELECTION CRITERIA**

| <b>Table 1: Selection Criteria</b> |  |
|------------------------------------|--|
| <b>Population</b>                  | Patients undergoing total hip replacement or total knee replacement  |
| <b>Intervention</b>                | Acetylsalicylic acid (ASA; aspirin)  |
| <b>Comparator</b>                  | Low molecular weight heparin (LMWH), warfarin, novel oral anticoagulant drugs (NOACs), or placebo                                    |
| <b>Outcomes</b>                    | Clinical benefits or harms; serious adverse events   |
| <b>Study Designs</b>               | Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies (safety only) |

**RESULTS**

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials and non-randomized studies.

Two systematic reviews, two randomized controlled trials, and two non-randomized studies were identified. No health technology assessments or meta-analyses were identified. Additional references of potential interest are provided in the appendix.

**OVERALL SUMMARY OF FINDINGS**

Two systematic reviews were identified.<sup>1,2</sup> One review<sup>1</sup> included eight randomized controlled trials (RCTs) of patients (n = 1,408) who received either aspirin or anticoagulants following major lower extremity orthopedic surgery. The authors concluded that aspirin was associated with a non-statistically significant lower bleeding risk than anticoagulants, and rates of deep vein thrombosis (DVT) did not differ significantly following knee or hip arthroplasty. The second systematic review<sup>2</sup> included five studies (study type not specified) of patients (n = 5,179) receiving either ASA or anticoagulants following total hip or total knee replacement. The review found that patients receiving ASA had higher rates of VTE, but could not reach firm conclusions due to the low quality of the included studies and heterogeneity of the findings.

Two RCTs<sup>3,4</sup> studied patients undergoing total knee arthroplasty (TKA). One trial<sup>3</sup> compared post-surgical patients (n = 120) receiving either aspirin or low-molecular-weight heparin (LMWH) sodium and rivaroxaban sequentially. Patients in both groups also received postoperative mechanical measures for the prevention of VTE. The authors of this study concluded that aspirin in combination with mechanical measures was effective in preventing VTE after TKA, resulting in less blood loss and less subcutaneous ecchymosis. A second RCT<sup>4</sup> compared patients (n = 324) receiving either aspirin, LMWH, or rivaroxaban postoperatively, and found no significant difference in DVT incidence between aspirin and LMWH.

Two non-randomized studies<sup>5,6</sup> reported on the safety aspects of aspirin therapy following TKA. One study<sup>5</sup> examined the safety of aspirin compared with Coumadin following TKA (n = 2,017), in combination with preoperative VTE risk stratification, mechanical prophylaxis, and early mobilization for both groups. There were no significant differences in bleeding, complications, readmission, or 90-day mortality between the two groups. A second study<sup>6</sup> used data from a UK

national joint registry to compare the safety of aspirin with LMWH following TKA (n = 156,798). There were no significant differences in 90-day mortality or major hemorrhage between the two groups, but the aspirin group was significantly more likely to need to return to the operating room (no further detail regarding reasons for this was provided in the abstract).

## REFERENCES SUMMARIZED

### Health Technology Assessments

No literature identified.

### Systematic Reviews and Meta-analyses

1. Drescher FS, Sirovich BE, Lee A, Morrison DH, Chiang WH, Larson RJ. Aspirin versus anticoagulation for prevention of venous thromboembolism major lower extremity orthopedic surgery: A systematic review and meta-analysis. *J Hosp Med*. 2014 Jul 17. [PubMed: PM25045166](#)
2. Lussana F, Squizzato A, Permunian ET, Cattaneo M. A systematic review on the effect of aspirin in the prevention of post-operative arterial thrombosis in patients undergoing total hip and total knee arthroplasty. *Thromb Res*. 2014 Jul 5. [PubMed: PM25064034](#)

### Randomized Controlled Trials

3. Jiang Y, Du H, Liu J, Zhou Y. Aspirin combined with mechanical measures to prevent venous thromboembolism after total knee arthroplasty: a randomized controlled trial. *Chin Med J (Engl)*. 2014;127(12):2201-5. [PubMed: PM24931228](#)
4. Zou Y, Tian S, Wang Y, Sun K. Administering aspirin, rivaroxaban and low-molecular-weight heparin to prevent deep venous thrombosis after total knee arthroplasty. *Blood Coagul Fibrinolysis*. 2014 Apr 2. [PubMed: PM24695091](#)

### Non-Randomized Studies (Safety Only)

5. Gesell MW, Gonzalez D, V, Bartolome GS, Memtsoudis SG, Ma Y, Haas SB, et al. Safety and efficacy of multimodal thromboprophylaxis following total knee arthroplasty: a comparative study of preferential aspirin vs. routine coumadin chemoprophylaxis. *J Arthroplasty*. 2013 Apr;28(4):575-9. [PubMed: PM23142450](#)
6. Jameson SS, Baker PN, Charman SC, Deehan DJ, Reed MR, Gregg PJ, et al. The effect of aspirin and low-molecular-weight heparin on venous thromboembolism after knee replacement: a non-randomised comparison using National Joint Registry Data. *J Bone Joint Surg Br*. 2012 Jul;94(7):914-8. [PubMed: PM22733945](#)

### PREPARED BY:

Canadian Agency for Drugs and Technologies in Health

Tel: 1-866-898-8439

[www.cadth.ca](http://www.cadth.ca)

**APPENDIX – FURTHER INFORMATION:**

**Randomized Controlled Trials – Combined Drug Therapy**

7. Anderson DR, Dunbar MJ, Bohm ER, Belzile E, Kahn SR, Zukor D, et al. Aspirin versus low-molecular-weight heparin for extended venous thromboembolism prophylaxis after total hip arthroplasty: a randomized trial. *Ann Intern Med.* 2013 Jun 4;158(11):800-6.  
[PubMed: PM23732713](#)

**Non-Randomized Studies (Safety Only) – Combined Drug Therapy**

8. Hamilton SC, Whang WW, Anderson BJ, Bradbury TL, Erens GA, Roberson JR. Inpatient enoxaparin and outpatient aspirin chemoprophylaxis regimen after primary hip and knee arthroplasty: a preliminary study. *J Arthroplasty.* 2012 Oct;27(9):1594-8.  
[PubMed: PM22480528](#)

**Economic Evaluations**

9. Schousboe JT, Brown GA. Cost-effectiveness of low-molecular-weight heparin compared with aspirin for prophylaxis against venous thromboembolism after total joint arthroplasty. *J Bone Joint Surg Am.* 2013 Jul 17;95(14):1256-64.  
[PubMed: PM23864173](#)

**Guidelines and Recommendations**

10. Falck-Ytter Y, Francis CW, Johanson NA, Curley C, Dahl OE, Schulman S, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* [Internet]. 2012 Feb [cited 2014 Aug 14];141(2 Suppl):e278S-e325S. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3278063>  
[PubMed: PM22315265](#)

**Review Articles**

11. Stewart DW, Freshour JE. Aspirin for the prophylaxis of venous thromboembolic events in orthopedic surgery patients: a comparison of the AAOS and ACCP guidelines with review of the evidence. *Ann Pharmacother.* 2013 Jan;47(1):63-74.  
[PubMed: PM23324504](#)
12. Donohoe CL, Sayana MK, Thakral R, Niall DM. Aspirin for lower limb arthroplasty thromboprophylaxis: review of international guidelines. *Ir J Med Sci.* 2011 Sep;180(3):627-32.  
[PubMed: PM21286842](#)