Author's response to reviews

Title: Warfarin Use in Hemodialysis Patients with Atrial Fibrillation: Decisions based on Uncertainty

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We have added the following to the discussion:

There would be clear challenges in funding, designing and carrying out a randomized controlled trial on warfarin use in hemodialysis. Since warfarin is inexpensive, readily available and bioequivalent (1), the funding for such a trial would need to come from public, rather than pharmaceutical company funding. Alternatively, a newer non-Vitamin K dependent anticoagulant could be evaluated against warfarin. However, such a study would be challenging in the absence of a placebo patient group, since the question of whether any anticoagulation of any kind is required in this setting would remain unanswered (2). Furthermore, there is limited experience and safety of newer anticoagulants in hemodialysis patients (3). Thus, a country with sufficient public funds would need to initiate this rigorously designed, randomized controlled trial.

Designing a randomized controlled trial in this clinical setting would need to overcome ethical challenges. Specifically, randomizing patients to the use of warfarin in hemodialysis patients may be unethical if clinicians believe that treatment to be inferior to no anticoagulation. Patients may have strong preferences that limit recruitment and bias outcomes (4). However, this study confirms that uncertainty is common in Canadian nephrologists, and that willingness to enter patients into a randomized trial is high. Thus, it would not be unethical for Canadian nephrologists to enter their patients into such a trial, since they don't feel that anticoagulation of hemodialysis patients with atrial fibrillation is either inferior or superior. Ultimately, randomized controlled trials are the most rigorous way of determining whether a cause-effect relation exists between treatment and outcome (5), and even despite the above challenges, remains the ideal way to assess the effect of anticoagulation of hemodialysis patients with atrial fibrillation.