Supplemental Material:

Supplementary Figure 1: Warfarin decisions by case
How likely are you to recommend warfarin to reduce this patient’s risk of stroke?
Supplementary Figure 2: Left atrial appendage occlusion device decisions by case
If the WATCHMAN left atrial appendage occlusion device was readily available at your centre how likely would you consider it as an alternative to chronic anticoagulation to reduce this patient’s risk of stroke?
Supplementary Figure 3: Apixaban decisions by case
How likely would you consider apixaban as an alternative to warfarin to reduce this patient’s risk of stroke?
Supplemental Figure 4: Willingness to enroll into a randomized controlled trial of a left atrial appendage occlusion device vs warfarin by case
If the WATCHMAN left atrial appendage occlusion device was readily available at your center, how likely would you consider enrolling this patient into a randomized controlled trial comparing the WATCHMAN to a control therapy to reduce this patient’s risk of stroke?
Supplemental Figure 5: Willingness to enroll into a randomized controlled trial apixaban vs warfarin by case
How likely would you consider enrolling this patient into a randomized controlled trial comparing apixaban to warfarin to reduce this patient’s risk of stroke?
Appendix:

**ORAL ANTICOAGULATION AND LEFT ATRIAL APPENDAGE OCCLUSION DEVICES FOR CARDIOEMBOLIC PREVENTION OF ARRHYTHMIAS IN CHRONIC KIDNEY DISEASE AND DIALYSIS SURVEY**

**PLEASE SELECT THE MOST APPROPRIATE RESPONSE**

1. Have you ever treated a patient with a left atrial appendage occlusion device for the prevention of stroke (e.g. a Watchman device)?
   - ☐ Yes
   - ☐ No

Left atrial appendage occlusion (LAAO) devices occlude the left atrial appendage to decrease the chance of clot formation and subsequent embolisms that cause strokes and systemic embolism. Once the LAAO device is inserted via a percutaneous procedure, it endothelializes and patients may stop their anticoagulation. LAAO devices may therefore be useful to avoid oral anticoagulation in patients at high risk of bleeding or with contraindications to oral anticoagulants.

PROTECT-AF was a multicenter non-inferiority randomized controlled trial of 707 adults with non-valvular atrial fibrillation, CHADS2 score of 1 or more, and normal renal function comparing WATCHMAN, a LAAO device, to warfarin. The WATCHMAN device was considered non-inferior to warfarin in terms of the primary composite endpoint of stroke, cardiovascular death and systemic embolism (3.0 per 100 patient years in WATCHMAN vs 4.9 per 100 patient years with warfarin, RR 0.62 95% C.I. 0.35-1.25).

The WATCHMAN was complicated by a 5.61% chance of an adverse event around the time of the LAAO procedure including pericardial effusion (4.8%), major bleeding (3.5%), procedure-related ischemic stroke (1.1%) and device embolization (0.6%) in follow-up. However, further follow-up analysis at a mean 3.0 (1.6) years met criteria for superiority with adverse events no longer being statistically significantly different between groups. Furthermore, as experience with WATCHMAN has increased, device/procedure-related complications have decreased to 3.6% through 30 days.

A patient level meta-analysis including PROTECT-AF and another randomized controlled trial comparing the WATCHMAN to warfarin (PREVAIL) and their respective registries including 2406 patients and 5931 patient-years of follow-up showed that the WATCHMAN device was associated with significantly less hemorrhagic strokes HR 0.22 P=0.004 and non-procedural bleeding HR 0.51 (0.006) with no difference in all-cause stroke or systemic embolism (HR 1.02) P=0.94 but an increase in ischemic strokes HR 1.95 P=0.05 due to procedural risks.
2. Have you ever treated a patient on dialysis with apixaban?
   □ Yes      □ No

Apixaban is a direct factor Xa inhibitor that decreases the risk of stroke and systemic embolism. In the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOLE) study, a randomized, double-blind, non-inferiority trial of 18201 patients with non-valvular atrial fibrillation and CHADS2 of 1 or more, apixaban 5mg orally twice daily compared to warfarin (target INR 2.0 to 3.0) significantly decreased the risk of stroke and systemic embolism with a hazard ratio of 0.79 (95% C.I. 0.66-0.95) while also significantly decreasing the risk of major bleeding with a hazard ratio of 0.69 (95% C.I. 0.60-0.80). Results were consistent in 16.6% of participants with eGFR<50ml/min/1.73m² including only a very few with eGFR<30ml/min/1.73m². A pharmacokinetic study suggests that dialysis patients exposed to the same dose of apixaban appear to have 30% higher levels of the drug and that dialyzability is negligible. No high quality clinical outcome data exists.
PLEASE SELECT THE MOST APPROPRIATE RESPONSE

3. You are caring for a 65 year old Caucasian male treated with intermittent hemodialysis with non-valvular atrial fibrillation and hypertension but no congestive heart failure, diabetes, stroke, liver disease, previous major bleeding, antiplatelet agents/non-steroidal anti-inflammatory drugs or alcohol use.

a) On a scale of 1-8 with 1 being the least and 8 being the most, how much do you value avoiding a stroke in this patient?

1 2 3 4 5 6 7 8 Don’t know

b) On a scale of 1-8 with 1 being the least and 8 being the most, how much do you value avoiding a major bleed requiring a hospitalization in this patient?

1 2 3 4 5 6 7 8 Don’t know

c) On a scale of 1-8 with 1 being definitely would not and 8 being definitively would, how likely are you to recommend warfarin to reduce this patient’s risk of stroke?

1 2 3 4 5 6 7 8 Don’t know

d) If the WATCHMAN left atrial appendage occlusion device was readily available at your centre, on a scale of 1-8 with 1 being definitely would not and 8 being definitely would, how likely would you consider it as an alternative to chronic anticoagulation to reduce this patient’s risk of stroke?

1 2 3 4 5 6 7 8 Don’t know

e) On a scale of 1-8 with 1 being definitely would not and 8 being definitely would, how likely would you consider apixaban as an alternative to warfarin to reduce this patient’s risk of stroke?

1 2 3 4 5 6 7 8 Don’t know

f) If the same patient was not dialysis dependent but had CKD with an eGFR of 15 ml/min/1.73m², on a scale of 1-8 with 1 being definitely would not and 8 being definitely would, how likely are you to recommend warfarin to reduce this patient’s risk of stroke?

1 2 3 4 5 6 7 8 Don’t know

g) If the WATCHMAN left atrial appendage occlusion device was readily available at your centre, on a scale of 1-8 with 1 being definitely would not and 8 being definitely would, how likely would you consider enrolling this patient into a randomized controlled trial comparing the WATCHMAN to a control therapy to reduce this patient’s risk of stroke?

1 2 3 4 5 6 7 8 Don’t know

h) On a scale of 1-8 with 1 being definitely would not and 8 being definitely would, how likely would you consider enrolling this patient into a randomized controlled trial comparing apixaban to warfarin to reduce this patient’s risk of stroke?

1 2 3 4 5 6 7 8 Don’t know
PLEASE SELECT THE MOST APPROPRIATE RESPONSE

4. You are caring for a 65 year old Caucasian male on intermittent hemodialysis with non-valvular atrial fibrillation and hypertension, previous upper gastrointestinal bleed, alcohol use but does not have congestive heart failure, diabetes, stroke, liver disease, or antiplatelet agents/non-steroidal anti-inflammatory drug use.

a) On a scale of 1-8 with 1 being the least and 8 being the most, how much do you value avoiding a stroke in this patient?

1 2 3 4 5 6 7 8 Don’t know

b) On a scale of 1-8 with 1 being the least and 8 being the most, how much do you value avoiding a major bleed requiring a hospitalization in this patient?

1 2 3 4 5 6 7 8 Don’t know

c) On a scale of 1-8 with 1 being definitely would not and 8 being definitively would, how likely are you to recommend warfarin to reduce this patient’s risk of stroke?

1 2 3 4 5 6 7 8 Don’t know

d) If the WATCHMAN left atrial appendage occlusion device was readily available at your centre, on a scale of 1-8 with 1 being definitely would not and 8 being definitely would, how likely would you consider it as an alternative to chronic anticoagulation to reduce this patient’s risk of stroke?

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e) On a scale of 1-8 with 1 being definitely would not and 8 being definitely would, how likely would you consider apixaban as an alternative to warfarin to reduce this patient’s risk of stroke?

1 2 3 4 5 6 7 8 Don’t know

f) If the same patient was not dialysis dependent but had CKD with an eGFR of 15 ml/min/1.73m², on a scale of 1-8 with 1 being definitely would not and 8 being definitely would, how likely are you to recommend warfarin to reduce this patient’s risk of stroke?

1 2 3 4 5 6 7 8 Don’t know

g) If the WATCHMAN left atrial appendage occlusion device was readily available at your centre, on a scale of 1-8 with 1 being definitely would not and 8 being definitely would, how likely would you consider enrolling this patient into a randomized controlled trial comparing the WATCHMAN to a control therapy to reduce this patient’s risk of stroke?

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1 2 3 4 5 6 7 8 Don’t know
5. You are caring for a 65 year old Caucasian male on intermittent hemodialysis with non-valvular atrial fibrillation and congestive heart failure, hypertension, diabetes, previous stroke but does not have liver disease, antiplatelet agents/non-steroidal anti-inflammatory or drug use or alcohol use.

a) On a scale of 1-8 with 1 being the least and 8 being the most, how much do you value avoiding a stroke in this patient?

1 2 3 4 5 6 7 8 Don’t know

b) On a scale of 1-8 with 1 being the least and 8 being the most, how much do you value avoiding a major bleed requiring a hospitalization in this patient?

1 2 3 4 5 6 7 8 Don’t know

c) On a scale of 1-8 with 1 being definitely would not and 8 being definitively would, how likely are you to recommend warfarin to reduce this patient’s risk of stroke?

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1 2 3 4 5 6 7 8 Don’t know
6. You are caring for a 65 year old Caucasian male on intermittent hemodialysis with non-valvular atrial fibrillation and congestive heart failure, hypertension, diabetes, previous stroke, previous upper gastrointestinal bleeding, alcohol use but does not have liver disease or antiplatelet agents/non-steroidal anti-inflammatory drug use.

a) On a scale of 1-8 with 1 being the least and 8 being the most, how much do you value avoiding a stroke in this patient?

1 2 3 4 5 6 7 8 Don’t know

b) On a scale of 1-8 with 1 being the least and 8 being the most, how much do you value avoiding a major bleed requiring a hospitalization in this patient?

1 2 3 4 5 6 7 8 Don’t know

c) On a scale of 1-8 with 1 being definitely would not and 8 being definitively would, how likely are you to recommend warfarin to reduce this patient’s risk of stroke?

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f) If the same patient was not dialysis dependent but had CKD with an eGFR of 15 ml/min/1.73m², on a scale of 1-8 with 1 being definitely would not and 8 being definitely would, how likely are you to recommend warfarin to reduce this patient’s risk of stroke?

1 2 3 4 5 6 7 8 Don’t know

g) If the WATCHMAN left atrial appendage occlusion device was readily available at your centre, on a scale of 1-8 with 1 being definitely would not and 8 being definitely would, how likely would you consider enrolling this patient into a randomized controlled trial comparing the WATCHMAN to a control therapy to reduce this patient’s risk of stroke?

1 2 3 4 5 6 7 8 Don’t know

h) On a scale of 1-8 with 1 being definitely would not and 8 being definitely would, how likely would you consider enrolling this patient into a randomized controlled trial comparing apixaban to warfarin to reduce this patient’s risk of stroke?

1 2 3 4 5 6 7 8 Don’t know
7. What is your specialty? □ Cardiology □ Nephrology □ Other

8. Number of years in independent practice: □ <5 □ 5-10 □ 10-15 □ 15-20 □ ≥20

9. Work environment:
   □ Community hospital   □ Community hospital with university affiliation   □ University hospital   □ Other

10. When deciding whether or not to prescribe an antiplatelet agent or oral anticoagulation for prevention of cardioembolism in a patient with non-valvular atrial fibrillation, do you refer to a risk prediction tool e.g. CHADS2 score or equivalent to stratify cardioembolic risk?
    □ Yes   □ No

11. When deciding whether or not to prescribe an antiplatelet agent or oral anticoagulation for prevention of cardioembolism in a patient with non-valvular atrial fibrillation, do you employ the HASBLED score or equivalent to stratify bleeding risk?
    □ Yes   □ No

12. In counselling CKD and dialysis patients with non-valvular atrial fibrillation about the benefits and risks of initiating oral anticoagulation, how many major bleeding episodes requiring hospitalization would you accept to prevent one ischemic stroke with disability?
    1) 0  2) 1  3) 2  4) 3  5) 4  6) 5  7) >5  8) Don’t know

Comments:

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