

New standards for trustworthy guidelines

Clinical scenario:
Anticoagulation treatment
for prevention of stroke
in atrial fibrillation

CLICK-IT studies in educational sessions
DECIDE WP1 2013

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CLICK-IT

How do clinicians like and understand trustworthy guidelines?
Mixed methods study using Clickers in educational sessions

Objectives:

- ✓ Determine understanding and preferences for guideline presentation formats
- ✓ Teach about new concepts for trustworthy guidelines
- Registered results and data will be used for research.
- We regard answering the questions is to give informed consent for us to use this in research. (You can walk out of the room now)
- The questions are in (if another language) , but some of the examples are in English

First, some demographic questions



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Q 1: My age is

1. 25-35
2. 36-45
3. 46-55
4. 56-65
5. 66-100

Q 2: My position is

1. Intern, medical student
2. Resident physician
3. Consultant physician

Q3: In terms of training in health research methodology (HRM), you have:

1. Never completed a formal course in HRM or epidemiology
2. Completed one or more formal courses in HRM or epidemiology
3. A masters degree or PhD degree in HRM or epidemiology



Meet Gabriel 68y

- **Medical history:** Type 2 diabetes. No medications
- **Chief complaint:** For the past 6 months intermittent episodes of heart palpitations and rapid heart rate; duration between 30 minutes to 3 days
- **Diagnosis:** Atrial fibrillation
- No risk factors indicating increased risk of bleeding
- Risk for stroke? Anticoagulation as prophylaxis?

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CHA2DS2-VASc Score for Atrial Fibrillation Stroke Risk

Calculates stroke risk for patients with atrial fibrillation, possibly better than the CHADS2 score.

Age?	<input type="radio"/> < 65 years old +0 <input type="radio"/> 65-74 years old +1 <input type="radio"/> ≥ 75 years old +2
Congestive Heart Failure History?	<input type="checkbox"/> Yes +1
Hypertension History?	<input type="checkbox"/> Yes +1
Stroke/TIA/Thromboembolism History?	<input type="checkbox"/> Yes +2
Vascular Disease History? (previous MI, peripheral arterial disease or aortic plaque)	<input type="checkbox"/> Yes +1
Diabetes Mellitus?	<input checked="" type="checkbox"/> Yes +1
Female?	<input type="checkbox"/> Yes +1

Score **2**

Baseline risk for stroke (no anticoagulation treatment) with CHA2DS2-VASc score 2

This means an assumed risk of 22 strokes per 1000 patients over 1 year

Treatment for Gabriel?

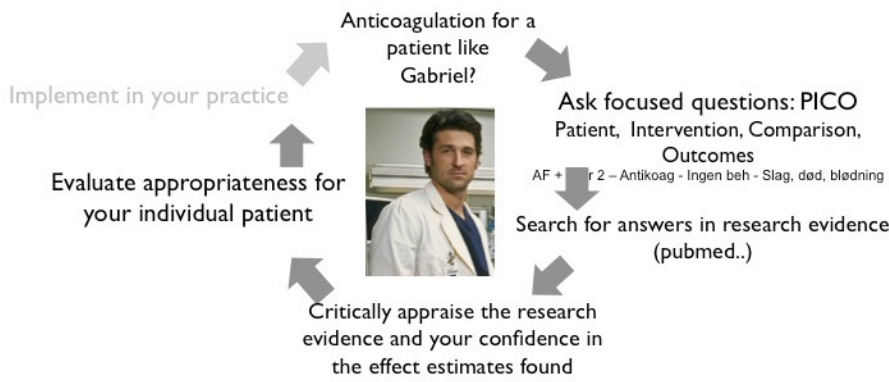


- **Diagnosis:** Atrial fibrillation
- Moderate risk of stroke (CHAD2S2-VASc score: 2)
- Low risk of bleeding
- Currently no antithrombotic treatment

Q 1: If you were unsure of which, if any, therapy to offer the patient, where would you first look for an answer?

1. Local guideline
2. Systematic review
3. EBM textbook (e.g. UpToDate)
4. Practice guideline (national or international)
5. Ask a colleague
6. Individual study

The traditional steps of evidence-based practice



Q 2a: "I consider traditional critical appraisal of research evidence to be feasible when I'm out in the clinics treating my patients"

1	2	3	4	5	6
Strongly Disagree	Disagree	Somewhat Disagree	Somewhat Agree	Agree	Strongly Agree

The traditional steps of evidence-based practice



Q 2b: In the clinics: How many times have you followed these traditional steps the last month

1	2	3	4
Never, rarely	Not followed all steps, but done critical appraisal of research evidence weekly	Followed all steps weekly	Followed all steps, daily

Several guidelines and EBM textbooks (e.g. UpToDate) use the GRADE system and label their recommendations with a number + letter.

We suggest that older patients receive supplementation with vitamin D3 (cholecalciferol) GRADE 2B

Q 3: What does the number (2) reflect?

1	2	3	4
It's a strong recommendation	It's moderate quality evidence	It's a moderate recommendation	It's a weak recommendation

Several guidelines and EBM textbooks (e.g. UpToDate) use the GRADE system and label their recommendations with a number + letter.

We suggest that older patients receive supplementation with vitamin D3 (cholecalciferol) GRADE 2B

Q 4: What does the letter (B) reflect?

1	2	3	4
Moderate quality evidence	Low quality evidence	Study design (based on a single Randomized study)	Study design (based on a smaller systematic review)

Several guidelines and EBM textbooks (e.g. UpToDate) use the GRADE system and label their recommendations with a number + letter.

We suggest that older patients receive supplementation with vitamin D3 (cholecalciferol) GRADE 2B

Q 5: GRADE provides either strong or weak recommendations. To what extent do you agree with the following statement:

"I fully understand the difference between strong and weak recommendations and the implications for clinical decision making"

1	2	3	4	5	6
Strongly Disagree	Disagree	Somewhat Disagree	Somewhat Agree	Agree	Strongly Agree

Now, let's get back to Gabriel



1. Two groups, 5 questions each
2. Different formats of guidelines for atrial fibrillation and anticoagulation
3. One group gets blindfolds (they are "blinded")
4. I will not read the questions or text out loud.
5. Read the text and give med a sign (waive/ raise you hand) when you are ready to answer
6. Then switch and the other group gets blindfolds

Imagine you search online for an answer to what to do with Gabriel, and you found the guideline on next slide!

Read through the text first and you'll get some questions later.

The questions will always come together with the text so there is no need to memorize!

- For patients with a CHA2DS2-VASc score greater than 1, we recommend chronic antithrombotic therapy (Grade 1A). (See "Prevention approach by CHA2DS2-VASc score" above.)
- For patients with a CHA2DS2-VASc score of 2, we suggest anticoagulant therapy in preference to aspirin (Grade 2A). In deciding between the two, it is particularly important to be sure patients are well informed about the benefits and risks of therapy, and that patient preferences are part of the decision. For patients at high risk of major bleeding (table 5 and table 6), aspirin is a reasonable choice. (See "Bleeding risk" above and "Net clinical benefit" above.)
- In patients with AF for whom anticoagulation therapy is chosen, we suggest an oral direct thrombin inhibitor or a factor Xa inhibitor (NOAC) rather than warfarin (Grade 2B). (See "Summary of anticoagulant monotherapy" above.)

Q 6: "These recommendations will help me manage my patient"

1	2	3	4	5	6
Strongly Disagree	Disagree	Somewhat Disagree	Somewhat Agree	Agree	Strongly Agree

- For patients with a CHA2DS2-VASc score greater than 1, we recommend chronic antithrombotic therapy (Grade 1A). (See "Prevention approach by CHA2DS2-VASc score" above.)
- For patients with a CHA2DS2-VASc score of 2, we suggest anticoagulant therapy in preference to aspirin (Grade 2A). In deciding between the two, it is particularly important to be sure patients are well informed about the benefits and risks of therapy, and that patient preferences are part of the decision. For patients at high risk of major bleeding (table 5 and table 6), aspirin is a reasonable choice. (See "Bleeding risk" above and "Net clinical benefit" above.)
- In patients with AF for whom anticoagulation therapy is chosen, we suggest an oral direct thrombin inhibitor or a factor Xa inhibitor (NOAC) rather than warfarin (Grade 2B). (See "Summary of anticoagulant monotherapy" above.)

Q 7 : How do you interpret these recommendations?

1	2	3	4
Strong recommendation for NOAC. Weak recommendation for warfarin or aspirin.	Weak recommendation for NOAC and warfarin.	Weak recommendation for any option.	Strong recommendation for treatment. Weak recommendation for NOAC over warfarin.

You also find the summary you will see on next slide!

Read through the text first and you'll get some questions later.

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Summary of anticoagulant monotherapy – Anticoagulation with each of the newer agents ([dabigatran](#), [rivaroxaban](#) and [apixaban](#)) leads to similar or lower rates both of ischemic stroke and major bleeding compared to [warfarin](#). Important additional advantages of these newer agents include convenience (no requirement for routine testing of the international normalized ratio), a small reduction in the risk of intracranial hemorrhage, and less susceptibility to dietary and drug interactions. Disadvantages include lack of an antidote and the potential that, with time, unidentified side effects will become evident, such as a potentially higher rate of myocardial infarction with [dabigatran](#) and twice daily regimen ([dabigatran](#) and [apixaban](#)). Should experience in real word populations mirror the net clinical benefit found in randomized trials, our confidence in the superiority of these drugs will increase. (See “[Dabigatran](#)” above.)

We believe that anticoagulation, when indicated, is reasonable with either [warfarin](#) or a newer agent. We believe the evidence suggests that the three newer agents have similar efficacy and safety.

Q 8 : “This information helps me apply the recommendation on my patient”

1	2	3	4	5	6
Strongly disagree	Disagree	Somewhat disagree	Somewhat Agree	Agree	Strongly Agree

Summary of anticoagulant monotherapy – Anticoagulation with each of the newer agents ([dabigatran](#), [rivaroxaban](#) and [apixaban](#)) leads to similar or lower rates both of ischemic stroke and major bleeding compared to [warfarin](#). Important additional advantages of these newer agents include convenience (no requirement for routine testing of the international normalized ratio), a small reduction in the risk of intracranial hemorrhage, and less susceptibility to dietary and drug interactions. Disadvantages include lack of an antidote and the potential that, with time, unidentified side effects will become evident, such as a potentially higher rate of myocardial infarction with [dabigatran](#) and twice daily regimen ([dabigatran](#) and [apixaban](#)). Should experience in real word populations mirror the net clinical benefit found in randomized trials, our confidence in the superiority of these drugs will increase. (See “[Dabigatran](#)” above.)

We believe that anticoagulation, when indicated, is reasonable with either [warfarin](#) or a newer agent. We believe the evidence suggests that the three newer agents have similar efficacy and safety.

Q 9 : What does this information tell you about NOAC vs warfarin?

1	2	3	4
Vastly superior treatment effect	Less burden of treatment and slightly better treatment effect	Large reduction in side effects	No difference in effect or side effects

How would you have treated Gabriel?



- Diagnosis: Atrial fibrillation
- Moderate risk of stroke (CHA2DS2-VASc score: 2)
- Low risk of bleeding
- Currently no antithrombotic treatment

Let’s look at the recommendations again

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- For patients with a CHA2DS2-VASc score greater than 1, we recommend chronic antithrombotic therapy (**Grade 1A**). (See “[Prevention approach by CHA2DS2-VASc score](#)” above.)
- For patients with a CHA2DS2-VASc score of 2, we suggest anticoagulant therapy in preference to aspirin (**Grade 2A**). In deciding between the two, it is particularly important to be sure patients are well informed about the benefits and risks of therapy, and that patient preferences are part of the decision. For patients at high risk of major bleeding ([table 5](#) and [table 6](#)), aspirin is a reasonable choice. (See “[Bleeding risk](#)” above and “[Net clinical benefit](#)” above.)
- In patients with AF for whom anticoagulation therapy is chosen, we suggest an oral direct thrombin inhibitor or a factor Xa inhibitor (NOAC) rather than warfarin (**Grade 2B**). (See “[Summary of anticoagulant monotherapy](#)” above.)

Q 10 : Which, if any, antithrombotic treatment would you consider appropriate for Gabriel?

1	2	3	4
NOAC (Dabigatran, rivaroxaban or apixaban)	Aspirin	Warfarin	No therapy

Now give your blindfold to an unblinded colleague



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Imagine you search online for an answer to what to do with Gabriel, and you found the guideline on next slide!

Read through the text first and you’ll get some questions later.

The questions will always come together with the text so there is no need to memorize!

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CHA2DS2-VASc score 2 or higher

Strong recommendation

We recommend treatment with oral anticoagulants (i.e. dabigatran, rivaroxaban, apixaban or warfarin) over aspirin or no treatment.

Choice of oral anticoagulation

Weak recommendation

We suggest treatment with dabigatran, rivaroxaban or apixaban (NOAC) rather than warfarin.

Q 11: "The recommendations will help me manage my patient"

1	2	3	4	5	6
Strongly Disagree	Disagree	Somewhat Disagree	Somewhat Agree	Agree	Strongly Agree

CHA2DS2-VASc score 2 or higher

Strong recommendation

We recommend treatment with oral anticoagulants (i.e. dabigatran, rivaroxaban, apixaban or warfarin) over aspirin or no treatment.

Choice of oral anticoagulation

Weak recommendation

We suggest treatment with dabigatran, rivaroxaban or apixaban (NOAC) rather than warfarin.

Q 12 : How do you interpret these recommendations?

1	2	3	4
Strong recommendation for NOAC. Weak recommendation for warfarin or aspirin.	Weak recommendation for NOAC and warfarin.	Weak recommendation for any option.	Strong recommendation for any treatment. Weak recommendation for NOAC over warfarin.

When you click one of the recommendations you find the summary you will see on next slide!

Read through the text first and you'll get some questions later.

The questions will always come together with the text so there is no need to memorize!

Benefits and harms

New oral anticoagulants versus warfarin per 1,000 patients treated for 1 year:

Death and stroke: No significant difference
Major bleeding: Overall no relevant difference, but there was seen a halving of the number intracranial bleeds with dabigatran, resulting in a absolute risk reduction of 2 fewer per 1000 patients
Myocardial infarction: No significant difference. The exception is dabigatran, which increased the risk compared to warfarin. The absolute risk, however, is generally very low: 5/1000 with warfarin, 6/1000 with dabigatran.
Treatment discontinuation (e.g. due to side effects): 31 interrupted with warfarin, 39 with NOAC.
Practical consequences: Daily medication with all. Regular INR controls and dietary restrictions with warfarin.

Quality of evidence

Moderate. The expected effects of NOAC compared with warfarin is taken from a systematic review with heterogeneity, and imprecise results (wide confidence intervals) for death and bleeding. Dabigatran was associated with an increase in myocardial infarction and treatment discontinuation in a reliable subgroup analysis.

Preference and values

Studies on patient preferences and values have shown that the average patient is prepared to suffer three major bleeds to avoid one stroke. These studies have guided our recommendation. They are however deemed to be of low quality and there was a high

Q 13 : "This information helps me apply the recommendation on my patient"

1	2	3	4	5	6
Strongly Disagree	Disagree	Somewhat Disagree	Somewhat Agree	Agree	Strongly Agree

Benefits and harms

New oral anticoagulants versus warfarin per 1,000 patients treated for 1 year:

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Q 14 : What does this information tell you about NOAC vs warfarin?

1	2	3	4
Vastly superior treatment effect	Less burden of treatment and slightly better treatment effect	Large reduction in side effects	No difference in effect or side effects

How would you have treated Gabriel?



- Diagnosis: Atrial fibrillation
- Moderate risk of stroke (CHA2DS2-VASc score: 2)
- Low risk of bleeding
- Currently no antithrombotic treatment

Let's look at the recommendations again

CHA2DS2-VASc score 2 or higher

Strong recommendation

We recommend treatment with oral anticoagulants (i.e. dabigatran, rivaroxaban, apixaban or warfarin) over aspirin or no treatment.

Choice of oral anticoagulation

Weak recommendation

We suggest treatment with dabigatran, rivaroxaban or apixaban (NOAC) rather than warfarin.

Q 15 : Which, if any, antithrombotic treatment would you consider appropriate for Gabriel?

1	2	3	4
NOAC (Dabigatran, rivaroxaban or apixaban)	Aspirin	Warfarin	No therapy



Now, let us all get unblinded and have a look at both formats for a few minutes



Format A

- For patients with a CHA2DS2-VASc score greater than 1, we recommend chronic antithrombotic therapy (Grade 1A). (See "Prevention approach by CHA2DS2-VASc score" above.)
- For patients with a CHA2DS2-VASc score of 2, we suggest anticoagulant therapy in preference to aspirin (Grade 2A). In deciding between the two, it is particularly important to be sure patients are well informed about the benefits and risks of therapy, and that patient preferences are part of the decision. For patients at high risk of major bleeding (table 5 and table 6), aspirin is a reasonable choice. (See "Bleeding risk" above and "Net clinical benefit" above.)
- In patients with AF for whom anticoagulation therapy is chosen, we suggest an oral direct thrombin inhibitor or a factor Xa inhibitor (NOAC) rather than warfarin (Grade 2B). (See "Summary of anticoagulant monotherapy" above.)

Summary of anticoagulant monotherapy – Anticoagulation with each of the newer agents (dabigatran, rivaroxaban and apixaban) leads to similar or lower rates both of ischemic stroke and major bleeding compared to warfarin. Important additional advantages of these newer agents include convenience (no requirement for routine testing of the international normalized ratio), a small reduction in the risk of intracranial hemorrhage, and less susceptibility to dietary and drug interactions. Disadvantages include lack of an antidote and the potential that, with time, unidentified side effects will become evident, such as a potentially higher rate of myocardial infarction with dabigatran and twice daily regimen (dabigatran and apixaban). Should experience in real world populations mirror the net clinical benefit found in randomized trials, our confidence in the superiority of these drugs will increase. (See "Dabigatran" above.)

We believe that anticoagulation, when indicated, is reasonable with either warfarin or a newer agent. We believe the evidence suggests that the three newer agents have similar efficacy and

Format B

CHA2DS2-VASc score 2 or higher

Strong recommendation

We recommend treatment with oral anticoagulants (i.e. dabigatran, rivaroxaban, apixaban or warfarin) over aspirin or no treatment.

Choice of oral anticoagulation

Weak recommendation

We suggest treatment with dabigatran, rivaroxaban or apixaban (NOAC) rather than warfarin.

Clicking a recommendation gives you a summary of key information

Benefits and harms

New oral anticoagulants versus warfarin per 1,000 patients treated for 1 year:

Death and stroke: No significant difference

Major bleeding: Overall no relevant difference, but the number of intracranial bleeds was halved with dabigatran, resulting in an absolute risk reduction of 2 fewer per 1000 patients

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Quality of evidence

Moderate. The expected effects of NOAC compared with warfarin is taken from a systematic review with heterogeneity, and imprecise results (wide confidence intervals) for death and bleeding. Dabigatran was associated with an increase in myocardial infarction and treatment discontinuation in a reliable subgroup analysis.

Preference and values

Studies on patient preferences and values have shown that the average patient is prepared to suffer three major bleeds to avoid one stroke. These studies have guided our recommendation. They are however deemed to be of low quality and there was a high degree of variability in preferences. We therefore suggest that the decision regarding treatment options is made together with the patient.

Resources

Cost did not influence this recommendation.

Q 16: Format B presents absolute effects for benefits and harms, whereas format A does not. What is your first reaction to being presented with the absolute effects?

1	2	3	4	5
Confusing distraction, leave it out	A little confusing but not a big problem	Doesn't help but doesn't hurt	Not crucial but helpful	Crucial information, should always be included

Benefits and harms

New oral anticoagulants versus warfarin per 1,000 patients treated for 1 year:

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Treatment discontinuation (e.g. due to side effects): 31 interrupted with warfarin, 39 with NOAC.

Practical consequences: Daily medication with all. Regular INR controls and dietary restrictions with warfarin.

Disadvantages include lack of an antidote and the potential that, with time, unidentified side effects will become evident, such as a potentially higher rate of myocardial infarction with dabigatran and twice daily regimen (dabigatran and apixaban). Should experience in real world populations mirror the net clinical benefit found in randomized trials, our confidence in the superiority of these drugs will increase. (See "Dabigatran" above.)

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Myocardial infarction: No significant difference. The exception is dabigatran, which increased the risk compared to warfarin. The absolute risk, however, is generally very low: 5/1000 with warfarin, 6/1000 with dabigatran.

Q 17: Overall, do you prefer format A or format B?

1	2	3
Format A	I have no preference	Format B

Format A

CHA2DS2-VASc score greater than 1, we recommend chronic antithrombotic therapy (Grade 1A). (See "Prevention approach by CHA2DS2-VASc score" above.)

For patients with a CHA2DS2-VASc score of 2, we suggest anticoagulant therapy in preference to aspirin (Grade 2A). In deciding between the two, it is particularly important to be sure patients are well informed about the benefits and risks of therapy, and that patient preferences are part of the decision. For patients at high risk of major bleeding (table 5 and table 6), aspirin is a reasonable choice. (See "Bleeding risk" above and "Net clinical benefit" above.)

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We believe that anticoagulation, when indicated, is reasonable with either warfarin or a newer agent. We believe the evidence suggests that the three newer agents have similar efficacy and safety.

Format B

CHA2DS2-VASc score 2 or higher

Strong recommendation

We recommend treatment with oral anticoagulants (i.e. dabigatran, rivaroxaban, apixaban or warfarin) over aspirin or no treatment.

Choice of oral anticoagulation

Weak recommendation

We suggest treatment with dabigatran, rivaroxaban or apixaban (NOAC) rather than warfarin.

Benefits and harms

New oral anticoagulants versus warfarin per 1,000 patients treated for 1 year:

Death and stroke: No significant difference

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Understand new definitions and standards for trustworthy guidelines

“Clinical Practice Guidelines are statements that include **recommendations** intended to optimize patient care. They are informed by a **systematic review** of evidence and an assessment of the **benefits and harms of alternative** care options“(2011)



Broad consensus **GRADE** Common methods for guidelines

GRADE defines **strength** of recommendation as:

“The strength of a recommendation reflects the extent to which we can, across the range of patients for whom the recommendations are intended, be confident that desirable effects of a management strategy outweigh undesirable effects.”

Strong recommendations:

Reflects clear benefit of the recommended treatment alternative.

Implications: Recommendation applies to all or nearly all patients. “Just do it”

Weak recommendations:

Reflects fine balance between benefits and harms for the treatment alternatives.

Implications: Recommendation applies to the majority of patients.

“Maybe”, “Depends on patient values and preferences”

Q18a: “I fully understand the difference between strong and weak recommendations and the implications for clinical decision making”

1	2	3	4	5	6
Strongly Disagree	Disagree	Somewhat Disagree	Somewhat Agree	Agree	Strongly Agree

GRADE defines **strength** by always considering 4 factors

Strong recommendations:

Reflects clear benefit of the recommended treatment alternative.

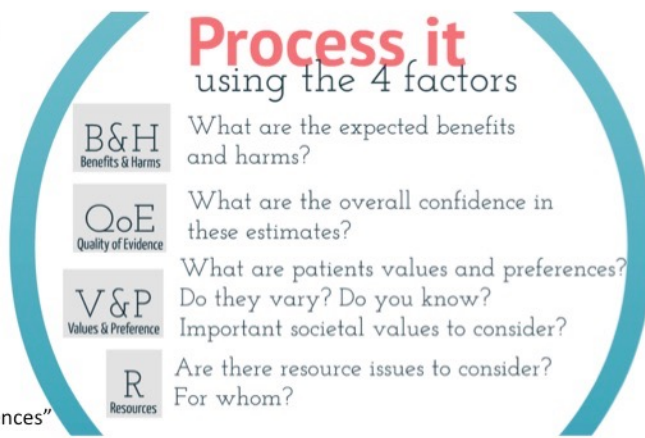
Applies to all or nearly all patients. “Just do it”

Weak recommendations:

Reflects fine balance between benefits and harms.

The majority of patients.

“Maybe”, “Depends on patient values and preferences”



Q18b: “This explanation is necessary to understand the difference between strong and weak recommendations and the implications for clinical decision making”

1	2	3	4	5	6
Strongly Disagree	Disagree	Somewhat Disagree	Somewhat Agree	Agree	Strongly Agree

GRADE defines **quality of evidence** as:

High quality: We are very confident that the true effect lies close to our effect estimates

Moderate quality: We are moderately confident in our effect estimates. The true effect is likely to be close to our effect estimates, but with the possibility to be substantially different.

Low quality: Our confidence in the effect estimates are limited. The true effect may be substantially different from our effect estimates.

Very low quality: We have very little confidence in our effect estimates. The true effect is likely to be substantially different from our effect estimates.

Q 19a: “I fully understand the difference between the different categories of quality and the implications for clinical decision making”

1	2	3	4	5	6
Strongly Disagree	Disagree	Somewhat Disagree	Somewhat Agree	Agree	Strongly Agree

Your confidence in the effect estimates (Quality Assessment)

Outcomes	Confidence In Effect Estimates
Mortality (during 1 year)	High
Stroke (during 1 year)	Moderate due to imprecise effect estimates
Major bleed (during 1 year)	Moderate due to imprecision and heterogeneity

Randomized trials with no serious limitations provide High confidence in effect estimates. Serious limitations as a result of risk of bias, Imprecision, Indirectness or publication bias lower your confidence in the effect estimates. Assess these 5 factors

Q 19b: “This explanation is necessary to understand the quality of evidence and the implications it has for clinical decision making”

1	2	3	4	5	6
Strongly Disagree	Disagree	Somewhat Disagree	Somewhat Agree	Agree	Strongly Agree

There is a lot of information included in a guideline

Do we need to see it all, all the time?

How do we like multilayered guidelines?

CHA2DS2-VASc score 2 or higher

Strong recommendation

We recommend treatment with oral anticoagulants (i.e. dabigatran, rivaroxaban, apixaban or warfarin) over aspirin or no treatment.

Choice of oral anticoagulation

Weak recommendation

We suggest treatment with dabigatran, rivaroxaban or apixaban (NOAC) rather than warfarin.

Choice of oral anticoagulation

Weak recommendation

It is less clear whether the benefits outweigh the drawbacks. We believe there will be variation in patients preferences

We suggest treatment with dabigatran, rivaroxaban or apixaban (NOAC) rather than warfarin.

- Effect estimates
- Key info**
- Rationale
- Practical advice
- Adaptation
- Reference

The new oral anticoagulants have equal effect to warfarin with regards to stroke reduction, they lower the incidence of intracranial bleeds and are more convenient to use. We therefore suggest the new oral anticoagulants over warfarin as first treatment of choice.
For patients that are already on warfarin therapy with stable INR values the cost/benefit ratio is similar to treatment with NOACs. We therefore suggest that patients well-established on warfarin therapy continue with this if they wish.

Weak recommendation

It is less clear whether the benefits outweigh the drawbacks. We believe there will be variation in patients preferences

We suggest treatment with dabigatran, rivaroxaban or apixaban (NOAC) rather than warfarin.

Benefits and harms

New oral anticoagulants versus warfarin per 1,000 patients treated for 1 year:

- Death and stroke:** No significant difference
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- Myocardial infarction:** No significant difference. The exception is dabigatran, which increased the risk compared to warfarin. The absolute risk, however, is generally very low: 5/1000 with warfarin, 6/1000 with dabigatran.
- Treatment discontinuation** (e.g. due to side effects): 31 interrupted with warfarin, 39 with NOAC.
- Practical consequences:** Daily medication with all. Regular INR controls and dietary restrictions with warfarin.

Quality of evidence

Moderate. The expected effects of NOAC compared with warfarin is taken from a systematic review with heterogeneity, and imprecise results (wide confidence intervals) for death and bleeding. Dabigatran was associated with an increase in myocardial infarction and treatment discontinuation in a reliable subgroup analysis.

Preference and values

Studies on patient preferences and values have shown that the average patient is prepared to suffer three major bleeds to avoid one stroke. These studies have guided our recommendation. They are however deemed to be of low quality and there was a high degree of variability in preferences. We therefore suggest that the decision regarding treatment options is made together with the patient.

Resources

Cost did not influence this recommendation.

Weak recommendation

It is less clear whether the benefits outweigh the drawbacks. We believe there will be variation in patients preferences

We suggest treatment with dabigatran, rivaroxaban or apixaban (NOAC) rather than warfarin.

- Effect estimates**
- Key info
- Rationale
- Practical advice
- Adaptation
- Reference

Patient	Intervention	Control	Outcome
Atrial fibrillation and low risk of stroke: CHA2DS2-VASc >2	NOAC	Warfarin	Mortality, stroke, major bleeding

Evidence profile Summary References

Outcomes	Confidence In Effect Estimates	Relative Effect	Warfarin	NOAC	Absolute Difference	Participants (Studies), Follow-Up
Mortality (during 1 year)	High	RR 0.88 (CI 0.82 - 0.96)	7 per 1000	6 per 1000	1 fewer per 1000 (CI 1 fewer - 0 fewer)	44,442 (3), 2 years
Stroke (during 1 year)	Moderate due to imprecise effect estimates	RR 0.89 (CI 0.78 - 1.02)	3 per 1000	3 per 1000	0 fewer per 1000 (CI 1 fewer - 0 fewer)	44,442 (3), 2 years
Major bleed (during 1 year)	Moderate due to imprecision and heterogeneity	RR 0.8 (CI 0.63 - 1.01)	25 per 1000	20 per 1000	5 fewer per 1000 (CI 9 fewer - 0 fewer)	44,442 (3), 2 years

“This is a smart layout for guidelines”

Thank you for your participation

For more information go to:

<http://www.decide-collaboration.eu>

<http://www.gradeworkinggroup.org>

<http://www.magicproject.org>

If there is time left we can look at your results

1	2	3	4	5	6
Strongly Disagree	Disagree	Somewhat Disagree	Somewhat Agree	Agree	Strongly Agree