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DO CLINICIANS WANT RECOMMENDATIONS? A RANDOMIZED TRIAL

On behalf of Ignacio Neumann & the group of authors

Disclosure

No financial conflicts

This study was not funded

The protocol was approved by the Hamilton Integrated Research Ethics Board and by the local Research Ethics Boards of each participating center.

Trial registration: NCT02006017

Background

- Evidence summaries have been used to bridge the gap between researcher and decision-makers

- The addition of recommendations may help to enhance the usefulness of evidence summaries

- However, not everyone agrees, especially in the context of "insufficient" or very low quality evidence.

Objective

To evaluate:

- Preferences

- Understanding of the evidence

- Interpretation of the evidence and

- Intended course of action

Evidence summaries with and without recommendations in the context of low or very-low quality evidence (GRADE).

Methods

Randomized trial with clinicians comparing evidence summaries plus recommendations versus evidence summaries alone

Participants

Eligibility:

- Medical doctors

- Working in internal medicine or family medicine

Clinical Grand Rounds in 14 centers in 10 countries (Canada, USA, Spain, Argentina, Chile, Switzerland, Norway, Costa Rica, Lebanon, Saudi Arabia)

First Randomization

Strong Recommendations Scenarios

Oseltamivir for treatment of avian influenza (H5N1)[1]

Aspirin for asymptomatic thrombophilia[2]
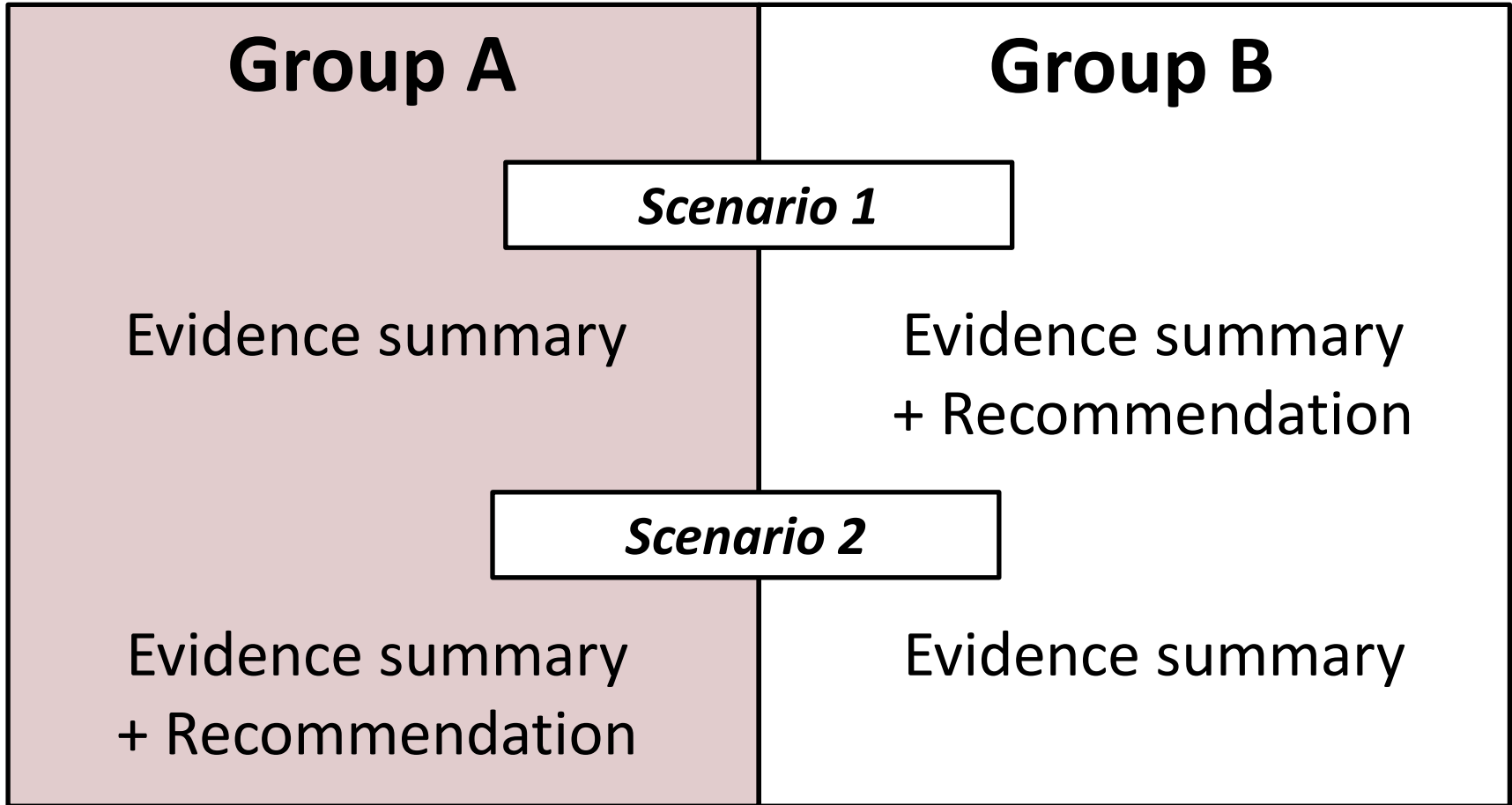
Weak Recommendations Scenarios

Potassium intake in adults[1]

Compression stockings for long-distance travelers[2]

[1]WHO Clinical Practice Guidelines
[2]ACCP 9th edition of the Antithrombotic Guidelines

Second Randomization

Group A	Group B
Scenario 1	
Evidence summary	Evidence summary + Recommendation
Scenario 2	
Evidence summary + Recommendation	Evidence summary

*Order of scenarios also at random

Evidence Summary:

No clinical trial has evaluated oseltamivir in the treatment of patients with Avian Influenza (H1N5). In 5 randomized trials conducted in healthy individuals with seasonal influenza, the use of oseltamivir resulted in a lower risk of pneumonia and other low respiratory tract infections. Serious adverse events and drug resistance were generally not reported.

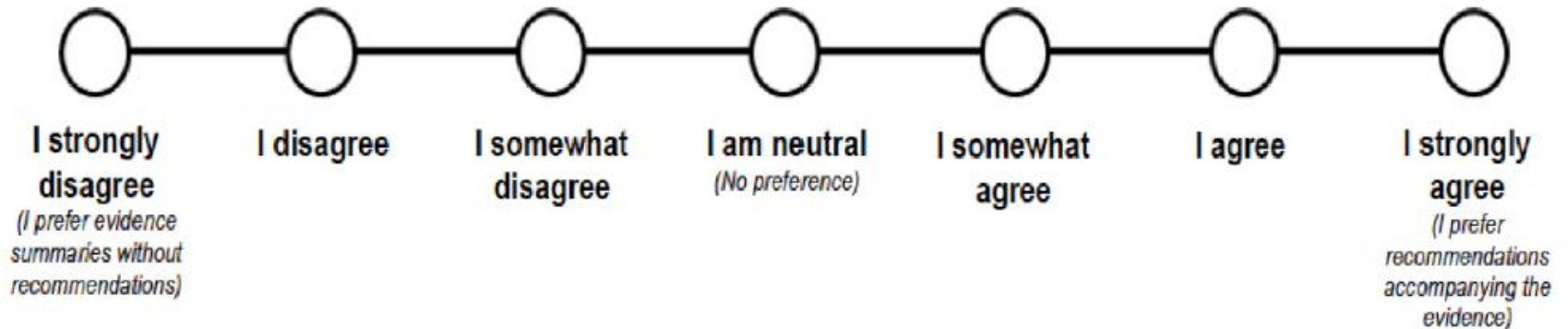| Outcome	No. of Studies	Relative Effect (95% CI)	Anticipated Absolute Effects		Confidence in effect estimates (GRADE)
			Baseline Risk	Risk Difference With oseltamivir (95% CI)	
Mortality	0	Not estimable	Not estimable	Not estimable	Not estimable
Pneumonia	5 RCT	RR 0.15 (0.03 to 0.69)	14 per 1000	12 fewer per 1,000 (from 4 to 14 fewer)	Very low due to very serious imprecision and very serious indirectness[a]
Duration of hospitalization	0	Not estimable	Not estimable	Not estimable	Not estimable
Serious adverse effects	0	Not estimable	Not estimable	Not estimable	Not estimable
Resistance	0	Not estimable	Not estimable	Not estimable	Not estimable

Recommendation:

In patients with confirmed or strongly suspected H5N1 infection, clinicians should administer oseltamivir treatment as soon as possible (Strong recommendation based on very low quality of evidence)

Remarks: *This recommendation places a high value on the prevention of death in an illness with a high case fatality. It places relatively low values on adverse reactions, the development of resistance and costs of treatment. Despite the lack of controlled treatment data for H5N1, this is a strong recommendation, in part, because there is a lack of known effective alternative pharmacological interventions at this time. The recommendation applies to adults, including pregnant women and children. Until further information becomes available, the current treatment regimen for H5N1 is as recommended for early treatment of adults, special patient groups (e.g. those with renal insufficiency) and children with seasonal influenza.*

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Primary Outcome

Clinicians' Preferences for the specific scenarios and in the context of their usual practice

I strongly disagree (I prefer evidence summaries without recommendations) | I disagree | I somewhat disagree | I am neutral (No preference) | I somewhat agree | I agree | I strongly agree (I prefer recommendations accompanying the evidence)

Secondary Outcomes

Understanding of the evidence

4 multiple choice questions regarding baseline risk, risk difference, confidence interval and confidence in effect estimates
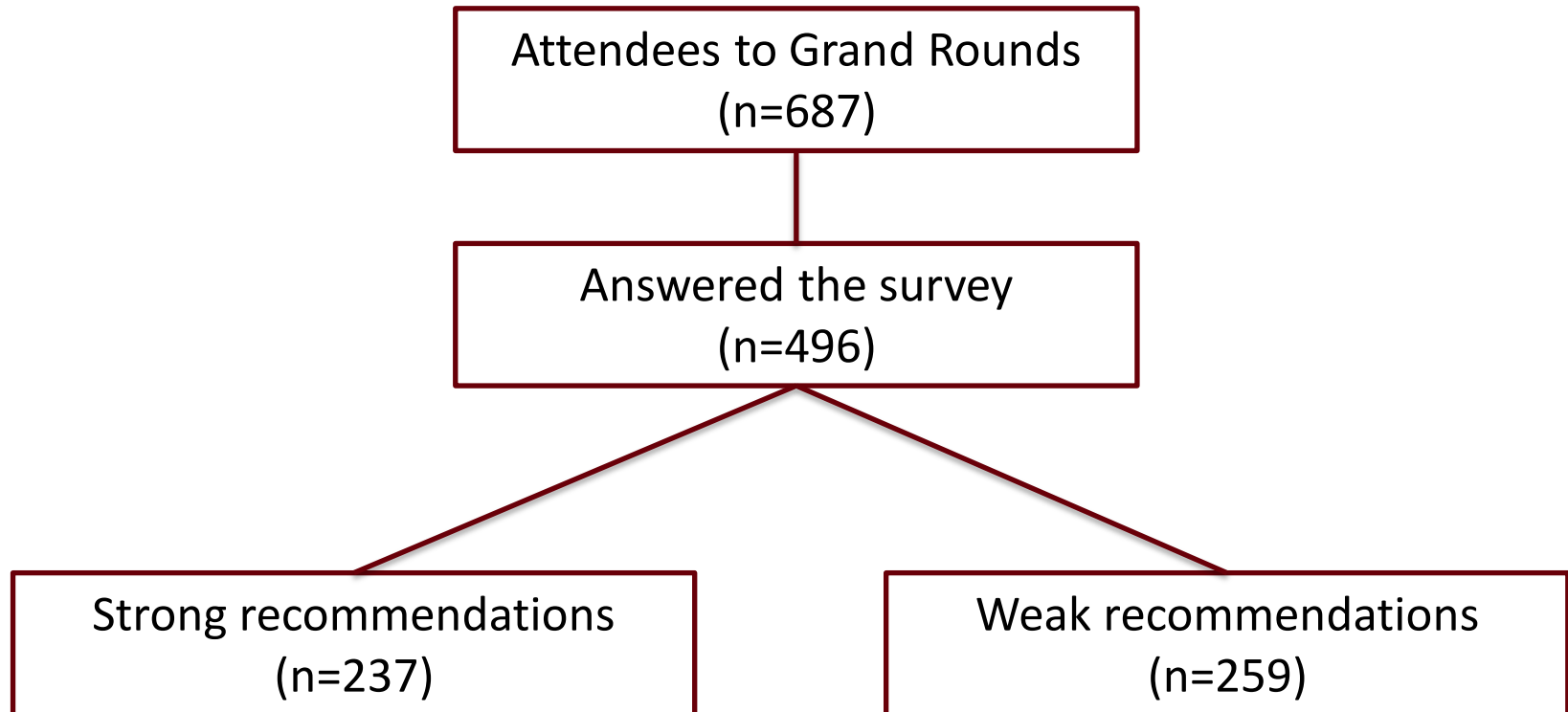
Interpretation of the evidence

4-point scale from "the benefits clearly outweigh the harms" to "the harms clearly outweigh the benefits"

Intended course of action

Would you use the intervention?

4-point scale: Yes – Probably Yes – Probably No – No

Results

Attendees to Grand Rounds
(n=687)

Answered the survey
(n=496)

Strong recommendations
(n=237)

Weak recommendations
(n=259)

Results

Strong recommendations
(n=237)

Group A
(n=123)

Oseltamivir for Avian Influenza
**Evidence summary +
recommendation**

Aspirin for asymptomatic
thrombophilia
Evidence summary only

Group B
(n=114)

Oseltamivir for Avian Influenza
Evidence summary only

Aspirin for asymptomatic
thrombophilia (AB)
**Evidence summary +
recommendation**

Results

Weak recommendations
(n=259)

Group A
(n=131)

Potassium intake
**Evidence summary +
recommendation**

Compression stockings for long-distance travelers
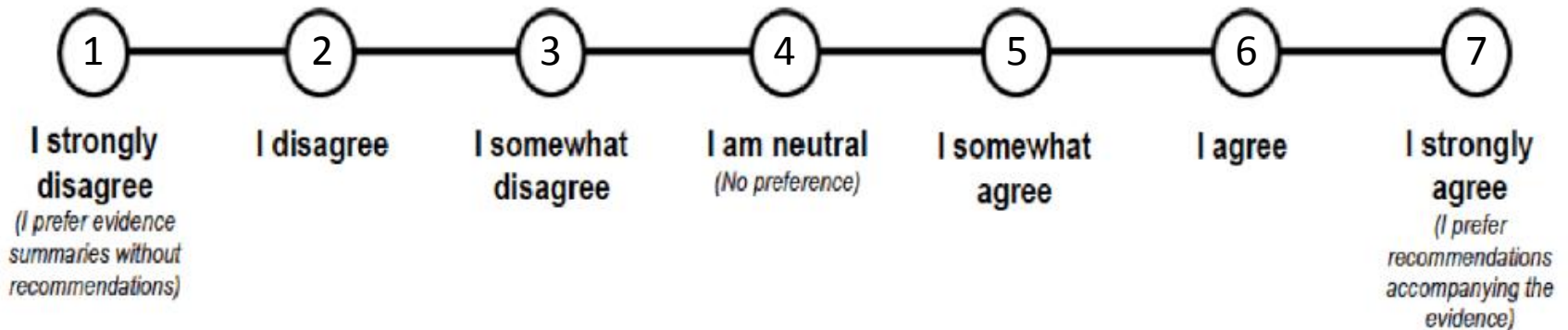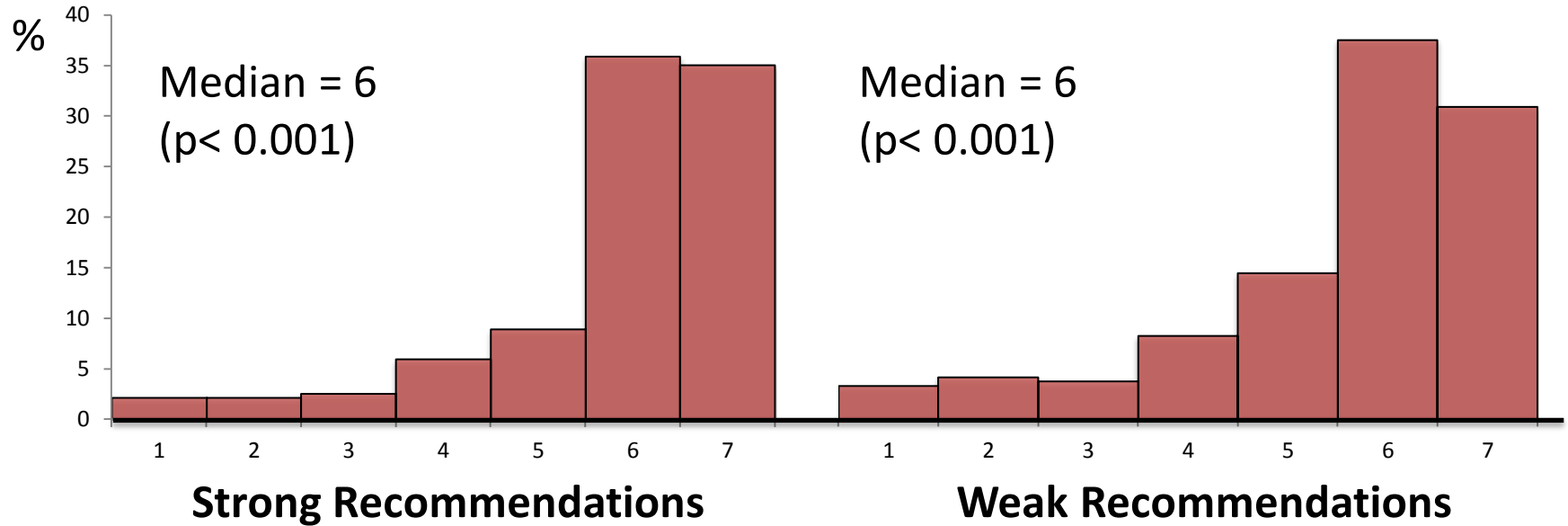**Evidence summary only**

Group B
(n=128)

Potassium intake
Evidence summary only

Compression stockings for long-distance travelers
**Evidence summary +
recommendation**

Results

	Strong Recommendations Scenarios		Weak Recommendations Scenarios	
	Group A (N=123)	Group B (N=114)	Group A (N=131)	Group B (N=128)
Mean Age (sd)	35.8 (11)	36.0 (11)	34.9 (10)	34.8 (10)
Female (%)	49 (40)	49 (43)	69 (52)	59 (46)
Professional status (%)				
Attending	49 (40)	47 (41)	53 (41)	55 (43)
Resident	66 (54)	62 (54)	73 (56)	64 (50)
Other	6 (6)	5 (5)	4 (3)	9 (7)
Training in Research (%)				
None	49 (40)	52 (46)	65 (50)	53 (42)
1 or more courses	67 (55)	57 (50)	62 (47)	68 (53)
M.Sc. Or Ph.D.	5 (5)	5 (4)	4 (3)	6 (5)

Preferences: specific scenarios

Median = 6
(p< 0.001)

Median = 6
(p< 0.001)

Strong Recommendations

Weak Recommendations

1 — 2 — 3 — 4 — 5 — 6 — 7

I strongly disagree
(I prefer evidence summaries without recommendations)

I disagree

I somewhat disagree

I am neutral
(No preference)

I somewhat agree

I agree

I strongly agree
(I prefer recommendations accompanying the evidence)

Understanding

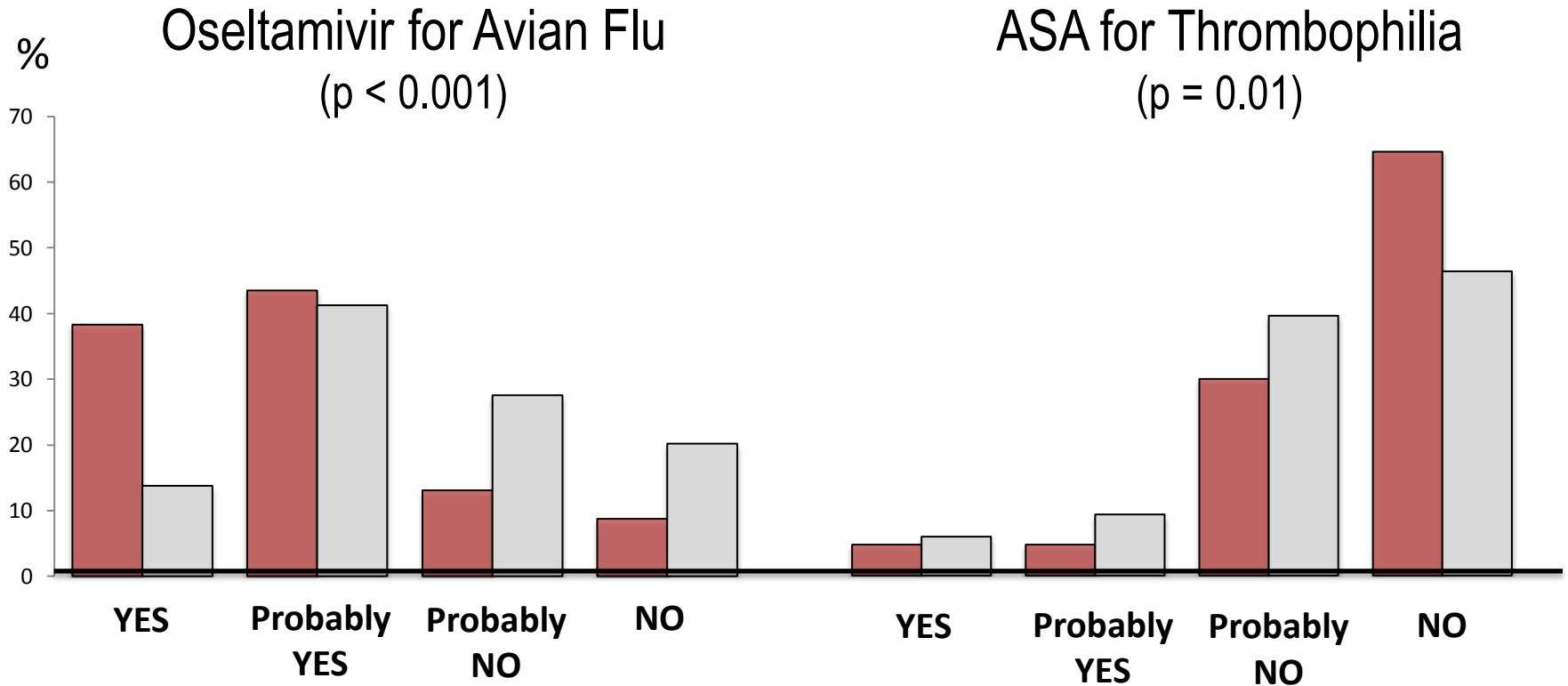| Evidence Summary		Evidence summary + recommendation
39%	Oseltamivir for Avian Flu	**39%**
32%	ASA for Thrombophilia	**25%**
43%	Potassium intake	**40%**
57%	Compression stockings*	**44%**

*statistically significant differences

Course of action

Would you use the intervention?

RED: With recommendation

Conclusions

- Clinicians value recommendations in the context of low or very low quality of evidence

- Recommendation can influence clinicians' course of action