MAGIC Evidence Ecosystem Foundation

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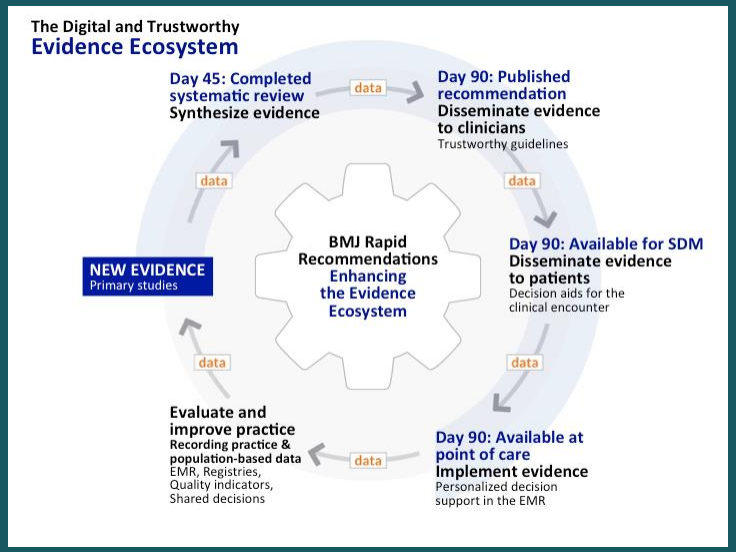
Playing with BMJ Rapid Recommendations in the MAGIC Evidence Ecosystem



Workshop EBHC Conference Taormina 2019

Per Olav Vandvik, on behalf of colleagues in the non-profit MAGIC Evidence Ecosystem Foundation

BMJ

folkehelseinstituttet

McMaster University

UiO : University of Oslo

UNIVERSITÉ DE GENÈVE
FACULTÉ DE MÉDECINE

Objectives

1. To understand how MAGICapp works for clinicians and patients, with trustworthy recommendations, evidence summaries and decision aids, exemplified through the BMJ Rapid Recommendations project for practice-changing evidence

2. To be introduced to the process of developing, publishing and dynamically updating a trustworthy recommendation from an existing systematic review, with the GRADE system and the MAGICapp

1. To get hands-on experience with use of the MAGICapp in the creation and dynamic updating of a living guideline recommendation.

Plan for workshop

1. Where does MAGIC and BMJ Rapid Recommendations belong in the Evidence Ecosystem?

2. Playing with a published BMJ Rapid Recommendation in groups, exploring new publication formats in The BMJ and MAGICapp
3. Plenary discussion follows

4. Testing authoring and dynamic updating in MAGICapp (if time permits)

5. In a final plenary discussion feedback on user experience of the MAGICapp will be discussed

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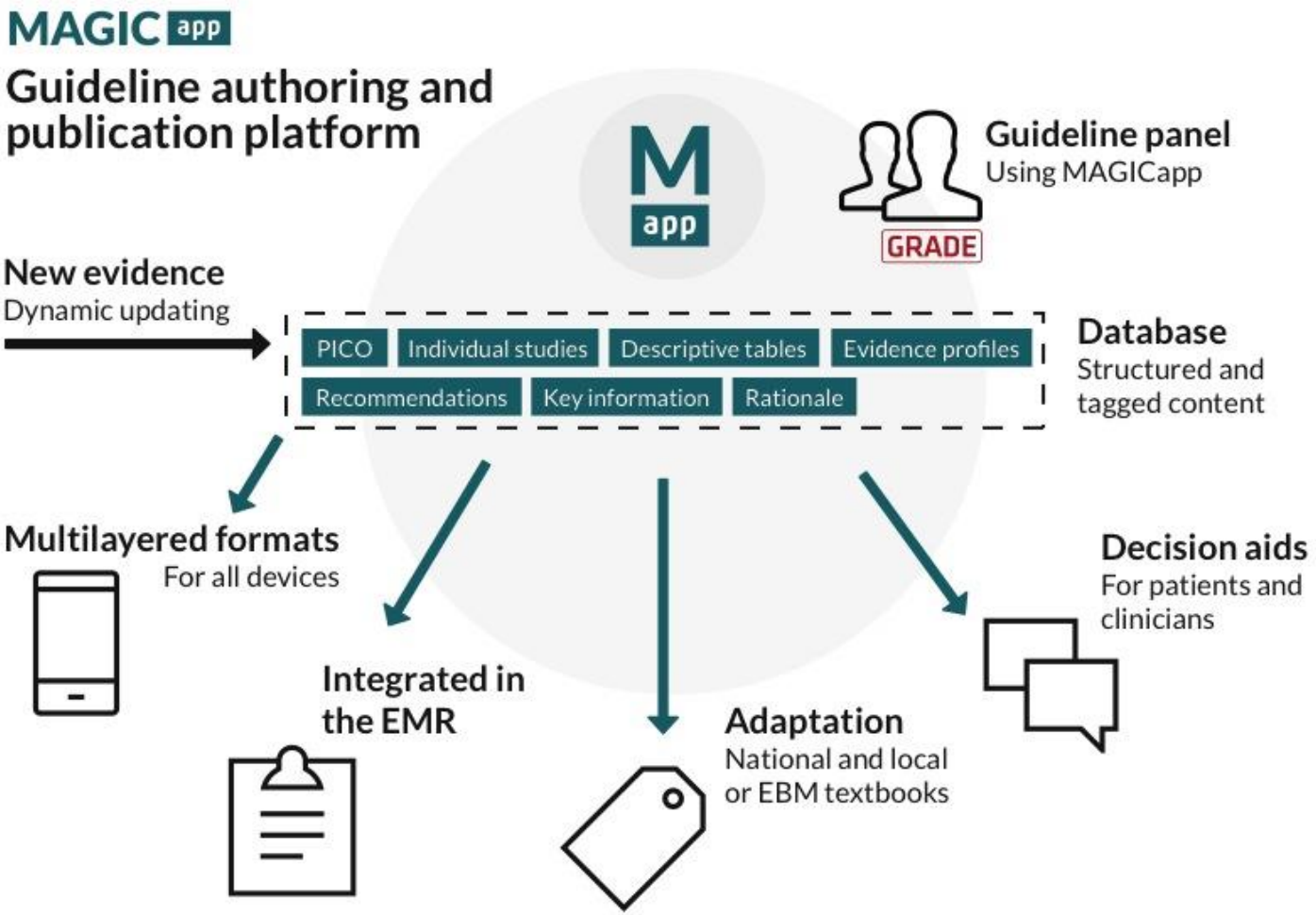
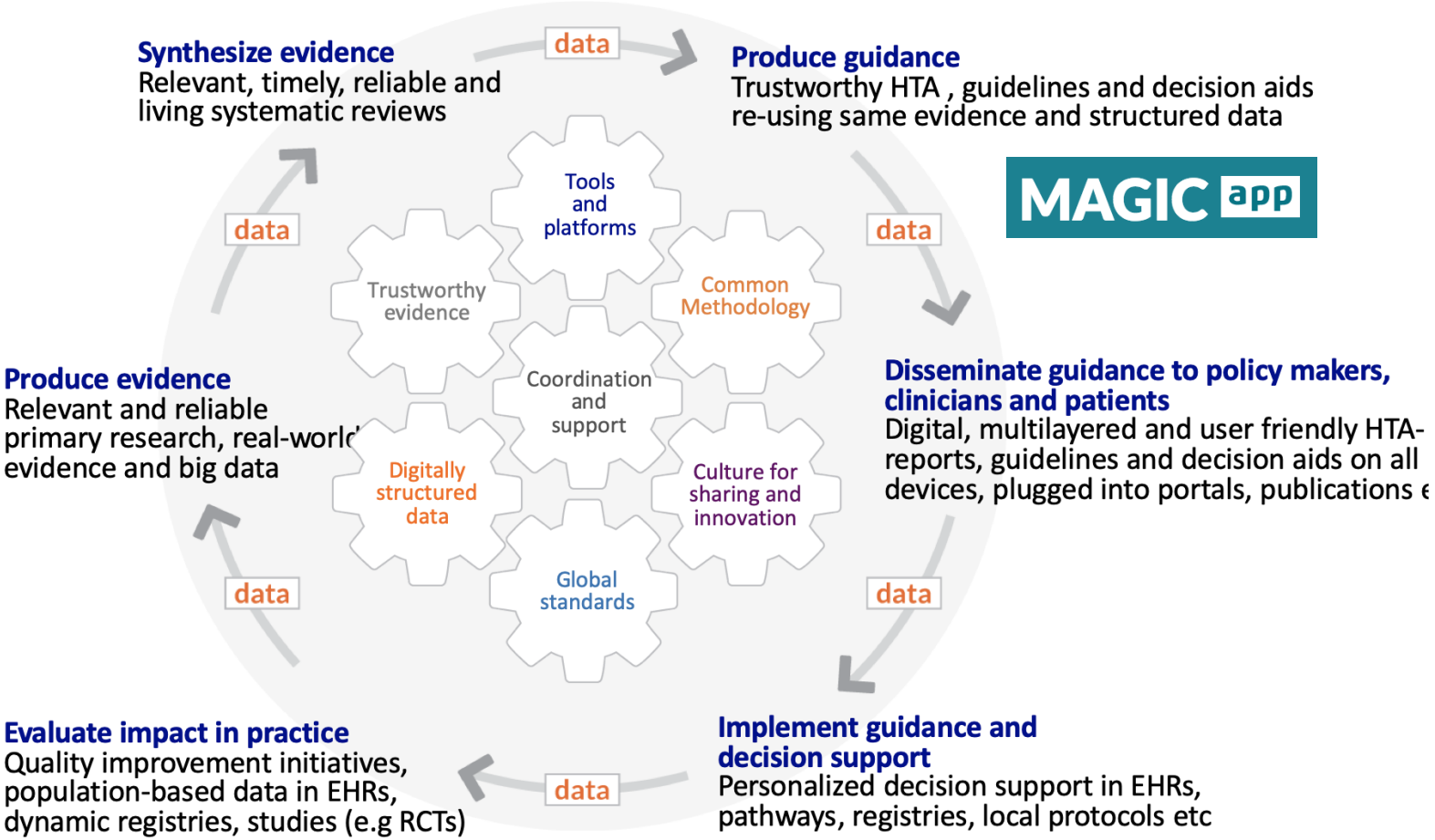
Creating, publishing and dynamically updating trustworthy recommendations, evidence summaries and decision aids in digitally structured formats



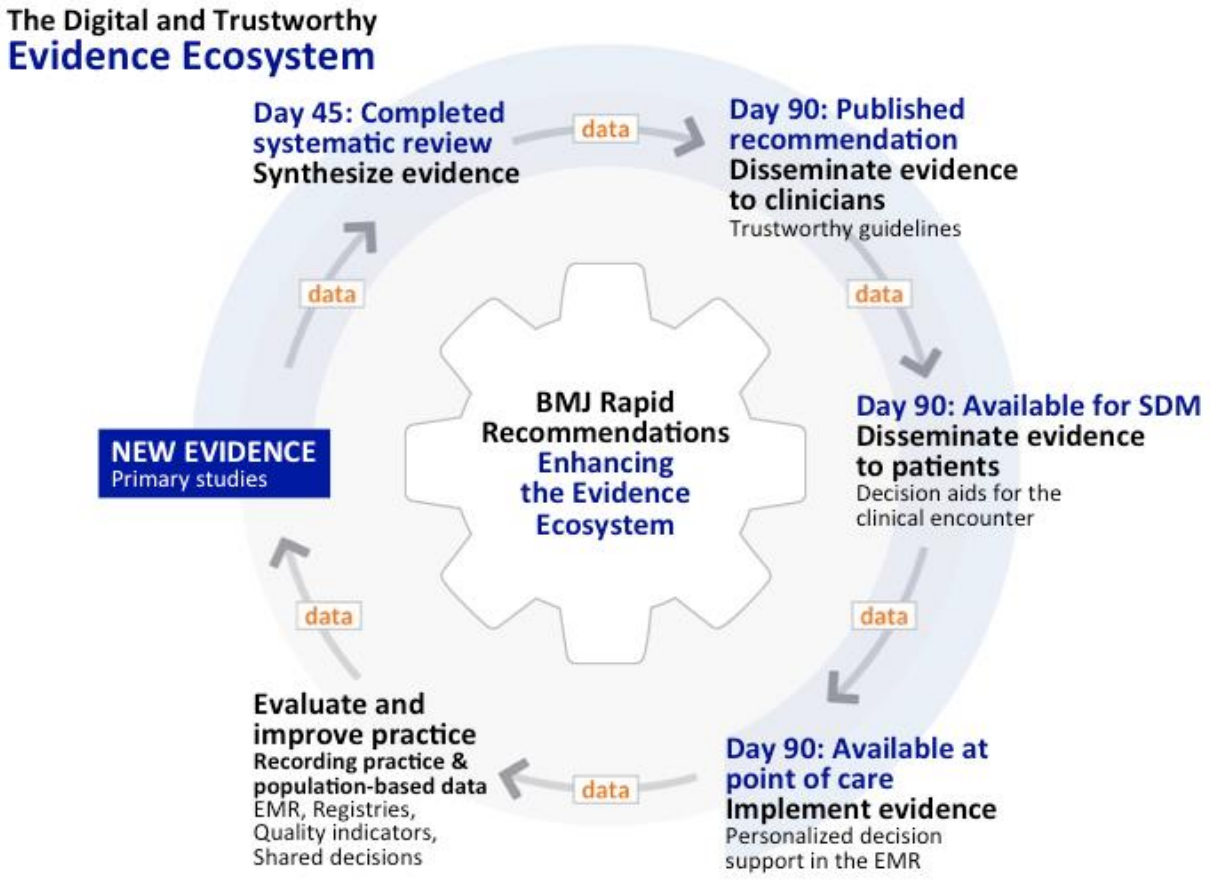
Our vision:
A Digital and Trustworthy Evidence Ecosystem
to increase value and reduce waste in health care



Some hurdles to overcome: Organizations fit for purpose?

How can we rapidly get potentially practice-changing evidence into practice?

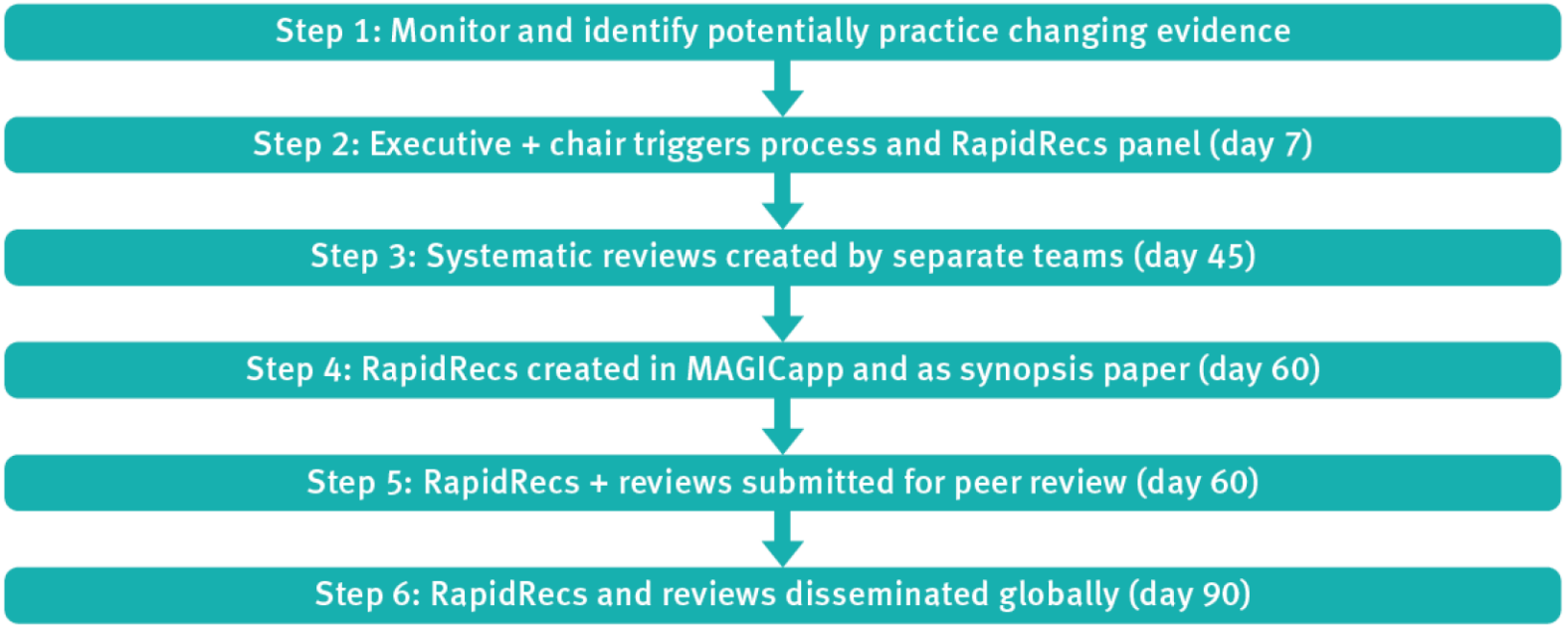
Collaborative network approach, partnering with innovative medical journal?



The BMJ-RapidRecs project: methods and process

- Guideline panel, network of the right people
  - ✓ Trustworthy guideline standards, GRADE
  - ✓ Focus on conflict of interest, patient involvement….
- Linked high quality systematic reviews
  - ✓ effects, prognosis, values and preferences
  - ✓ Separate teams, closely interacting with guideline panel

Rapid Recommendations process step by step (with target times)



Potentially practice-changing evidence for Daniel?

Triggering our first BMJ- RapidRecs, published September 28 2016

- Daniel, 69 years old
- Heart failure, not feeling well..
- Severe aortic stenosis, all set up for open heart surgery in Norway
- Read newspaper, questions if he could have "TAVI"...

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 28, 2016 VOL. 374 NO. 17

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

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ABSTRACT

BACKGROUND

Previous trials have shown that among high-risk patients with aortic stenosis, survival rates are similar with transcatheter aortic-valve replacement (TAVR) and surgical aortic-valve replacement. We evaluated the two procedures in a randomized trial involving intermediate-risk patients.

METHODS

We randomly assigned 2032 intermediate-risk patients with severe aortic stenosis, at 57 centers, to undergo either TAVR or surgical replacement. The primary end point was death from any cause or disabling stroke at 2 years. The primary hypothesis was that TAVR would not be inferior to surgical replacement. Before randomization, patients were entered into one of two cohorts on the basis of clinical and imaging findings; 76.5% of the patients were included in the transfemoral-access cohort and 23.7% in the transthoracic-access cohort.

RESULTS

The rate of death from any cause or disabling stroke was similar in the TAVR group and the surgery group (P=0.001 for noninferiority). At 2 years, the Kaplan–Meier event rates were 19.3% in the TAVR group and 21.1% in the surgery group (hazard ratio in the TAVR group, 0.89; 95% confidence interval [CI], 0.73 to 1.09; P=0.25). In the transfemoral-access cohort, TAVR resulted in a lower rate of death or disabling stroke than surgery (hazard ratio, 0.79; 95% CI, 0.62 to 1.00; P=0.05), whereas in the transthoracic-access cohort, outcomes were similar in the two groups. TAVR resulted in larger aortic-valve areas than did surgery and also resulted in lower rates of acute kidney injury, severe bleeding, and new-onset atrial fibrillation; surgery resulted in fewer major vascular complications and less paravalvular aortic regurgitation.

CONCLUSIONS

In intermediate-risk patients, TAVR was similar to surgical aortic-valve replacement with respect to the primary end point of death or disabling stroke. (Funded by Edwards Life-sciences; PARTNER 2 ClinicalTrials.gov number, NCT01314313.)

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Leon at Columbia University Medical Center, 161 Ft. Washington Ave., 6th Floor, New York, NY 10032, or at mleon@crf.org.

*A complete list of investigators in the Placement of Aortic Transcatheter Valves (PARTNER) 2 trial is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on April 2, 2016, at NEJM.org.

N Engl J Med 2016;374:1609-20.
DOI: 10.1056/NEJMoa1514616

BMJ-RapidRecs for TAVI , let us have a look before you explore it together…*

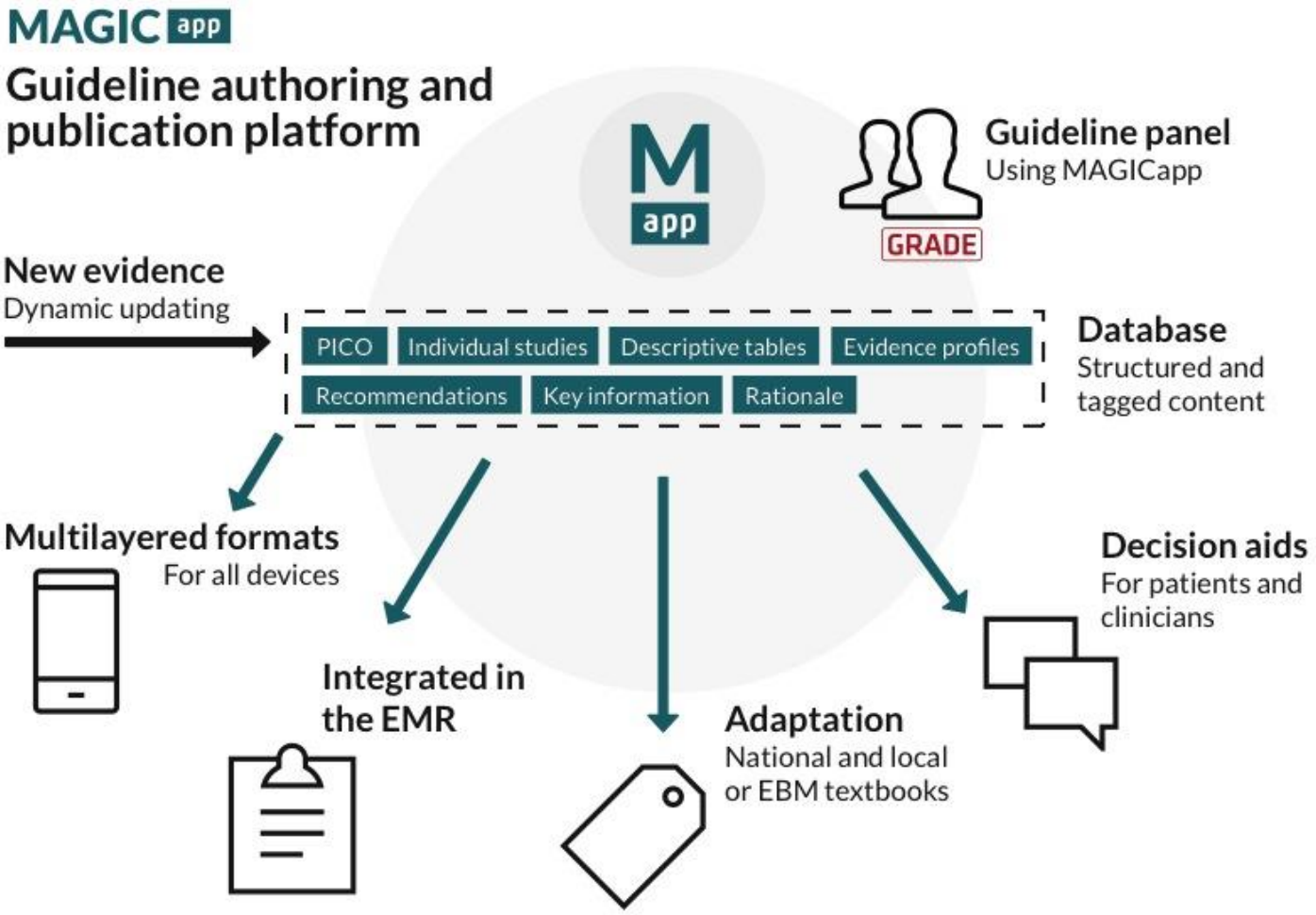
* All papers open access and for you to scrutinize, adapt and use for your purposes

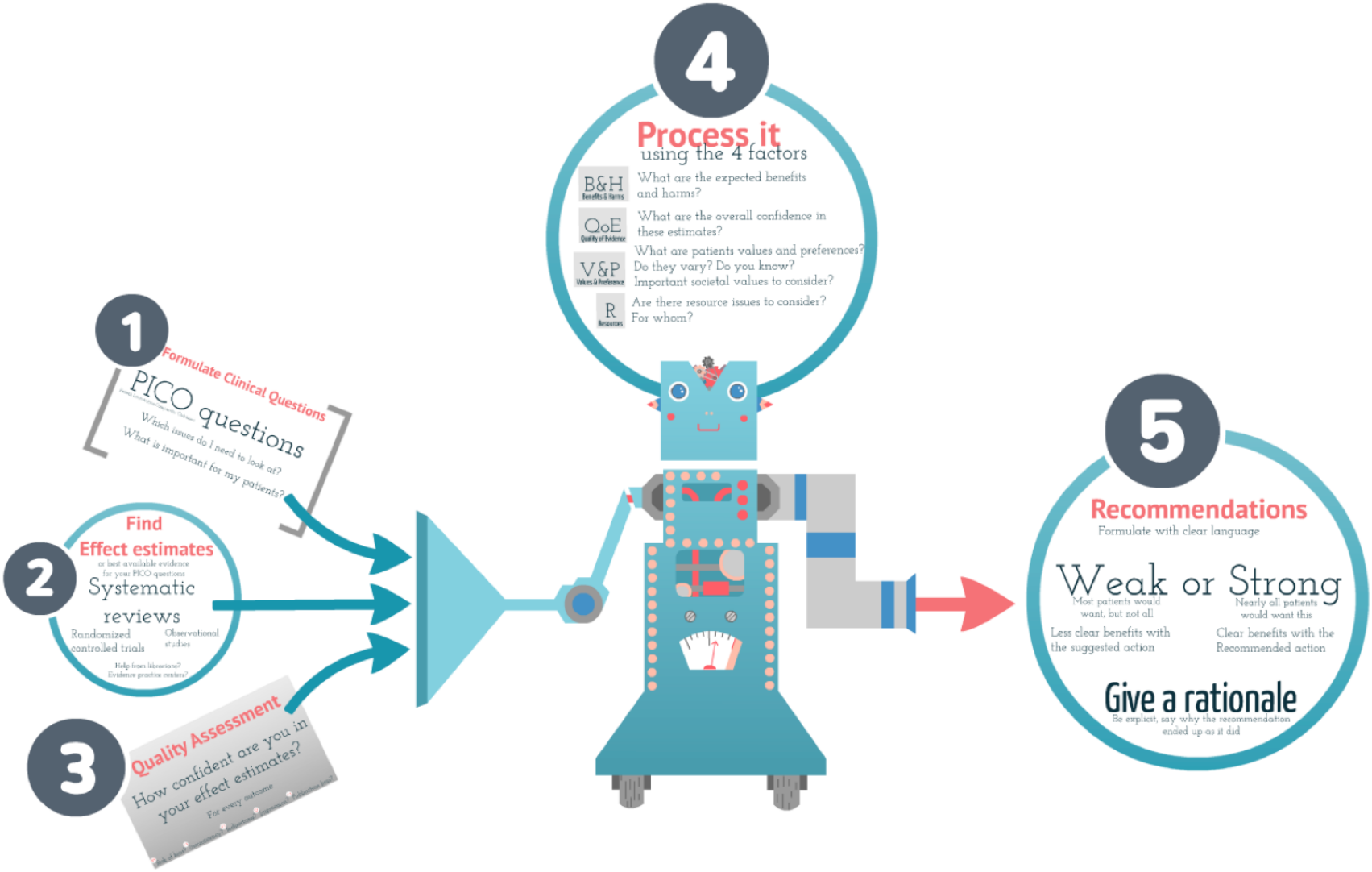
Plenary discussion

- How does this way of displaying evidence and recommendations work for clinicians, you, people?

- How can we further improve MAGICapp?

How to develop and update an evidence summary and a trustworthy recommendation in MAGICapp





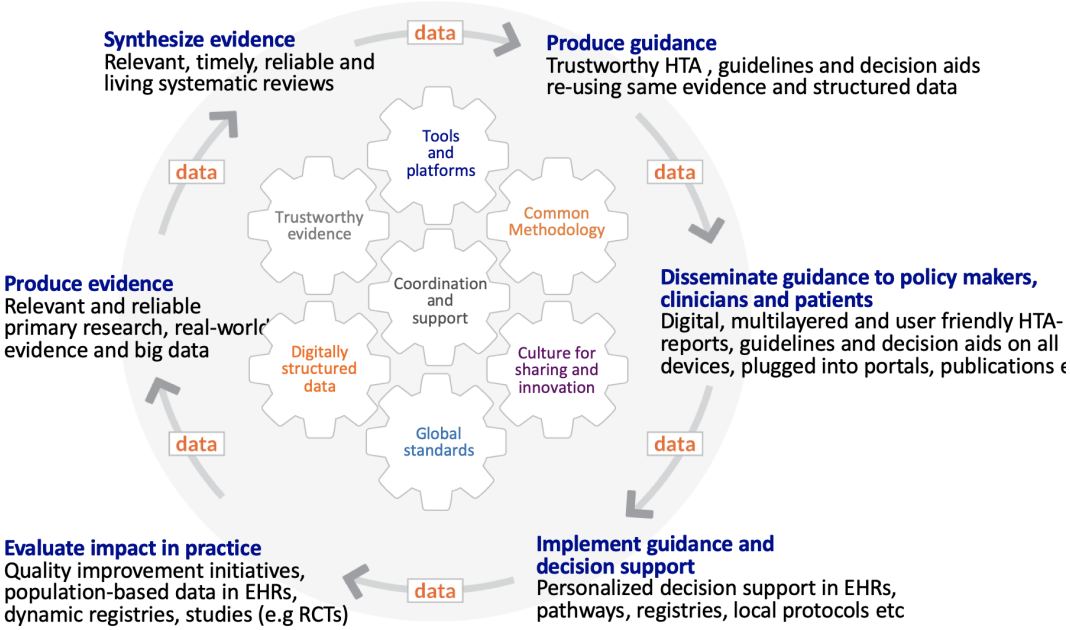
BASICs of making GRADE guidelines

NEWS: Two new trials on TAVI published recently,

We now need to update our living BMJ Rapid Recommendations

Updated SR (6 trials, 6478 patients)
Practice-changing moderate certainty evidence for key outcome:
Long-term aortic valve reintervention TAVI vs SAVR : **RR 2.2 (1.7-2.7)**

2 RCTs at low risk of bias



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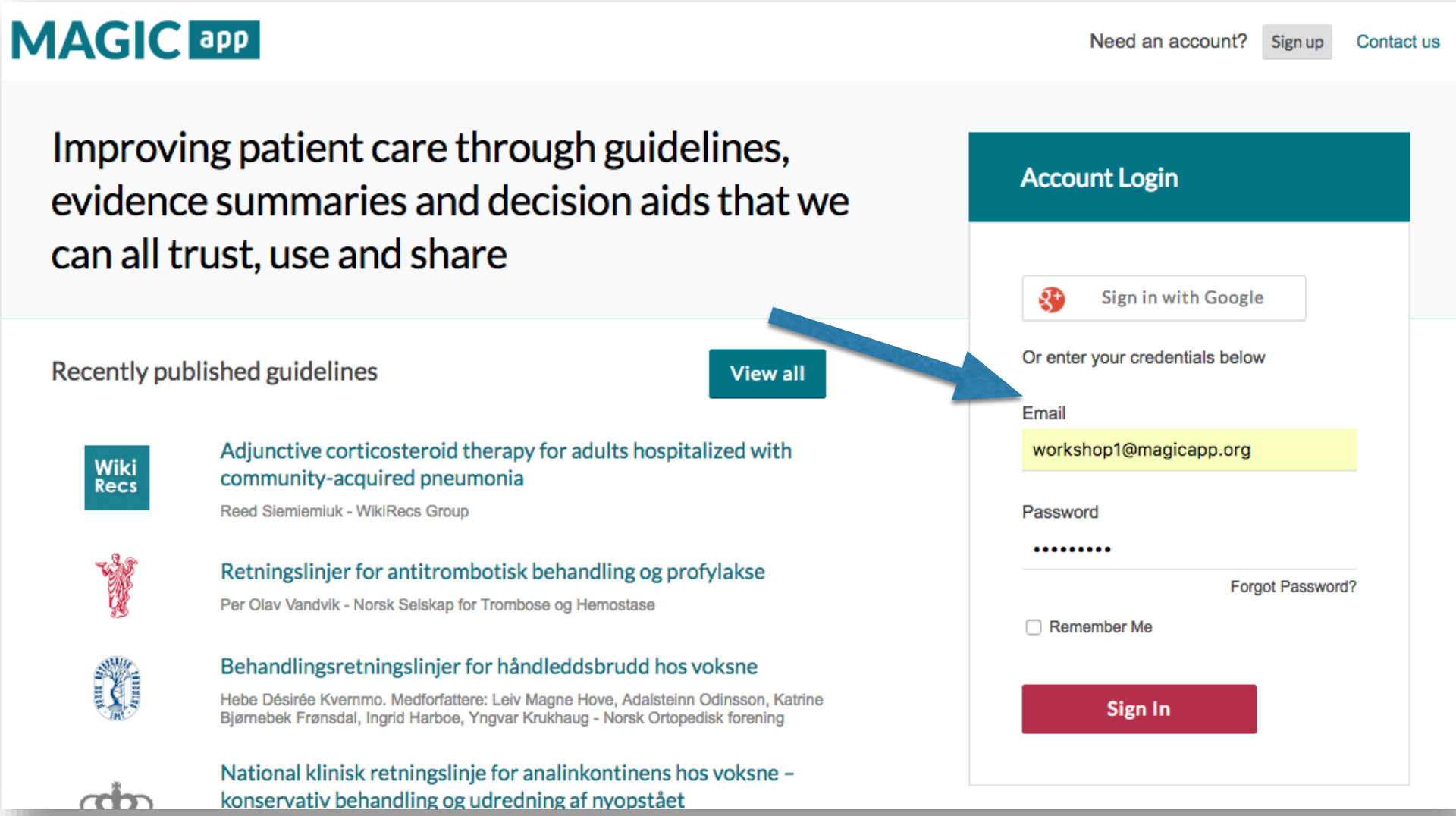

Log in

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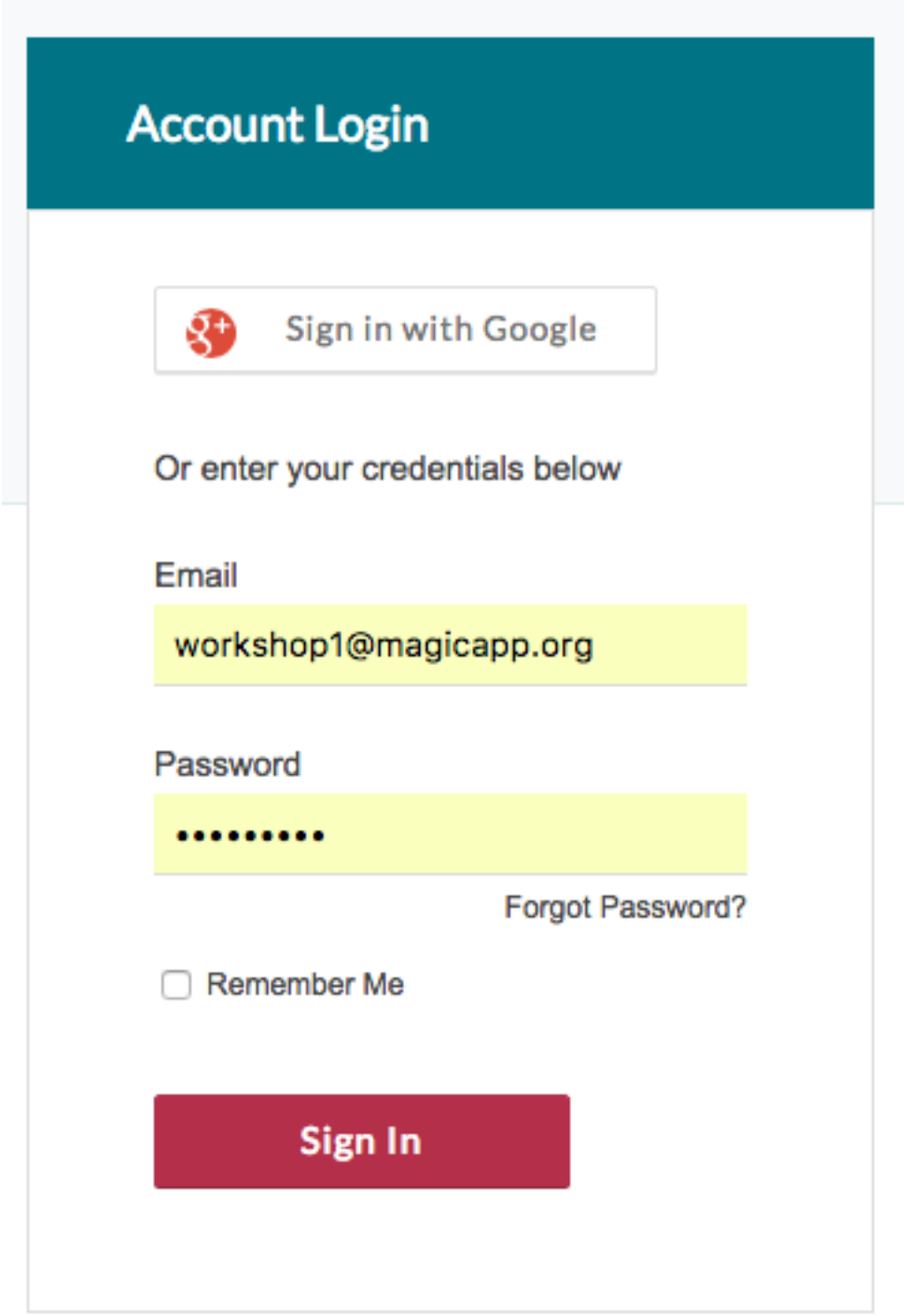

Transfemoral Transcatheter aortic valve insertion (TAVI) vs Surgical aortic valve replacement (SAVR)

Patients 65-75 years with severe symptomatic aortic stenosis who are at low or intermediate perioperative risk

15 Outcomes Summary

Outcome Timeframe	Study results and measurements	Absolute effect estimates SAVR	 Transfemoral TAVI	Certainty in effect estimates (Quality of evidence)	Plain text summary
Mortality, age adjusted 2 years	Hazard Ratio 0.79 (CI 95% 0.66 - 0.94) Based on data from 2576 patients in 3 studies Follow up: 2 years.	**92** per 1000	**73** per 1000 Difference: 19 fewer per 1000 (CI 95% 30 fewer - 5 fewer)	**Moderate** Due to serious imprecision	TAVI probably reduces the risk of death.
Stroke (includes perioperative events) 2 years	Relative risk 0.8 (CI 95% 0.63 - 1.01) Based on data from 2576 patients in 3 studies Follow up: 2 years.	**70** per 1000	**56** per 1000 Difference: 14 fewer per 1000 (CI 95% 1 more - 26 fewer)	**Moderate** Due to serious imprecision	TAVI probably reduces the risk of stroke.
Aortic valve reintervention 2 years	Relative risk 1.5 (CI 95% 1.2 - 1.8) Based on data from 3058 patients in 3 studies Follow up: 2 years.	**3** per 1000	**5** per 1000 Difference: 2 more per 1000 (CI 95% 1 more - 2 more)	**High**	TAVI probably increases the risk of aortic valve reintervention.
Aortic valve reintervention - long term 10 years	Relative risk 1.5 (CI 95% 1.2 - 1.8) Based on data from 3058 patients in 3 studies Follow up: 2 years.	**61** per 1000	**92** per 1000 Difference: 31 more per 1000 (CI 95% 12 more - 49 more)	**High**	TAVI may increase need for aortic reintervention due to structural valve deterioration

Reference | Evidence | Recommendations

Search for recommendations

1 TAVI versus SAVR for patients with severe symptomatic aortic stenosis at low to intermediate perioperative risk

View Section Text | ▼ Add PICO

1.1

▼ Options

POPULATION	INTERVENTION	COMPARATOR
Patients 65-75 years with severe symptomatic aortic stenosis who are at low or intermediate perioperative risk	Transfemoral Transcatheter aortic valve insertion (TAVI)	Surgical aortic valve replacement (SAVR)

OUTCOMES

Under development | Mortality, age adjusted | Stroke (includes perioperative events) | Aortic valve reintervention | Aortic valve reintervention - long term | Permanent pacemaker insertion | Life threatening bleeding | Atrial fibrillation (includes transient postoperative) | Moderate/severe heart failure symptoms (NYHA ≥III) | Myocardial infarction | Acute kidney injury (includes transient events) | something | Health-related quality of life | Length of index hospitalization | Pain | Recovery time

VIEW MORE DETAILS

Literature search | **Evidence profile** | Summary | References | PICO codes | Evidence Matrix

Outcome Timeframe	Study results and measurements	Absolute effect estimates SAVR	 Transfemoral TAVI	Certainty in effect estimates (Quality of evidence)	Plain text summary	+ Outcome
Dichotomous Outcome						
Mortality, age adjusted 2 years	Hazard Ratio 0.79 (CI 95% 0.66 - 0.94) Based on data from 2576 patients in 3 studies Follow up: 2 years.	**92** per 1000	**73** per 1000 Difference: 19 fewer per 1000 (CI 95% 30 fewer - 5 fewer)	**Moderate** Due to serious imprecision	TAVI probably reduces the risk of death.	Development
Stroke (includes perioperative events) 2 years	Relative risk 0.8 (CI 95% 0.63 - 1.01) Based on data from 2576 patients in 3 studies Follow up: 2 years.	**70** per 1000	**56** per 1000 Difference: 14 fewer per 1000 (CI 95% 1 more - 26 fewer)	**Moderate** Due to serious imprecision	TAVI probably reduces the risk of stroke.	Development
Aortic valve reintervention 2 years	Relative risk 3.25 (CI 95% 1.29 - 8.14) Based on data from 3058 patients in 3 studies Follow up: 2 years.	**3** per 1000	**10** per 1000 Difference: 7 more per 1000 (CI 95% 1 more - 21 more)	**High**	TAVI probably increases the risk of aortic valve reintervention.	Development
Aortic valve reintervention - long term 10 years	Relative risk 3.25 (CI 95% 1.29 - 8.14) Based on data from 3058 patients in 3 studies Follow up: 2 years.	**61** per 1000	**198** per 1000 Difference: 137 more per 1000 (CI 95% 18 more - 436 more)	**High**	TAVI may increase need for aortic reintervention due to structural valve deterioration	Development

Aortic valve reintervention 2 years	Relative risk 3.25 (CI 95% 1.29 - 8.14) Based on data from 3058 patients in 3 studies Follow up: 2 years.	**3** per 1000	**10** per 1000 Difference: 7 more per 1000 (CI 95% 1 more - 21 more)	**High**	TAVI probably increases the risk of aortic valve reintervention.

Development

Outcome | Save | Close | Certainty in effect estimates

Changed fields | Undo all changes

1 Relative effect of intervention vs. comparator

SOURCE OF EVIDENCE

Systematic review/ meta-

Systematic review:
Studies: 0
Add and show evidence

DATA FROM INCLUDED STUDIES Autofill from added studies

3,058 patients in 3 Studies.

Follow up (in studies)
2 years

Randomized controlled

RELATIVE EFFECT (FROM STUDIES)

Relative risk 3.25

CI 95% (1.29 - 8.14)

2 Baseline risk (result of the outcome in the comparison group): SAVR

SOURCE OF EVIDENCE

Control arm of reference

Studies: 0
Add and show evidence

BASELINE RISK/ EFFECT WITH COMPARATOR

3

per 1000

3 Expected difference and best estimate of effect with intervention: Transfemoral TAVI

Calculate estimates

CALCULATED ESTIMATE WITH INTERVENTION

10

per 100

ESTIMATED ABSOLUTE DIFFERENCE OF INTERVENTION VS. COMPARATOR (CALCULATED)

Difference: 7 more per 1000

CI 95% (1 more - 21 more)

Updating the recommendation: What would the panel recommend be for patients 65-75 years old? (screenshot current)

Patients aged 65 to < 75 years and eligible for transfemoral TAVI or SAVR

Weak recommendation

We suggest SAVR rather than TAVI

This recommendation considers benefits and harms of treatment alternatives with a particular weight on the uncertainty regarding the long-term durability of TAVI valves for those under 75. The age thresholds reflect the key issue, which is expected life span; clinicians need to also consider other factors such as comorbidity.

VIEW MORE DETAILS

Aortic valve reintervention - long term 10 years	Relative risk 3.25 (CI 95% 1.29 - 8.14) Based on data from 3,058 patients in 3 studies. (Randomized controlled) Follow up 2 years	**61** per 1000 — **198** per 1000 Difference: **137 more** per 1000 (CI 95% 436 more - 18 more)	**Very Low** Due to inconsistency, indirectness and imprecision	TAVI may increase need for aortic reintervention due to structural valve deterioration

Updating the recommendation: What would the panel recommend be for patients 65-75 years old? (screenshot new)

Patients aged 65 to < 75 years and eligible for transfemoral TAVI or SAVR

Weak recommendation

We suggest SAVR rather than TAVI

This recommendation considers benefits and harms of treatment alternatives with a particular weight on the uncertainty regarding the long-term durability of TAVI valves for those under 75. The age thresholds reflect the key issue, which is expected life span; clinicians need to also consider other factors such as comorbidity.

Aortic valve reintervention 2 years	Relative risk 1.5 (CI 95% 1.2 - 1.8) Based on data from 3058 patients in 3 studies Follow up: 2 years.	**3** per 1000 vs **5** per 1000 Difference: 2 more per 1000 (CI 95% 1 more - 2 more)	**High**	TAVI probably increases the risk of aortic valve reintervention.
Aortic valve reintervention - long term 10 years	Relative risk 1.5 (CI 95% 1.2 - 1.8) Based on data from 3058 patients in 3 studies Follow up: 2 years.	**61** per 1000 vs **92** per 1000 Difference: 31 more per 1000 (CI 95% 12 more - 49 more)	**High**	TAVI may increase need for aortic reintervention due to structural valve deterioration

Patients aged 65 to < 75 years and eligible fo

Weak recommendation · Set ▼

Benefits outweigh harms for the majority, but not for every
Learn more

We suggest SAVR rather than TAVI

This recommendation considers benefits and harms of tre
uncertainty regarding the long-term durability of TAVI valv
issue, which is expected life span; clinicians need to also

VIEW LESS D

esearch evidence | **Key info** | Rationale | Pra

Benefits and harms

Benefits of TAVI include reduced deaths, strokes, ma
hospital over 2 year follow-up. Harms include increa
aortic reinterventions in the short term over 2 year fo
to be reduced compared to SAVR biological valves v
reinterventions within the first 10 years.

Quality of evidence

Benefits and harms

▼ Small net benefit, or little difference between alternatives

Benefits of TAVI include reduced deaths, strokes, major bleeds, new onset atrial fibrillations and days in hospital over 2 year follow-up. Harms include increased heart failure, need for pacemaker insertions and aortic reinterventions in the short term over 2 year follow-up. Long term durability of TAVI valves is likely to be reduced compared to SAVR biological valves which suggests increased need for aortic valve reinterventions within the first 10 years.

Quality of evidence

▼ Moderate

For transfemoral TAVI versus SAVR, high certainty for decrease in acute kidney injury, bleeding, atrial fibrillation, and hospital length of stay; moderate certainty for decrease in mortality, stroke, recovery time and increase in short term (2 year) aortic valve reintervention, permanent pacemaker, and moderate/severe heart failure; low certainty for decrease in postoperative pain and very low certainty for increase in long term (10 year) aortic valve reintervention.

Preference and values

▼ Substantial variability is expected or uncertain

Patients are likely to place different value on benefits and harms associated with TAVI. Patients aged 75 or younger - with a life expectancy well beyond 10 years - are likely to place a particularly high value on avoiding need for a second aortic valve replacement and are likely to choose surgery. Patients who place a high value on avoiding initial open heart surgery and are willing to accept an increased risk for aortic valve reintervention are likely to choose TAVI. A systematic review of values and preferences provided limited evidence to inform our judgements. One study showed that patients have high risk willingness for mortality in exchange for perfect health (someone of equal age without aortic stenosis) [14].

Resources and other considerations

▼ Important issues, or potential issues not investigated

TAVI should be considered only in centres with sufficient expertise utilizing specialized TAVI teams consisting of interventional cardiologists, general cardiologists, cardiac surgeons,and appropriate nursing and adjunctive personnel. Cost-effectiveness of SAVR versus TAVI in low to intermediate risk patients remains uncertain in the absence of available cost-benefit analyses.

Plenary discussion

- Digital authoring of evidence summaries, recommendations and decision aids: Feasible or too big of a leap for you?
- How could MAGICapp work for you, in creating, publishing and updating evidence summaries for systematic reviews?
- Want to be part of the Evidence Ecosystem?

In summary

- MAGICapp allows creation, dissemination and dynamic updating of evidence summaries, recommendations and decision aids

- Within an emerging evidence ecosystem, the BMJ-RapidRecs provide a model for rapidly responding to potentially practice-changing evidence through systematic reviews and trustworthy recommendations: Organizations fit for purpose?

- Authoring, publishing and updating of evidence summaries for systematic reviews an emerging opportunity: Will Cochrane and other review groups benefit from our services?

Per Olav Vandvik, MD PhD

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PLUGGED-IN, technology and collaboration

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