BMJ Rapidrecs for Transcatheter aortic valve implantation versus surgical aortic valve replacement for severe aortic stenosis in low-intermediate risk patients

Main editor
Per Olav Vandvik, on behalf of the RapidRecs panel

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The BMJ-RapidRecs project represents a collaboration between MAGIC and The BMJ. In response to potentially practice-changing evidence a guideline panel creates recommendations and all underlying content in MAGICapp, informed by linked systematic reviews. The BMJ publishes the recommendations and systematic reviews in their journals.

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Disclaimer
These recommendations are made according to standards for trustworthy guidelines and targets an international audience with an individual patient perspective. Adaptation to specific countries or contexts should be considered, including the cost-effectiveness of interventions.
Sections

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Summary of recommendations

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

Patients aged 85 years or older and eligible for transfemoral TAVI or SAVR

**Strong Recommendation**

We recommend transfemoral TAVI rather than SAVR.

Patients aged 75 to < 85 years and eligible for transfemoral TAVI or SAVR

**Weak Recommendation**

We suggest transfemoral TAVI rather than SAVR

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

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.*

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

**Strong Recommendation**

We recommend SAVR rather than TAVI

*This recommendation considers benefits and harms of treatment alternatives with a particular weight on the lacking evidence on use of TAVR in patients below 65 years of age and the uncertainty regarding the long-term durability of TAVI valves.*

Patients not eligible for transfemoral approach but eligible for transapical approach or SAVR

**Strong Recommendation**

We recommend SAVR rather than TAVI with a transapical approach
2 - Flow chart of management alternatives for severe aortic stenosis

- Severe symptomatic AS
  - Life expectancy >1 year if AVR performed
    - No: Palliative therapy*
    - Yes: Bioprosthetic AVR planned
      - No: Surgical AVR possible
      - Yes: Transfemoral AVR approach possible
        - Low to intermediate surgical risk
        - High or prohibitive surgical risk
          - Transfemoral TAVI*
          - SAVR over transapical TAVI
            - Strong recommendation

- Mechanical SAVR*

3 - Background and methods for BMJ-Rapidrecs
1 - TAVI versus SAVR for patients with severe symptomatic aortic stenosis at low to intermediate perioperative risk

Please see the BMJ RapidRecs publication for details about the RapidRecs panel, their affiliations and declarations of interest. [4]

Background for these recommendations:
Symptomatic severe aortic stenosis - affecting approximately 3% of people over the age of 75 – results in symptoms of heart failure, reduced quality of life and a in the absence of prompt aortic valve replacement, a 50% mortality rate at 2 years. There is no effective medical therapy for severe aortic stenosis so palliative care is the only option for those in whom aortic valve replacement is not feasible. Previous evidence addressing TAVI vs SAVR focused on patients with severe aortic stenosis at high risk of peri-operative death suggested that TAVI was beneficial for such patients. [5] TAVI is now frequently used in patients with a prohibitive surgical risk and as an alternative to SAVR for patients with severe aortic stenosis at high risk for perioperative death. This, in turn, has led to interest in use of TAVI in patients at low to intermediate perioperative risk.

The Partner 2A trial published in April 2016 holds the potential to change practice as it suggests a benefit to patients at low to intermediate perioperative risk. [1][2] We - representing the Rapidrecs group – have created systematic reviews for effect- estimates, prognostic risk estimates and values and preferences followed by trustworthy recommendations, evidence summaries and decision aids in order to provide clinicians and patients with guidance about use of TAVI in patients at low to intermediate perioperative risk. The systematic reviews and a short synopsis publication are published in the BMJ. [4] Below you will find recommendations, full evidence summaries (GRADE SoF-tables), practical information and decision aids for use in the clinical encounter. A detailed account of the background, methods and processes for BMJ Rapidrecs is available through the Background and methods section (below the recommendations) and through the BMJ Rapidrecs publication. [4]

**Patients aged 85 years or older and eligible for transfemoral TAVI or SAVR**

**Strong Recommendation**
We recommend transfemoral TAVI rather than SAVR.

**Practical Info**

**Calculation of perioperative risk:** Patients should be assessed regarding their postoperative risk by using a validated risk score such as the STS-PROM online calculator [http://riskcalc.sts.org/stswebriskcalc/#/](http://riskcalc.sts.org/stswebriskcalc/#/). The risk assessment, which includes many questions regarding cardiac investigations, is performed by the multi-professional heart team. This risk score serves as a starting point for risk assessment. Other considerations, not included in this score, include frailty, severe and circumferential calcification of the ascending aorta (“porcelain aorta”), non-cardiovascular comorbid conditions, cognitive impairment, physical functioning, life expectancy and patient values and expectations.

**Valve durability:** With TAVI, the need for aortic valve reintervention at 2-year follow-up with TAVI, is low but higher relative to SAVR (1.5% vs. 0.5%). There is insufficient data at this time regarding longer term durability of the TAVI devices. Preliminary evidence suggests that long term durability (10 years and longer) may be an issue: in the only long-term followup study reported to date, up to 50% of 378 patients undergoing TAVI with a first generation balloon-expandable device showed signs of degeneration (at least moderate or more aortic stenosis or regurgitation) at 8 years. However, large uncertainty remains. If the relative effect over two years persists long-term, using best estimates of the need for aortic valve reintervention in 8% of patients post SAVR at 10 years, up to 20-30% of patients post TAVI may require repeat intervention in the long term.

This issue should be discussed with patients considering TAVI with special attention paid to future life expectancy of each patient. Although tables of life expectancy for patients who have reached their current age may overestimate life expectancy in patients with aortic stenosis, this information can be used as a starting point (https://www.ssa.gov/OACT/population/longevity.html). Patients who have a life expectancy of 10 or more years at time of their initial procedure who want to avoid repeat valve intervention will be likely to prefer SAVR. Repeat TAVIs (valve in valve procedures) are being performed although experience with this approach remains limited. This may mitigate some patients' concerns about unknown durability of their initial TAVI particularly if they place a high value on avoiding open heart surgery. Finally, the limited durability data that is available is in patients receiving first generation TAVI devices. It is possible 2nd generation devices will have greater durability; this remains to be seen.

**Type of TAVI device:** Devices used in trials include the balloon-expandable Edwards SAPIEN-XT and the self-expanding Medtronic
CoreValve. Due to its delivery catheter, the self-expanding CoreValve can be implanted by transfemoral, direct aortic, subclavian/axillar and trans-carotid, but not via transapical approach. The balloon-expandable SAPIEN-XT can be implanted by any access route; the only difference is that for the transapical approach, the delivery system is much shorter and has a bigger outer-diameter. Logically, due to the “antegrade” nature of the transapical access, the bioprosthesis is mounted upside-down as compared for the “retrograde” accesses. The balloon-expandable has merits in terms of less need for permanent pacemaker implantation and less paravalvular leakage.

Transfemoral TAVI versus non-transfemoral approaches: Non-transfemoral approaches, in most cases the transapical route, have been associated with an increased risk of deaths, strokes and acute kidney injury relative to SAVR; therefore, we provide a strong recommendation for SAVR rather than non-transfemoral TAVI. The transfemoral approach is the least invasive approach, and many centres perform TAVI as a fully-percutaneous procedure using local anesthesia along with conscious sedation. Patients undergoing transfemoral TAVI spend their acute recovery period in the coronary care unit. Transfemoral TAVI patients experience limited post-procedural pain, allowing early ambulation and a shorter length of stay in the hospital. The transfemoral approach has therefore become the access of choice for TAVI centres following a “minimalist” invasive strategy.

Key Info

<table>
<thead>
<tr>
<th>Benefits and harms</th>
<th>Substantial net benefits of the recommended alternative</th>
</tr>
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<tbody>
<tr>
<td>Benefits of transfemoral TAVI include reduced deaths, strokes, major bleeds, new onset atrial fibrillation, acute kidney injury, and fewer days in hospital. Harms include increased heart failure, need for pacemaker insertions and need for aortic valve reinterventions.</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Quality of evidence</th>
<th>Moderate</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Preference and values</th>
<th>No substantial variability expected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients are likely to place different value on benefits and harms associated with TAVI. Patients aged 85 or above are likely to place a high value on avoiding open heart surgery and benefits of TAVI on mortality, stroke, atrial fibrillation and life-threatening bleeds. A systematic review of values and preferences provided limited evidence to inform our judgments. One study showed that patients are ready to trade off longevity in exchange for quality of life (someone of equal age without aortic stenosis) [14]. Experience in shared decision-making suggests that many patients will wish to avoid a surgical procedure if the nonsurgical procedure, such as TAVI, provides similar or superior short-term results, even with uncertainty about long term durability.</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Resources and other considerations</th>
<th>Important issues, or potential issues not investigated</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAVI should be considered only in centres with established heart team consisting of valve disease experts, interventional cardiologists, cardiac surgeons, cardiovascular imaging specialists, cardiac anesthetists, and appropriate nursing and adjunctive personnel. TAVI is likely to represent a cost-effective alternative to SAVR in patients at low to moderate perioperative risk but we have not identified any cost-benefit analyses to support this assumption.</td>
<td></td>
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</tbody>
</table>

Rationale

We issue a strong recommendation for transfemoral TAVI in patients aged 85 or above because we believe that the desirable consequences clearly outweigh the undesirable consequences when compared to SAVR. The uncertain long term durability of TAVI - which suggests a need for reintervention in a substantial proportion of patients within the first 10 years - does not constitute a major concern given limited expected life expectancy in this population.
Clinical Question/ PICO

Population: Patients above 85 years with severe symptomatic aortic stenosis, at low or intermediate perioperative risk
Intervention: Transfemoral Transcatheter aortic valve insertion (TAVI)
 Comparator: Surgical aortic valve replacement

Summary
Comments to the evidence profile:
- Effect-estimates come from a linked systematic review of trials comparing TAVI and SAVR, except for pain and recovery time (not reported in trials) which come from two observational studies [15][16].
- Baseline risk estimates come from linked systematic reviews of observational studies (for mortality, stroke, long term aortic valve reintervention, atrial fibrillation) and trials (for the other outcomes). Baseline risks are age-stratified only for mortality in those above 85 years old.
- Aortic valve reintervention long term (at 10 years) was not reported in observational studies identified in the systematic review. Studies report structural valve deterioration which we used as an intermediate outcome reflecting need for aortic valve reintervention. Therefore we rated down for very serious indirectness both for baseline risk and for effect-estimates, the latter coming from trials reporting short term aortic valve reintervention. We also rated down for imprecision, resulting in very low certainty in the absolute effect estimates.

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality - age adjusted 2 years</td>
<td>Hazard Ratio 0.79 (CI 95% 0.66 - 0.94) Based on data from 2,576 patients in 3 studies. (Randomized controlled) Follow up 2 years</td>
<td><strong>242</strong> per 1000 <strong>197</strong> per 1000</td>
<td>Moderate Due to serious imprecision</td>
<td>TAVI probably reduces the risk of death.</td>
</tr>
<tr>
<td>Stroke (includes perioperative events)</td>
<td>Relative risk 0.8 (CI 95% 0.63 - 1.01) Based on data from 2,576 patients in 3 studies. (Randomized controlled) Follow up 2 years</td>
<td><strong>99</strong> per 1000 <strong>79</strong> per 1000</td>
<td>Moderate Due to serious imprecision</td>
<td>TAVI probably reduces the risk of stroke.</td>
</tr>
<tr>
<td>Aortic valve reintervention - short term 2 years</td>
<td>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</td>
<td><strong>3</strong> per 1000 <strong>10</strong> per 1000</td>
<td>Moderate Due to borderline risk of bias and imprecision</td>
<td>TAVI probably increases the risk of aortic valve reintervention.</td>
</tr>
<tr>
<td>Event</td>
<td>Relative Risk</td>
<td>CI 95%</td>
<td>Patients</td>
<td>Studies</td>
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<td>---------</td>
</tr>
<tr>
<td>Aortic valve reintervention - long term 10 years</td>
<td>3.25</td>
<td>1.29 - 8.14</td>
<td>3,058</td>
<td>3</td>
</tr>
<tr>
<td>Permanent pacemaker insertion 2 years</td>
<td>2.46</td>
<td>1.17 - 5.15</td>
<td>3,128</td>
<td>4</td>
</tr>
<tr>
<td>Life threatening bleeding 2 years</td>
<td>0.39</td>
<td>0.29 - 0.54</td>
<td>3,128</td>
<td>3</td>
</tr>
<tr>
<td>Atrial fibrillation (includes transient postoperative) 2 years</td>
<td>0.43</td>
<td>0.35 - 0.52</td>
<td>3,058</td>
<td>3</td>
</tr>
<tr>
<td>Moderate/ severe heart failure symptoms (NYHA ≥III) 2 years</td>
<td>1.29</td>
<td>1.08 - 1.55</td>
<td>2,146</td>
<td>4</td>
</tr>
<tr>
<td>Myocardial infarction 2 years</td>
<td>0.87</td>
<td>0.59 - 1.29</td>
<td>3,128</td>
<td>4</td>
</tr>
<tr>
<td>Acute kidney injury (includes)</td>
<td>0.38</td>
<td>0.27 - 0.54</td>
<td>2,576</td>
<td>2</td>
</tr>
<tr>
<td>Practical issues</td>
<td>Surgical aortic valve replacement</td>
<td>Transfemoral Transcatheter aortic valve insertion (TAVI)</td>
<td>Both</td>
<td></td>
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</tr>
<tr>
<td>Medication routine</td>
<td>- Antiplatelet or anticoagulation medication after procedure, as needed</td>
<td>- Pain medication after procedure, as needed</td>
<td>- Resume medications for concomitant cardiac conditions, as needed</td>
<td></td>
</tr>
</tbody>
</table>
- Tests and visits
  - Dental care may be needed before the intervention, and is not recommended for 3-6 months afterwards
  - Post operative visits are typically within 1-2 months, and then yearly to check that the valve is working

- Procedure and device
  - The doctor will make a small puncture (opening) in the groin for the catheter (long, thin tube), which carries the new valve into the heart, where it is put inside the unhealthy valve
  - The new heart valve is made of natural tissue (from the heart of a cow or pig) attached to a flexible, metallic mesh frame
  - This procedure allows one to be awake (conscious sedation)
  - The procedure takes under 2 hours
  - TAVI valves are durable for 3 to 5 years but longer term durability data is not yet available
  - The doctors will make a cut in the middle of the chest, divide the breastbone, and surgically replace the unhealthy heart valve
  - The new heart valve is made of tissue (from the heart of a cow or pig)
  - The heart may be stopped and supported by a machine
  - One is asleep during the procedure (general anesthesia)
  - The procedure takes 3-5 hours
  - SAVR valves are durable for 10 to 20 years with long term data in large numbers of patients

- Recovery and adaptation
  - After the procedure, in-hospital stay will usually last 2-5 days
  - It could take about a month to recover
  - Pain from the insertion site usually resolves within a few weeks
  - After the procedure, in-hospital stay will usually last 5-10 days
  - It could take about 2-3 months to recover
  - About 1 patient in 4 report persisting pain in the sternum at after 1 year, with 1 in 10 with more serious pain

- Coordination of care
  - It is useful to have someone to help with activities during recovery as one regains their strength

- Adverse effects, interactions and antidote
  - Long-term effects of TAVI are less well known than surgery
  - See summary of findings
  - Additional adverse effects include endocarditis, a rare (risk less than 1% per year) but serious condition of the heart, requiring antibiotics and hospitalization
  - Some symptoms can remain after the procedure
  - Another procedure may be needed if this one is unsuccessful
  - Cognitive decline might occur after the procedure but how often is not clear
Physical well-being
- Some patients report less appetite and constipation as they recover
- Some patients report poor sleep as they recover

Emotional well-being
- Data on emotional well-being after TAVI is scant
- Some patients report mood swings, irritability, anxiety, and depression as they recover, although these symptoms may also have been present before surgery

Costs and access
- Travel costs if intervention happens far from home
- Insurance plans may or may not cover some or all aspects of the procedure

Food and drinks
- Dietary restrictions apply if blood thinners are needed

Exercise and activities
- Need to avoid strenuous activity during recovery
- Rehabilitation may help recovery
- If blood thinners are needed, may limit activities with high risk injury

Work and education
- May be 2-6 weeks
- May be 6-8 weeks
- Time until return to work depends on speed of recovery

Travel and driving
- Driving may be limited during recovery
- Driving is limited for 6 weeks until the sternal bone heals

Details about studies used and certainty down- and upgrading

Mortality - age adjusted
**Intervention:** Systematic review [3]
**Baseline/comparator:** Systematic review [5]
**Risk of bias:** No serious Robust to worst-plausible but not worst-case lost to follow-up sensitivity analysis
**Inconsistency:** No serious We found subgroup analyses of transfemoral versus transapical approach to be credible so did not rate down for inconsistency. I²=0% within each subgroup.
<table>
<thead>
<tr>
<th>Event</th>
<th>Intervention</th>
<th>Baseline/comparator</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
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<th>Imprecision</th>
<th>Publication bias</th>
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<tr>
<td><strong>Aortic valve reintervention - short term</strong></td>
<td>Systematic review</td>
<td>Control arm of reference</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
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<td>Systematic review</td>
<td>Systematic review [5]</td>
<td>No serious</td>
<td>No serious</td>
<td>Very Serious</td>
<td>Serious</td>
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</tr>
<tr>
<td><strong>Permanent pacemaker insertion</strong></td>
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<td>Control arm of reference</td>
<td>No serious</td>
<td>No serious</td>
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<tr>
<td><strong>Life threatening bleeding</strong></td>
<td>Systematic review</td>
<td>Control arm of reference</td>
<td>No serious</td>
<td>No serious</td>
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<tr>
<td><strong>Atrial fibrillation (includes transient</strong></td>
<td>Systematic review</td>
<td>Control arm of reference</td>
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<td>No serious</td>
<td>No serious</td>
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**Stroke (includes perioperative events)**

- **Intervention:** Systematic review
- **Baseline/comparator:** Control arm of reference used for intervention

- **Risk of bias:** No serious
- **Inconsistency:** No serious
- **Indirectness:** No serious
- **Imprecision:** Very Serious
- **Publication bias:** No serious

**Aortic valve reintervention - short term**

- **Intervention:** Systematic review
- **Baseline/comparator:** Control arm of reference used for intervention

- **Risk of bias:** No serious
- **Inconsistency:** No serious
- **Indirectness:** No serious
- **Imprecision:** No serious
- **Publication bias:** No serious

**Aortic valve reintervention - long term**

- **Intervention:** Systematic review
- **Baseline/comparator:** Systematic review [5]

- **Risk of bias:** No serious
- **Inconsistency:** No serious
- **Indirectness:** Very Serious
- **Imprecision:** No serious
- **Publication bias:** No serious

**Permanent pacemaker insertion**

- **Intervention:** Systematic review
- **Baseline/comparator:** Control arm of reference used for intervention

- **Risk of bias:** No serious
- **Inconsistency:** No serious
- **Indirectness:** No serious
- **Imprecision:** No serious
- **Publication bias:** No serious

**Life threatening bleeding**

- **Intervention:** Systematic review
- **Baseline/comparator:** Control arm of reference used for intervention

- **Risk of bias:** No serious
- **Inconsistency:** No serious
- **Indirectness:** No serious
- **Imprecision:** No serious
- **Publication bias:** No serious

**Atrial fibrillation (includes transient postoperative)**

- **Intervention:** Systematic review
- **Baseline/comparator:** Control arm of reference used for intervention

- **Risk of bias:** No serious
- **Inconsistency:** No serious
- **Indirectness:** No serious
- **Imprecision:** No serious
- **Publication bias:** No serious
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<td>No serious</td>
<td>No serious</td>
<td>Serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Health-related quality of life</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>Serious</td>
<td>No serious</td>
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<tr>
<td>Length of index hospitalization</td>
<td>Primary study</td>
<td>Systematic review</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
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<tr>
<td>Pain</td>
<td>Systematic review Other [15][16]</td>
<td></td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
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<td>No serious</td>
</tr>
<tr>
<td>Recovery time</td>
<td>Systematic review Other [3]</td>
<td></td>
<td>No serious</td>
<td>No serious</td>
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</tr>
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References


Patients aged 75 to < 85 years and eligible for transfemoral TAVI or SAVR

Weak Recommendation

We suggest transfemoral TAVI rather than SAVR

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

Practical Info

Calculation of perioperative risk: Patients should be assessed regarding their postoperative risk by using a validated risk score such as the STS-PROM online calculator [http://riskcalc.sts.org/stswebriskcalc/#] The risk assessment, which includes many questions regarding cardiac investigations, is performed by the multi-professional heart team. This risk score serves as a starting point for risk assessment. Other considerations, not included in this score, include frailty, severe and circumferential calcification of the ascending aorta (“porcelain aorta”), non-cardiovascular comorbid conditions, cognitive impairment, physical functioning, life expectancy and patient values and expectations.

Valve durability: With TAVI, the need for aortic valve reintervention at 2-year follow-up with TAVI, is low but higher relative to SAVR (1.5% vs. 0.5%). There is insufficient data at this time regarding longer term durability of the TAVI devices. Preliminary evidence suggests that long term durability (10 years and longer) may be an issue: in the only long-term followup study reported to date, up to 50% of 378 patients undergoing TAVI with a first generation balloon-expandable device showed signs of degeneration (at least moderate or more aortic stenosis or regurgitation) at 8 years. However, large uncertainty remains. If the relative effect over two years persists long-term, using best estimates of the need for aortic valve reintervention in 8% of patients post SAVR at 10 years, up to 20-30% of patients post TAVI may require repeat intervention in the long term.

This issue should be discussed with patients considering TAVI with special attention paid to future life expectancy of each patient. Although tables of life expectancy for patients who have reached their current age may overestimate life expectancy in patients with aortic stenosis, this information can be used as a starting point ([https://www.ssa.gov/OACT/population/longevity.html]). Patients who have a life expectancy of 10 or more years at time of their initial procedure who want to avoid repeat valve intervention will be likely to prefer SAVR. Repeat TAVIs (valve in valve procedures) are being performed although experience with this approach remains limited. This may mitigate some patients' concerns about unknown durability of their initial TAVI particularly if they place a high value on avoiding open heart surgery. Finally, the limited durability data that is available is in patients receiving first generation TAVI devices. It is possible 2nd generation devices will have greater durability; this remains to be seen.

Type of TAVI device: Devices used in trials include the balloon-expandable Edwards SAPIEN-XT and the self-expanding Medtronic CoreValve. Due to its delivery catheter, the self-expanding CoreValve can be implanted by transfemoral, direct aortic, subclavian/axillar and trans-carotid, but not via transapical approach. The balloon-expandable SAPIEN-XT can be implanted by any access route; the only difference is that for the transapical approach, the delivery system is much shorter and has a bigger outer-diameter. Logically, due to the “antegrade” nature of the transapical access, the bioprosthesis is mounted upside-down as compared for the “retrograde” accesses. The balloon-expandable has merits in terms of less need for permanent pacemaker implantation and less paravalvular leakage.

Transfemoral TAVI versus non-transfemoral approaches: Non-transfemoral approaches, in most cases the transapical route, have been associated with an increased risk of deaths, strokes and acute kidney injury relative to SAVR; therefore, we provide a strong recommendation for SAVR rather than non-transfemoral TAVI. The transfemoral approach is the least invasive approach, and many centres perform TAVI as a fully-percutaneous procedure using local anesthesia along with conscious sedation. Patients undergoing transfemoral TAVI spend their acute recovery period in the coronary care unit. Transfemoral TAVI patients experience limited post-procedural pain, allowing early ambulation and a shorter length of stay in the hospital. The transfemoral approach has therefore become the access of choice for TAVI centres following a “minimalist” invasive strategy.

Key Info

Benefits and harms

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 with biological valves which suggests...
increased need for aortic valve reinterventions within the first 10 years. This issue may be of less clinical importance in older patients.

Quality of evidence
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
Patients are likely to place different value on benefits and harms associated with TAVI. Patients who place a high value on avoiding initial open heart surgery are likely to choose TAVI. Patients who place a particularly high value on avoiding need for a second aortic valve replacement are likely to choose surgery. 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
TAVI should be considered only in centres with established heart team consisting of interventional cardiologists, general cardiologists, cardiac surgeons, and appropriate nursing and adjunctive personnel. TAVI is likely to represent a cost-effective alternative to SAVR in patients at moderate to low perioperative risk but we have not identified any cost-benefit analyses to support this assumption.

Rationale
We issue a weak recommendation for transfemoral TAVR in patients aged 75 to 85 because we believe that the desirable consequences are finely balanced with the undesirable consequences when compared to SAVR. The uncertain long term durability of TAVR - which suggests a need for reintervention in a substantial proportion of patients within the first 10 years - represents a concern in this population where a substantial proportion of patients are likely to have expected life expectancy beyond 10 years and therefore need for aortic reinterventions after TAVR. Whereas the age thresholds reflect the key issue, which is expected life span; clinicians need to also consider other factors such as comorbidity.

Clinical Question/ PICO
- Population: Patients 75-85 years with severe symptomatic aortic stenosis who are at low or intermediate perioperative risk
- Intervention: Transfemoral Transcatheter aortic valve insertion (TAVI)
- Comparator: Surgical aortic valve replacement (SAVR)

Summary
Comments to the Evidence profile
- Effect-estimates come from a linked systematic review of trials comparing TAVI and SAVR, except for pain and recovery time (not reported in trials) which come from two observational studies [15]/[16].
- Baseline risk estimates come from linked systematic reviews of observational studies (for mortality, stroke, long term aortic valve reintervention, atrial fibrillation) and trials (for the other outcomes). [5]/[3] Baseline risks are age-stratified only for mortality in patients between 75 and 85.
- Aortic valve reintervention long term (at 10 years) was not reported in observational studies identified in the systematic review. Studies report structural valve deterioration which we used as an intermediate outcome reflecting need for aortic valve reintervention. Therefore we rated down for very serious indirectness both for baseline risk and for effect-estimates, the latter coming from trials reporting short term aortic valve reintervention. We also rated down for imprecision, resulting in very low certainty in the absolute effect estimates.
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality, age adjusted</td>
<td>2 years</td>
<td>Hazard Ratio 0.79 (CI 95% 0.66 - 0.94) Based on data from 2,576 patients in 3 studies. (Randomized controlled) Follow up 2 years</td>
<td>152 per 1000</td>
<td>122 per 1000</td>
<td>Moderate Due to serious imprecision TAVI probably reduces the risk of death.</td>
</tr>
<tr>
<td>Stroke (includes perioperative events)</td>
<td></td>
<td>Relative risk 0.8 (CI 95% 0.63 - 1.01) Based on data from 2,576 patients in 3 studies. (Randomized controlled) Follow up 2 years</td>
<td>99 per 1000</td>
<td>79 per 1000</td>
<td>Moderate Due to serious imprecision TAVI probably reduces the risk of stroke.</td>
</tr>
<tr>
<td>Life threatening bleeding</td>
<td>2 years</td>
<td>Relative risk 0.39 (CI 95% 0.29 - 0.54) Based on data from 2,576 patients in 3 studies. (Randomized controlled) Follow up 2 years</td>
<td>413 per 1000</td>
<td>161 per 1000</td>
<td>High TAVI reduces the risk of life threatening or disabling bleeding.</td>
</tr>
<tr>
<td>Aortic valve reintervention short term</td>
<td>2 years</td>
<td>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</td>
<td>3 per 1000</td>
<td>10 per 1000</td>
<td>Moderate Due to borderline risk of bias and imprecision TAVI probably increases the risk of aortic valve reintervention.</td>
</tr>
<tr>
<td>Aortic valve reintervention - long term</td>
<td>10 years</td>
<td>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</td>
<td>61 per 1000</td>
<td>198 per 1000</td>
<td>Very Low Due to serious inconsistency, indirectness, imprecision TAVI may increase need for aortic reintervention due to structural valve deterioration</td>
</tr>
<tr>
<td>Permanent pacemaker insertion</td>
<td>2 years</td>
<td>Relative risk 2.46 (CI 95% 1.17 - 5.15) Based on data from 3,128 patients in 4 studies. (Randomized controlled) Follow up 2 years</td>
<td>92 per 1000</td>
<td>226 per 1000</td>
<td>Moderate Due to serious inconsistency TAVI probably increases the risk for permanent pacemaker insertion.</td>
</tr>
<tr>
<td>Condition</td>
<td>Relative Risk or Odds Ratio</td>
<td>Confidence Interval</td>
<td>Difference</td>
<td>Classification</td>
<td>Notes</td>
</tr>
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<td>-----------------------------------------------</td>
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<tr>
<td><strong>Atrial fibrillation</strong> (includes transient postoperative) 2 years</td>
<td>Relative risk 0.43 (CI 95% 0.35 - 0.52)</td>
<td>Based on data from 3,058 patients in 3 studies. (Randomized controlled) Follow up 2 years</td>
<td>312 per 1000 - 134 per 1000</td>
<td>High</td>
<td>TAVI reduces the risk of new onset atrial fibrillation.</td>
</tr>
<tr>
<td><strong>Moderate/severe heart failure symptoms (NYHA ≥III) 2 years</strong></td>
<td>Odds Ratio 1.29 (CI 95% 1.08 - 1.55)</td>
<td>Based on data from 2,146 patients in 4 studies. (Randomized controlled) Follow up 2 years</td>
<td>69 per 1000 - 87 per 1000</td>
<td>Moderate</td>
<td>TAVI probably slightly increases risk of moderate or severe heart failure symptoms.</td>
</tr>
<tr>
<td><strong>Myocardial infarction 2 years</strong></td>
<td>Relative risk 0.87 (CI 95% 0.59 - 1.29)</td>
<td>Based on data from 3,128 patients in 4 studies. (Randomized controlled) Follow up 2 years</td>
<td>36 per 1000 - 31 per 1000</td>
<td>Moderate</td>
<td>TAVI may have little or no impact on myocardial infarction.</td>
</tr>
<tr>
<td><strong>Acute kidney injury (includes transient events) 2 years</strong></td>
<td>Relative risk 0.38 (CI 95% 0.27 - 0.54)</td>
<td>Based on data from 2,576 patients in 3 studies. (Randomized controlled) Follow up 2 years</td>
<td>85 per 1000 - 32 per 1000</td>
<td>High</td>
<td>TAVI reduces the risk of AKI.</td>
</tr>
<tr>
<td><strong>Health-related quality of life 2 years</strong></td>
<td>Measured by: Difference from baseline in KCCQ Score. Minimal important difference is 5 points. Scale: 0-100 High better</td>
<td>Based on data from 797 patients in 1 studies. (Randomized controlled) Follow up 2 years</td>
<td>18.7 points (Mean) - 22.2 points (Mean)</td>
<td>Low</td>
<td>TAVI may have little or no impact compared to SAVR on HRQoL.</td>
</tr>
<tr>
<td><strong>Length of index hospitalization</strong></td>
<td>Measured by: Days in hospital after procedure Lower better</td>
<td>Based on data from: 2,032 patients in 1 studies. (Randomized controlled)</td>
<td>12 days (Median) - 8 days (Median)</td>
<td>High</td>
<td>TAVI reduces the length of hospital stay.</td>
</tr>
</tbody>
</table>
### BMJ Rapidrecs for Transcatheter aortic valve implantation versus surgical aortic valve replacement for severe aortic stenosis in low-intermediate risk

#### Pain

| Based on data from 379 patients in 2 studies | A large prospective observational study showed that ~28% have chronic post-sternotomy pain at 1 year and ~13% have pain >3/10 on visual analog scale. One smaller unadjusted observational study showed no difference in pain scores between TAVI and SAVR at 3 months. | Low |

TAVI may result in less short and long-term pain.

#### Recovery time

| Based on data from 3,028 patients in 3 studies | TAVI was associated with significantly less shortness of breath at one month (2 RCTs). Patients in the TAVI group had a shorter index hospital stay (2 RCTs). | Moderate |

Due to serious indirectness TAVI probably reduces recovery time.

<table>
<thead>
<tr>
<th>Practical issues</th>
<th>Surgical aortic valve replacement (SAVR)</th>
<th>Transfemoral Transcatheter aortic valve insertion (TAVI)</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication routine</strong></td>
<td>- Antiplatelet or anticoagulation medication after procedure, as needed</td>
<td>- Pain medication after procedure, as needed</td>
<td>- Dental care may be needed before the intervention, and is not recommended for 3-6 months afterwards</td>
</tr>
<tr>
<td><strong>Tests and visits</strong></td>
<td>- Resume medications for concomitant cardiac conditions, as needed</td>
<td></td>
<td>- Post operative visits are typically within 1-2 months, and then yearly to check that the valve is working</td>
</tr>
<tr>
<td><strong>Procedure and device</strong></td>
<td>- The doctor will make a small puncture (opening) in the groin for the catheter (long, thin tube), which carries the new valve into the heart, where it is put inside the unhealthy valve</td>
<td>- The doctors will make a cut in the middle of the chest, divide the breastbone, and surgically replace the unhealthy heart valve</td>
<td>- The new heart valve is made of tissue (from the heart of a cow or pig)</td>
</tr>
<tr>
<td></td>
<td>- The new heart valve is made of natural tissue (from the heart of a cow or pig) attached to a flexible, metallic mesh frame</td>
<td>- The heart may be stopped and supported by a machine</td>
<td>- The procedure takes 3-5 hours</td>
</tr>
<tr>
<td></td>
<td>- This procedure allows one to be awake (conscious sedation)</td>
<td>- One is asleep during the procedure (general anesthesia)</td>
<td>- SAVR valves are durable for 10 to 20 years with long term data in large numbers of patients</td>
</tr>
<tr>
<td></td>
<td>- The procedure takes under 2 hours</td>
<td>- The procedure takes 3-5 hours</td>
<td>- TAVI valves are durable for 3 to 5 years but longer term durability data is not yet available</td>
</tr>
<tr>
<td>Category</td>
<td>Details</td>
<td></td>
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<tr>
<td>-------------------------------</td>
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<tr>
<td>Recovery and adaptation</td>
<td>- After the procedure, in-hospital stay will usually last 2-5 days&lt;br&gt;- It could take about a month to recover&lt;br&gt;- Pain from the insertion site usually resolves within a few weeks&lt;br&gt;- About 1 patient in 4 report persisting pain in the sternum at after 1 year, with 1 in 10 with more serious pain</td>
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<tr>
<td>Coordination of care</td>
<td>- It is useful to have someone to help with activities during recovery as one regains their strength</td>
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<tr>
<td>Adverse effects, interactions and antidote</td>
<td>- Long-term effects of TAVI are less well known than surgery</td>
<td></td>
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<tr>
<td>Physical well-being</td>
<td>- Some patients report less appetite and constipation as they recover&lt;br&gt;- Some patients report poor sleep as they recover</td>
<td></td>
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<tr>
<td>Emotional well-being</td>
<td>- Some patients report mood swings, irritability, anxiety, and depression as they recover, although these symptoms may also have been present before surgery</td>
<td></td>
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<tr>
<td>Costs and access</td>
<td>- Travel costs if intervention happens far from home&lt;br&gt;- Insurance plans may or may not cover some or all aspects of the procedure</td>
<td></td>
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</tr>
</tbody>
</table>

BMJ Rapidrecs for Transcatheter aortic valve implantation versus surgical aortic valve replacement for severe aortic stenosis in low-intermediate risk

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## Details about studies used and certainty down- and upgrading

<table>
<thead>
<tr>
<th>Event</th>
<th>Intervention</th>
<th>Baseline/comparator</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Publication bias</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality, age adjusted</strong></td>
<td>Systematic review</td>
<td>Systematic review</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
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<tr>
<td><strong>Stroke (includes perioperative events)</strong></td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
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<tr>
<td><strong>Life threatening bleeding</strong></td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>No serious</td>
<td>No serious</td>
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<td>No serious</td>
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<tr>
<td><strong>Aortic valve</strong></td>
<td>Systematic review</td>
<td>Systematic review</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
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</tbody>
</table>

**Notes:**

- Dietary restrictions apply if blood thinners are needed.
- Need to avoid strenuous activity during recovery.
- Rehabilitation may help recovery.
- If blood thinners are needed, may limit activities with high risk injury.
- Time until return to work depends on speed of recovery.
- Driving may be limited during recovery.
- Driving is limited for 6 weeks until the sternal bone heals.

**Intervention:** Systematic review

**Baseline/comparator:** Systematic review

**Risk of bias:** No serious Robust to worst-plausible but not worst-case lost to follow-up sensitivity analysis;

**Inconsistency:** No serious We found subgroup analyses of transfemoral versus transapical approach to be credible so did not rate down for inconsistency;

**Indirectness:** No serious

**Imprecision:** Serious Confidence intervals include important benefit and no benefit from TAVR;

**Publication bias:** No serious

**Intervention:** Systematic review

**Baseline/comparator:** Control arm of reference used for intervention

**Risk of bias:** No serious

**Inconsistency:** No serious We found subgroup analyses of transfemoral versus transapical approach to be credible so did not rate down for inconsistency;

**Indirectness:** No serious

**Imprecision:** Serious Wide confidence intervals;

**Publication bias:** No serious

**Intervention:** Systematic review

**Baseline/comparator:** Control arm of reference used for intervention

**Risk of bias:** No serious Unclear whether outcome adjudicators were blinded;

**Inconsistency:** No serious

**Indirectness:** No serious

**Imprecision:** No serious

**Publication bias:** No serious

**Intervention:** Systematic review

**Risk of bias:** No serious We considered rating down for unblinded healthcare providers;
<table>
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<tr>
<th>Condition</th>
<th>Intervention</th>
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<th>Publication bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic valve reintervention</td>
<td>Systematic review [5]</td>
<td>Control arm of reference used for intervention</td>
<td>No serious</td>
<td>Serious</td>
<td>No serious</td>
<td>Serious</td>
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<tr>
<td>Aortic valve reintervention - long term</td>
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<td></td>
<td>Serious</td>
<td>No serious</td>
<td>No serious</td>
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<td>Atrial fibrillation (includes transient postoperative)</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
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<tr>
<td>Moderate/severe heart failure symptoms (NYHA ≥III)</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>No serious</td>
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<td>Myocardial infarction</td>
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<td>Control arm of reference used for intervention</td>
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</tbody>
</table>
### References


8. Adams DH, Popma JJ, Reardon MJ, Yakubov SJ, Coselli JS, Deeb GM, Gleason TG, Buchbinder M, Hermiller J, Kleiman NS,
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.

Practical Info

Calculation of perioperative risk: Patients should be assessed regarding their postoperative risk by using a validated risk score such as the STS-PROM online calculator [http://riskcalc.sts.org/stswebriskcalc/#/](http://riskcalc.sts.org/stswebriskcalc/#/). The risk assessment, which includes many questions regarding cardiac investigations, is performed by the multi-professional heart team. This risk score serves as a starting point for risk assessment. Other considerations, not included in this score, include frailty, severe and circumferential calcification of the ascending aorta (“porcelain aorta”), non-cardiovascular comorbid conditions, cognitive impairment, physical functioning, life expectancy and patient values and expectations.

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This issue should be discussed with patients considering TAVI with special attention paid to future life expectancy of each patient. Although tables of life expectancy for patients who have reached their current age may overestimate life expectancy in patients with
aortic stenosis, this information can be used as a starting point (https://www.ssa.gov/OACT/population/longevity.html). Patients who have a life expectancy of 10 or more years at time of their initial procedure who want to avoid repeat valve intervention will be likely to prefer SAVR. Repeat TAVIs (valve in valve procedures) are being performed although experience with this approach remains limited. This may mitigate some patients' concerns about unknown durability of their initial TAVI particularly if they place a high value on avoiding open heart surgery. Finally, the limited durability data that is available is in patients receiving first generation TAVI devices. It is possible 2nd generation devices will have greater durability; this remains to be seen.

**Type of TAVI device:** Devices used in trials include the balloon-expandable Edwards SAPIEN-XT and the self-expanding Medtronic CoreValve. Due to its delivery catheter, the self-expanding CoreValve can be implanted by transfemoral, direct aortic, subclavian/axillar and trans-carotid, but not via transapical approach. The balloon-expandable SAPIEN-XT can be implanted by any access route; the only difference is that for the transapical approach, the delivery system is much shorter and has a bigger outer-diameter. Logically, due to the “antegrade” nature of the transapical access, the bioprosthesis is mounted upside-down as compared for the “retrograde” accesses. The balloon-expandable has merits in terms of less need for permanent pacemaker implantation and less paravalvular leakage.

**Transfemoral TAVI versus non-transfemoral approaches:** Non-transfemoral approaches, in most cases the transapical route, have been associated with an increased risk of deaths, strokes and acute kidney injury relative to SAVR; therefore, we provide a strong recommendation for SAVR rather than non-transfemoral TAVI. The transfemoral approach is the least invasive approach, and many centres perform TAVI as a fully-percutaneous procedure using local anesthesia along with conscious sedation. Patients undergoing transfemoral TAVI spend their acute recovery period in the coronary care unit. Transfemoral TAVI patients experience limited post-procedural pain, allowing early ambulation and a shorter length of stay in the hospital. The transfemoral approach has therefore become the access of choice for TAVI centres following a “minimalist” invasive strategy.

### Key Info

<table>
<thead>
<tr>
<th>Benefits and harms</th>
<th>Small net benefit, or little difference between alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
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</table>

<table>
<thead>
<tr>
<th>Quality of evidence</th>
<th>Moderate</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Preference and values</th>
<th>Substantial variability is expected or uncertain</th>
</tr>
</thead>
<tbody>
<tr>
<td>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].</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resources and other considerations</th>
<th>Important issues, or potential issues not investigated</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
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</table>
Rationale
We issue a weak recommendation for SAVR in patients aged 75 or younger because we believe that the desirable consequences are finely balanced with the undesirable consequences when compared to TAVI. The uncertain long term durability of TAVI - which suggests a need for reintervention in a substantial proportion of patients within the first 10 years - represents a key concern in this population where a majority are likely to have expected life expectancy beyond 10 years and therefore need for aortic reinterventions after TAVI. Whereas the age thresholds reflect the key issue, which is expected life span; clinicians need to also consider other factors such as comorbidity and engage in shared decision-making as needed.

Clinical Question/ PICO

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

Summary
Comments to the Evidence profile
- Effect-estimates come from a linked systematic review of trials comparing TAVI and SAVR, except for pain and recovery time (not reported in trials) which come from two observational studies [15][16].
- Baseline risk estimates come from linked systematic reviews of observational studies (for mortality, stroke, long term aortic valve reintervention, atrial fibrillation) and trials (for the other outcomes), [5][3] Baseline risks are age-stratified only for mortality and stroke in patients between 65 and 75 years old. The age adjustment for stroke was performed by taking the overall baseline risk estimate from the systematic review on observational studies and assuming a similar age distribution for incidence of stroke as in the general population.
- Aortic valve reintervention long term (at 10 years) was not reported in observational studies identified in the systematic review. Studies report structural valve deterioration which we used as an intermediate outcome reflecting need for aortic valve reintervention. Therefore we rated down for very serious indirectness both for baseline risk and for effect-estimates, the latter coming from trials reporting short term aortic valve reintervention. We also rated down for imprecision, resulting in very low certainty in the absolute effect estimates.

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality, age adjusted</td>
<td>Hazard Ratio 0.79 (CI 95% 0.66 - 0.94) Based on data from 2,576 patients in 3 studies. (Randomized controlled) Follow up 2 years</td>
<td>Surgical aortic valve replacement (SAVR)</td>
<td>92 per 1000</td>
<td>Moderate Due to serious imprecision</td>
</tr>
<tr>
<td>Stroke (includes perioperative events)</td>
<td>Relative risk 0.8 (CI 95% 0.63 - 1.01) Based on data from 2,576 patients in 3 studies. (Randomized controlled) Follow up 2 years</td>
<td>Transthoracic Transcatheter aortic valve insertion (TAVI)</td>
<td>73 per 1000</td>
<td>TAVI probably reduces the risk of death.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Difference: 19 fewer per 1000 ( CI 95% 30 fewer - 5 fewer )</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>TAVI probably reduces the risk of stroke.</td>
</tr>
</tbody>
</table>
Aortic valve reintervention 2 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

Difference: 7 more per 1000
( CI 95% 21 more - 1 more )

Moderate
Due to borderline risk of bias and imprecision
TAVI probably increases the risk of aortic valve reintervention.

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

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

Permanent pacemaker insertion 2 years
Relative risk 2.46 (CI 95% 1.17 - 5.15)
Based on data from 3,128 patients in 4 studies.
(Randomized controlled)
Follow up 2 years

Difference: 134 more per 1000
( CI 95% 382 more - 16 more )

Moderate
Due to serious inconsistency
TAVI probably increases the risk for permanent pacemaker insertion.

Life threatening bleeding 2 years
Relative risk 0.39 (CI 95% 0.29 - 0.54)
Based on data from 3,128 patients in 3 studies.
(Randomized controlled)
Follow up 2 years

Difference: 252 fewer per 1000
( CI 95% 190 fewer - 293 fewer )

High
TAVI reduces the risk of life threatening or disabling bleeding.

Atrial fibrillation (includes transient postoperative) 2 years
Relative risk 0.43 (CI 95% 0.35 - 0.52)
Based on data from 3,058 patients in 3 studies.
(Randomized controlled)
Follow up 2 years

Difference: 178 fewer per 1000
( CI 95% 150 fewer - 203 fewer )

High
TAVI reduces the risk of new onset atrial fibrillation.

Moderate/severe heart failure symptoms (NYHA ≥III) 2 years
Odds Ratio 1.29 (CI 95% 1.08 - 1.55)
Based on data from 2,146 patients in 4 studies.
(Randomized controlled)
Follow up 2 years

Difference: 18 more per 1000
( CI 95% 5 more - 34 more )

Moderate
Due to serious imprecision
TAVI increases risk of moderate or severe heart failure symptoms

Myocardial infarction
Relative risk 0.87 (CI 95% 0.59 - 1.29)
Based on data from 3,128

36
31

Low
Due to serious risk
TAVI may have little or no impact on myocardial infarction.
<table>
<thead>
<tr>
<th>Practical issues</th>
<th>Surgical aortic valve replacement (SAVR)</th>
<th>Transfemoral Transcatheter aortic valve insertion (TAVI)</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 years</td>
<td>patients in 4 studies. (Randomized controlled)</td>
<td>Follow up 2 years</td>
<td></td>
</tr>
<tr>
<td>Acute kidney injury (includes transient events) 2 years</td>
<td>Relative risk 0.38 (CI 95% 0.27 - 0.54)</td>
<td>Based on data from 2,576 patients in 3 studies. (Randomized controlled)</td>
<td>Follow up 2 years</td>
</tr>
<tr>
<td>Health-related quality of life 2 years</td>
<td>Measured by: Difference from baseline in KCCQ Score. Minimal important difference is 5 points. Scale: 0-100 High better</td>
<td>Based on data from: 797 patients in 1 studies. (Randomized controlled)</td>
<td></td>
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<tr>
<td>Length of index hospitalization</td>
<td>Measured by: Days in hospital after procedure</td>
<td>Lower better</td>
<td>Based on data from: 2,308 patients in 2 studies. (Randomized controlled)</td>
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<tr>
<td>Pain</td>
<td>Based on data from 397 patients in 2 studies</td>
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<tr>
<td>Recovery time</td>
<td>Based on data from 3,058 patients in 3 studies</td>
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<tr>
<th></th>
<th>per 1000</th>
<th>per 1000</th>
<th>of bias and serious imprecision</th>
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<tbody>
<tr>
<td>Acute kidney injury</td>
<td>85</td>
<td>32</td>
<td>High</td>
</tr>
<tr>
<td>Health-related quality of life</td>
<td>18.7</td>
<td>22.2</td>
<td>Low</td>
</tr>
<tr>
<td>Length of index hospitalization</td>
<td>12</td>
<td>8</td>
<td>High</td>
</tr>
<tr>
<td>Pain</td>
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<td>Low</td>
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</tbody>
</table>

A large prospective observational study showed that ~28% have chronic post-sternotomy pain at 1 year and ~13% have pain >3/10 on visual analog scale. One smaller unadjusted observational study showed no difference in pain scores between TAVI and SAVR at 3 months.

TAVI was associated with significantly less shortness of breath at one month (2 RCTs). Patients in the TAVI group had a shorter index hospital stay (2 RCTs).

TAVI reduces the risk of AKI

TAVI may have little or no impact compared to SAVR on HRQoL

TAVI reduces the length of hospital stay.

TAVI may reduce post-intervention pain.

TAVI probably reduces recovery time.

Due to serious risk of bias and serious imprecision

Due to serious indirectness
Medication routine

- Antiplatelet or anticoagulation medication after procedure, as needed
- Pain medication after procedure, as needed
- Resume medications for concomitant cardiac conditions, as needed

Tests and visits

- Dental care may be needed before the intervention, and is not recommended for 3-6 months afterwards
- Post operative visits are typically within 1-2 months, and then yearly to check that the valve is working

Procedure and device

- The doctor will make a small puncture (opening) in the groin for the catheter (long, thin tube), which carries the new valve into the heart, where it is put inside the unhealthy valve
- The new heart valve is made of natural tissue (from the heart of a cow or pig) attached to a flexible, metallic mesh frame
- This procedure allows one to be awake (conscious sedation)
- The procedure takes under 2 hours
- TAVI valves are durable for 3 to 5 years but longer term durability data is not yet available
- The doctors will make a cut in the middle of the chest, divide the breastbone, and surgically replace the unhealthy heart valve
- The new heart valve is made of tissue (from the heart of a cow or pig)
- The heart may be stopped and supported by a machine
- One is asleep during the procedure (general anesthesia)
- The procedure takes 3-5 hours
- SAVR valves are durable for 10 to 20 years with long term data in large numbers of patients

Recovery and adaptation

- After the procedure, in-hospital stay will usually last 2-5 days
- It could take about a month to recover
- Pain from the insertion site usually resolves within a few weeks
- After the procedure, in-hospital stay will usually last 5-10 days
- It could take about 2-3 months to recover
- About 1 patient in 4 report persisting pain in the sternum at after 1 year, with 1 in 10 with more serious pain
- Recovery

Coordination of care

- It is useful to have someone to help with activities during recovery as one regains their strength
| **Adverse effects, interactions and antidote** | Long-term effects of TAVI are less well known than surgery |
| **Physical well-being** | Some patients report less appetite and constipation as they recover |
| **Emotional well-being** | Data on emotional well-being after TAVI is scant. Some patients report mood swings, irritability, anxiety, and depression as they recover, although these symptoms may also have been present before surgery. |
| **Costs and access** | Travel costs if intervention happens far from home. Insurance plans may or may not cover some or all aspects of the procedure. |
| **Food and drinks** | Dietary restrictions apply if blood thinners are needed. Dietary restrictions apply if blood thinners are needed. |
| **Exercise and activities** | Need to avoid strenuous activity during recovery. Rehabilitation may help recovery. If blood thinners are needed, may limit activities with high risk injury. |
| **Work and education** | May be 2-6 weeks. May be 6-8 weeks. Time until return to work depends on speed of recovery. |
### Details about studies used and certainty down- and upgrading

<table>
<thead>
<tr>
<th>Event Description</th>
<th>Intervention: Systematic review</th>
<th>Baseline/comparator: Systematic review [5]</th>
<th>Risk of bias: <strong>No serious</strong></th>
<th>Inconsistency: <strong>No serious</strong></th>
<th>Indirectness: <strong>No serious</strong></th>
<th>Imprecision: <strong>Serious</strong></th>
<th>Publication bias: <strong>No serious</strong></th>
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<tbody>
<tr>
<td>Mortality, age adjusted</td>
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<tr>
<td>Stroke (includes perioperative events)</td>
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<tr>
<td>Aortic valve reintervention</td>
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<tr>
<td>Aortic valve reintervention - long term</td>
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<tr>
<td>Permanent pacemaker insertion</td>
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<tr>
<td>Atrial fibrillation (includes transient postoperative)</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>No serious</td>
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<td>Moderate/severe heart failure symptoms (NYHA ≥III)</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>No serious</td>
<td>No serious</td>
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<tr>
<td>Myocardial infarction</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
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<tr>
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<tr>
<td>Length of index hospitalization</td>
<td>Primary study</td>
<td>Systematic review</td>
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<tr>
<td>Pain</td>
<td>Primary study Other[15][16]</td>
<td>Systematic review</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
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<td>No serious</td>
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</table>

We did not rate down certainty in evidence for statistical heterogeneity (I²=53.5%) because there were significantly fewer atrial fibrillation events in the TAVI group in all 3 trials.

Outcome included transient postoperative atrial fibrillation and trials do not report permanent atrial fibrillation at 2 years. Therefore the effects do not likely represent permanent atrial fibrillation at two years, in need of long term anticoagulation.

Differences between the outcomes of interest and those reported (e.g., short-term/ surrogate, not patient-important):

Confidence intervals include important harm and no harm from TAVR.

Confidence interval includes benefit and serious harm with TAVI.

Only data from one study.

Confidence intervals were not provided, but P-value was very low (<0.0001) and results were consistent with the NOTION study (n=280): 8.9 (SD 6.2) days in TAVI group and 12.9 (SD 11.6) days in SAVR group (P=0.0001).

Only data from one study. We considered rating down 2 because confidence intervals were not provided, but P-value was very low (<0.0001) and results were consistent with the NOTION study (n=280): 8.9 (SD 6.2) days in TAVI group and 12.9 (SD 11.6) days in SAVR group (P=0.0001).
References


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

Strong Recommendation

We recommend SAVR rather than TAVI

This recommendation considers benefits and harms of treatment alternatives with a particular weight on the lacking evidence on use of TAVR in patients below 65 years of age and the uncertainty regarding the long-term durability of TAVI valves.

Practical Info

Calculation of perioperative risk: Patients should be assessed regarding their postoperative risk by using a validated risk score such as the STS-PROM online calculator [http://riskcalc.sts.org/stswebriskcalc/#/](http://riskcalc.sts.org/stswebriskcalc/#/). The risk assessment, which includes many questions regarding cardiac investigations, is performed by the multi-professional heart team. This risk score serves as a starting point for risk assessment. Other considerations, not included in this score, include frailty, severe and circumferential calcification of the ascending aorta (“porcelain aorta”), non-cardiovascular comorbid conditions, cognitive impairment, physical functioning, life expectancy and patient values and expectations.

Valve durability: With TAVI, the need for aortic valve reintervention at 2-year follow-up with TAVI, is low but higher relative to SAVR (1.5% vs. 0.5%). There is insufficient data at this time regarding longer term durability of the TAVI devices. Preliminary evidence suggests that long term durability (10 years and longer) may be an issue: in the only long-term followup study reported to date, up to 50% of 378 patients undergoing TAVI with a first generation balloon-expandable device showed signs of degeneration (at least moderate or more aortic stenosis or regurgitation) at 8 years. However, large uncertainty remains. If the relative effect over two years persists long-term, using best estimates of the need for aortic valve reintervention in 8% of patients post SAVR at 10 years, up to 20-30% of patients post TAVI may require repeat intervention in the long term.

This issue should be discussed with patients considering TAVI with special attention paid to future life expectancy of each patient. Although tables of life expectancy for patients who have reached their current age may overestimate life expectancy in patients with aortic stenosis, this information can be used as a starting point (https://www.ssa.gov/OACT/population/longevity.html). Patients who have a life expectancy of 10 or more years at time of their initial procedure who want to avoid repeat valve intervention will be likely to prefer SAVR. Repeat TAVIs (valve in valve procedures) are being performed although experience with this approach remains limited. This may mitigate some patients’ concerns about unknown durability of their initial TAVI particularly if they place a high value on avoiding open heart surgery. Finally, the limited durability data that is available is in patients receiving first generation TAVI devices. It is possible 2nd generation devices will have greater durability; this remains to be seen.

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Transfemoral TAVI versus non-transfemoral approaches: Non-transfemoral approaches, in most cases the transapical route, have been associated with an increased risk of deaths, strokes and acute kidney injury relative to SAVR; therefore, we provide a strong recommendation for SAVR rather than non-transfemoral TAVI. The transfemoral approach is the least invasive approach, and many centres perform TAVI as a fully-percutaneous procedure using local anesthesia along with conscious sedation. Patients undergoing transfemoral TAVI spend their acute recovery period in the coronary care unit. Transfemoral TAVI patients experience limited post-procedural pain, allowing early ambulation and a shorter length of stay in the hospital. The transfemoral approach has therefore become the access of choice for TAVI centres following a “minimalist” invasive strategy.

Key Info

Benefits and harms

Benefits of SAVR - when compared to TAVI - include established long term durability of mechanical and biological valves, reduced heart failure, need for pacemaker insertions and aortic reinterventions. Harms include a potential for increased deaths, strokes, major bleeds, new onset atrial fibrillations and days in hospital after surgery. 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.

Substantial net benefits of the recommended alternative
Rationale

We issue a strong recommendation for SAVR in patients below 65 years of age because of the uncertain long term durability of TAVI - which suggests a need for reintervention in a substantial proportion of patients within the first 10 years. This represents a key concern in this population where a significant majority are likely to have expected life expectancy beyond 10 years and therefore need for aortic reinterventions after TAVI. Whereas the age thresholds reflect the key issue, which is expected life span; clinicians need to also consider other factors such as comorbidity and engage in shared decision-making as needed. In addition, very few patients aged < 65 years were included in RCTs therefore very little data is available for TAVI in this subset.

Quality of evidence

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

Preference and values

We expect that patients aged 65 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 the uncertain benefits of TAVI and the 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

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 remains uncertain in the absence of available cost-benefit analyses.

Rationale

We issue a strong recommendation for SAVR in patients below 65 years of age because of the uncertain long term durability of TAVI - which suggests a need for reintervention in a substantial proportion of patients within the first 10 years. This represents a key concern in this population where a significant majority are likely to have expected life expectancy beyond 10 years and therefore need for aortic reinterventions after TAVI. Whereas the age thresholds reflect the key issue, which is expected life span; clinicians need to also consider other factors such as comorbidity and engage in shared decision-making as needed. In addition, very few patients aged < 65 years were included in RCTs therefore very little data is available for TAVI in this subset.

Clinical Question/ PICO

Population: Patients 65 years and below with severe symptomatic aortic symptomatic stenosis who are at low or intermediate perioperative risk

Intervention: Transfemoral Transcatheter aortic valve insertion (TAVI)

Comparator: Surgical aortic valve replacement (TAVR)

Summary

Comments to the Evidence profile

- Effect-estimates come from a linked systematic review of trials comparing TAVI and SAVR, except for pain and recovery time (not reported in trials) which come from two observational studies [15][16].
- Baseline risk estimates come from linked systematic reviews of observational studies (for mortality, stroke, long term aortic valve reintervention, atrial fibrillation) and trials (for the other outcomes), [5][3] Baseline risks are age-stratified only for mortality and stroke in patients below 65 years old. The age adjustment for stroke was performed by taking the overall baseline risk estimate from the systematic review on observational studies and assuming a similar age distribution for incidence of stroke as in the general population.
- Aortic valve reintervention long term (at 10 years) was not reported in observational studies identified in the systematic review. Studies report structural valve deterioration which we used as an intermediate outcome reflecting need for aortic valve reintervention. Therefore we rated down for very serious indirectness both for baseline risk and for effect-estimates, the latter coming from trials reporting short term aortic valve reintervention. We also rated down for imprecision, resulting in very low certainty in the absolute effect estimates.

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty in effect estimates (Quality of evidence)</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality, age adjusted 2 years</td>
<td>Hazard Ratio 0.79 (CI 95% 0.66 - 0.94) Based on data from 2,576 patients in 3 studies. (Randomized controlled) Follow up 2 years</td>
<td>72 per 1000 57 per 1000</td>
<td>Low Due to indirectness and imprecision</td>
<td>TAVI probably reduces the risk of death.</td>
</tr>
<tr>
<td>Stroke - age adjusted</td>
<td>Relative risk 0.8 (CI 95% 0.63 - 1.01) Based on data from 2,576 patients in 3 studies. (Randomized controlled) Follow up 2 years</td>
<td>50 per 1000 40 per 1000</td>
<td>Low</td>
<td>TAVI probably reduces the risk of stroke.</td>
</tr>
<tr>
<td>Aortic valve reintervention 2 years</td>
<td>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</td>
<td>3 per 1000 10 per 1000</td>
<td>Low</td>
<td>TAVI probably increases the risk of aortic valve reintervention.</td>
</tr>
<tr>
<td>Aortic valve reintervention - long term 10 years</td>
<td>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</td>
<td>61 per 1000 198 per 1000</td>
<td>Very Low</td>
<td>TAVI may increase need for aortic reintervention due to structural valve deterioration</td>
</tr>
<tr>
<td>Permanent pacemaker insertion 2 years</td>
<td>Relative risk 2.46 (CI 95% 1.17 - 5.15) Based on data from 3,128 patients in 4 studies. (Randomized controlled) Follow up 2 years</td>
<td>92 per 1000 226 per 1000</td>
<td>Low</td>
<td>TAVI increases the risk for permanent pacemaker insertion.</td>
</tr>
<tr>
<td>Condition</td>
<td>Relative Risk</td>
<td>Confidence Interval</td>
<td>Patients</td>
<td>Follow up</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>---------------</td>
<td>---------------------</td>
<td>----------</td>
<td>-----------</td>
</tr>
<tr>
<td>Life threatening bleeding</td>
<td>0.39</td>
<td>(0.29 - 0.54)</td>
<td>3,128</td>
<td>2 years</td>
</tr>
<tr>
<td>Atrial fibrillation, age-adjusted</td>
<td>0.43</td>
<td>(0.35 - 0.52)</td>
<td>3,058</td>
<td>2 years</td>
</tr>
<tr>
<td>Moderate/ severe heart failure symptoms (NYHA ≥III)</td>
<td>1.29</td>
<td>(1.08 - 1.55)</td>
<td>2,146</td>
<td>2 years</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0.87</td>
<td>(0.59 - 1.29)</td>
<td>3,128</td>
<td>2 years</td>
</tr>
<tr>
<td>Acute kidney injury (including transient events)</td>
<td>0.38</td>
<td>(0.27 - 0.54)</td>
<td>2,576</td>
<td>2 years</td>
</tr>
<tr>
<td>Health-related quality of life</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**
- Relative risk and confidence interval are based on data from specified number of patients in studies.
- Follow up period is 2 years.
- Difference is calculated per 1000 patients.
- Moderate/low risk indicates different levels of confidence in the assessment.
## Length of Index Hospitalization

<table>
<thead>
<tr>
<th></th>
<th>Lower better</th>
<th>Difference: MD 4 fewer (CI 95% 3 fewer - 5 fewer)</th>
<th>Moderate Due to serious indirectness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Based on data:</td>
<td>2,032 patients in 1 studies. (Randomized controlled)</td>
<td>TAVI probably reduces the length of hospital stay.</td>
<td>12 days (Median) 8 days (Median)</td>
</tr>
<tr>
<td></td>
<td>A large prospective observational study showed that ~28% have chronic post-sternotomy pain at 1 year and ~13% have pain &gt;3/10 on visual analog scale. One smaller unadjusted observational study showed no difference in pain scores between TAVI and SAVR at 3 months.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Pain

<table>
<thead>
<tr>
<th></th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>Based on data:</td>
<td>397 patients in 3 studies</td>
</tr>
<tr>
<td></td>
<td>TAVI may reduce post-intervention pain.</td>
</tr>
</tbody>
</table>

## Recovery Time

<table>
<thead>
<tr>
<th></th>
<th>Moderate Due to serious indirectness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Based on data:</td>
<td>3,058 patients in 3 studies</td>
</tr>
<tr>
<td></td>
<td>TAVI probably reduces recovery time.</td>
</tr>
<tr>
<td></td>
<td>TAVI was associated with significantly less shortness of breath at one month (2 RCTs). Patients in the TAVI group had a shorter index hospital stay (2 RCTs).</td>
</tr>
</tbody>
</table>

## Practical Issues

<table>
<thead>
<tr>
<th>Practical issues</th>
<th>Surgical aortic valve replacement (TAVR)</th>
<th>Transfemoral Transcatheter aortic valve insertion (TAVI)</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication routine</strong></td>
<td>- Antiplatelet or anticoagulation medication after procedure, as needed</td>
<td>- Pain medication after procedure, as needed</td>
<td>- Resume medications for concomitant cardiac conditions, as needed</td>
</tr>
<tr>
<td><strong>Tests and visits</strong></td>
<td>- Dental care may be needed before the intervention, and is not recommended for 3-6 months afterwards</td>
<td>- Post operative visits are typically within 1-2 months, and then yearly to check that the valve is working</td>
<td></td>
</tr>
<tr>
<td><strong>Procedure and device</strong></td>
<td>- The doctor will make a small puncture (opening) in the groin for the catheter (long, thin tube), which carries the new valve into the heart, where it is put inside the unhealthy valve</td>
<td>- The doctors will make a cut in the middle of the chest, divide the breastbone, and surgically replace the unhealthy heart valve</td>
<td>- The new heart valve is made of natural tissue (from the heart of a cow or pig) attached to a flexible, metallic mesh frame</td>
</tr>
<tr>
<td></td>
<td>- The new heart valve is made of tissue (from the heart of a cow or pig)</td>
<td>- The heart may be stopped and supported by a machine</td>
<td>- One is asleep during the procedure (general anesthesia)</td>
</tr>
<tr>
<td></td>
<td>- This procedure allows one to be awake (conscious sedation)</td>
<td>- The procedure takes 3-5 hours</td>
<td></td>
</tr>
</tbody>
</table>

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BMJ Rapidrecs for Transcatheter aortic valve implantation versus surgical aortic valve replacement for severe aortic stenosis in low-intermediate risk
-The procedure takes under 2 hours
-TAVI valves are durable for 3 to 5 years but longer term durability data is not yet available
-SAVR valves are durable for 10 to 20 years with long term data in large numbers of patients

-Recovery and adaptation
-After the procedure, in-hospital stay will usually last 2-5 days
-It could take about a month to recover
-Pain from the insertion site usually resolves within a few weeks
-After the procedure, in-hospital stay will usually last 5-10 days
-It could take about 2-3 months to recover
-About 1 patient in 4 report persisting pain in the sternum at after 1 year, with 1 in 10 with more serious pain

-Coordination of care
-It is useful to have someone to help with activities during recovery as one regains their strength

-Adverse effects, interactions and antidote
-Long-term effects of TAVI are less well known than surgery
-See summary of findings
-Additional adverse effects include endocarditis, a rare (risk less than 1% per year) but serious condition of the heart, requiring antibiotics and hospitalization
-Some symptoms can remain after the procedure
-Another procedure may be needed if this one is unsuccessful
-Cognitive decline might occur after the procedure but how often is not clear

-Physical well-being
-Some patients report less appetite and constipation as they recover
-Some patients report poor sleep as they recover

-Emotional well-being
-Data on emotional well-being after TAVI is scant
-Some patients report mood swings, irritability, anxiety, and depression as they recover, although these symptoms may also have been present before surgery
Costs and access

- Travel costs if intervention happens far from home
- Insurance plans may or may not cover some or all aspects of the procedure

Food and drinks

- Dietary restrictions apply if blood thinners are needed

Exercise and activities

- Need to avoid strenuous activity during recovery
- Rehabilitation may help recovery
- If blood thinners are needed, may limit activities with high risk injury

Work and education

- May be 2-6 weeks
- May be 6-8 weeks
- Time until return to work depends on speed of recovery

Travel and driving

- Driving may be limited during recovery
- Driving is limited for 6 weeks until the sternal bone heals

Details about studies used and certainty down- and upgrading

| Mortality, age adjusted | Intervention: Systematic review | Baseline/comparator: Systematic review | Risk of bias: No serious | Loss to follow up robust to worst plausible LFU scenarios; Inconsistency: No serious We found subgroup analyses of transfemoral versus transapical approach to be credible so did not rate down for inconsistency; Indirectness: Serious Differences between the young population of interest and those studied in TAVR studies; Imprecision: Serious Confidence intervals for absolute effects considered to include important benefit and no benefit for patients; Publication bias: No serious |
| Stroke - age adjusted | Intervention: Systematic review | Baseline/comparator: Systematic review [3] | Risk of bias: No serious | Inconsistency: No serious We found subgroup analyses of transfemoral versus transapical approach to be credible so did not rate down for inconsistency. I²=0% in each subgroup; Indirectness: Serious Differences between the young population of interest and those studied in TAVR studies; Imprecision: Serious Confidence intervals for absolute effects include benefit to no difference; Publication bias: No serious |
## Aortic valve reintervention

**Intervention:** Systematic review  
**Baseline/comparator:** Control arm of reference used for intervention

- **Risk of bias:** No serious  
  We considered rating down for unblinded healthcare providers.  
  **Indirectness:** No serious  
  Younger patients are probably more physically active than the older patients, which may lead to more structural valve degeneration and aortic valve reinterventions.  
  **Imprecision:** Serious  
  Very few total events. Confidence interval includes no difference and harm with TAVI.  
  **Publication bias:** No serious

## Aortic valve reintervention - long term

**Intervention:** Systematic review  
**Baseline/comparator:** Systematic review [5]

- **Inconsistency:** Serious  
  Trials suggest inconsistent aortic valve regurgitation short term, may impact on valve reintervention long term.  
  **Indirectness:** Serious  
  Relative effects on aortic reintervention at 2 years (from trials) applied to 10 years time frame.  
  **Imprecision:** Serious  
  Confidence intervals include substantial harm and no important harm from TAVR.

## Permanent pacemaker insertion

**Intervention:** Systematic review  
**Baseline/comparator:** Control arm of reference used for intervention

- **Risk of bias:** No serious  
- **Inconsistency:** Serious  
  The magnitude of statistical heterogeneity was high, with I^2: 87.8%. However, we chose not to rate down for inconsistency because all RCTs suggested an increase in permanent pacemaker insertion.  
  **Indirectness:** Serious  
  Differences between patients <65 and those studied in trials.  
  **Imprecision:** No serious  
  **Publication bias:** No serious

## Life threatening bleeding

**Intervention:** Systematic review  
**Baseline/comparator:** Control arm of reference used for intervention

- **Risk of bias:** No serious  
  Unclear whether outcome adjudicators were blinded.  
  **Indirectness:** No serious  
  Differences between the population of interest and those studied.  
  **Imprecision:** No serious  
  **Publication bias:** No serious

## Atrial fibrillation, age-adjusted

**Intervention:** Systematic review  
**Baseline/comparator:** Systematic review

- **Risk of bias:** No serious  
- **Inconsistency:** No serious  
  We did not rate down certainty in evidence for statistical heterogeneity (I^2=53.5%) because there were significantly fewer atrial fibrillation events in the TAVI group in all 3 trials.  
  **Indirectness:** No serious  
  Differences between the population of interest and those studied.  
  **Imprecision:** No serious  
  **Publication bias:** No serious

## Moderate/severe heart failure symptoms (NYHA ≥III)

**Intervention:** Systematic review  
**Baseline/comparator:** Control arm of reference used for intervention

- **Risk of bias:** No serious  
- **Inconsistency:** No serious  
  Differences between patients <65 and those studied in trials.  
  **Imprecision:** No serious  
  Confidence intervals include harm and no harm with TAVR.

## Myocardial infarction

**Intervention:** Systematic review  
**Baseline/comparator:** Control arm of reference used for intervention

- **Risk of bias:** Serious  
  Inadequate/lack of blinding of outcome assessors, resulting in potential for detection bias.  
  **Indirectness:** No serious  
  Differences between the population of interest and those studied.  
  **Imprecision:** No serious  
  Confidence interval includes benefit and serious harm with TAVR.  
  **Publication bias:** No serious
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Reference</th>
<th>Bias/Imprecision</th>
</tr>
</thead>
</table>
| Acute kidney injury (including transient events) | Reference 1 | Risk of bias: No serious  
Indirectness: Serious Differences between the population of interest and those studied  
Inconsistency: No serious  
Imprecision: No serious  
Publication bias: No serious |
| Baseline/comparator:        | Control arm of reference used for intervention                           |
| Health-related quality of life | Reference 2 | Risk of bias: Serious  
Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Selective outcome reporting  
Indirectness: No serious  
Inconsistency: No serious  
Imprecision: Serious Only data from one study  
Publication bias: No serious |
| Length of index hospitalization | Reference 3 | Risk of bias: No serious  
Indirectness: Serious Patients <65 years old were not well represented in the RCTs. Inferred from studies of older patients.  
Inconsistency: No serious  
Imprecision: No serious Only data from one study. We considered rating down 2 because confidence intervals were not provided, but P-value was very low (<0.0001) and results were consistent with the NOTION study (n=280): 8.9 (SD 6.2) days in TAVI group and 12.9 (SD 11.6) days in SAVR group (P=0.0001).  
Publication bias: No serious |
| Intervention:                | Primary study                                                              |
| Baseline/comparator:        | Systematic review                                                          |
| Pain                         | Reference 4 | Risk of bias: No serious  
Indirectness: No serious  
Inconsistency: No serious  
Imprecision: No serious  
Publication bias: No serious |
| Recovery time                | Reference 5 | Risk of bias: No serious  
Inconsistency: No serious  
Indirectness: No serious  
Imprecision: No serious  
Publication bias: No serious |
| Intervention:                | Systematic review                                                          |
| Other                        | Other[16][15]                                                              |

References


Patients not eligible for transfemoral approach but eligible for transapical approach or SAVR

**Strong Recommendation**

We recommend SAVR rather than TAVI with a transapical approach

**Practical Info**

**Calculation of perioperative risk:** Patients should be assessed regarding their postoperative risk by using a validated risk score such as the STS-PROM online calculator [http://riskcalc.sts.org/stswebriskcalc/#](http://riskcalc.sts.org/stswebriskcalc/#). The risk assessment, which includes many questions regarding cardiac investigations, is performed by the multi-professional heart team. This risk score serves as a starting point for risk assessment. Other considerations, not included in this score, include frailty, severe and circumferential calcification of the ascending aorta (“porcelain aorta”), non-cardiovascular comorbid conditions, cognitive impairment, physical functioning, life expectancy and patient values and expectations.

**Valve durability:** With TAVI, the need for aortic valve reintervention at 2-year follow-up with TAVI, is low but higher relative to SAVR (1.5% vs. 0.5%). There is insufficient data at this time regarding longer term durability of the TAVI devices. Preliminary evidence suggests that long term durability (10 years and longer) may be an issue: in the only long-term followup study reported to date, up to 50% of 378 patients undergoing TAVI with a first generation balloon-expandable device showed signs of degeneration (at least moderate or more aortic stenosis or regurgitation) at 8 years. However, large uncertainty remains. If the relative effect over two years persists long-term,
using best estimates of the need for aortic valve reintervention in 8% of patients post SAVR at 10 years, up to 20-30% of patients post TAVI may require repeat intervention in the long term.

This issue should be discussed with patients considering TAVI with special attention paid to future life expectancy of each patient. Although tables of life expectancy for patients who have reached their current age may overestimate life expectancy in patients with aortic stenosis, this information can be used as a starting point ([https://www.ssa.gov/OACT/population/longevity.html](https://www.ssa.gov/OACT/population/longevity.html)). Patients who have a life expectancy of 10 or more years at time of their initial procedure who want to avoid repeat valve intervention will be likely to prefer SAVR. Repeat TAVIs (valve in valve procedures) are being performed although experience with this approach remains limited. This may mitigate some patients’ concerns about unknown durability of their initial TAVI particularly if they place a high value on avoiding open heart surgery. Finally, the limited durability data that is available is in patients receiving first generation TAVI devices. It is possible 2nd generation devices will have greater durability; this remains to be seen.

**Type of TAVI device:** Devices used in trials include the balloon-expandable Edwards SAPIEN-XT and the self-expanding Medtronic CoreValve. Due to its delivery catheter, the self-expanding CoreValve can be implanted by transfemoral, direct aortic, subclavian/axillar and trans-carotid, but not via transapical approach. The balloon-expandable SAPIEN-XT can be implanted by any access route; the only difference is that for the transapical approach, the delivery system is much shorter and has a bigger outer-diameter. Logically, due to the “antegrade” nature of the transapical access, the bioprosthesis is mounted upside-down as compared for the “retrograde” accesses. The balloon-expandable has merits in terms of less need for permanent pacemaker implantation and less paravalvular leakage.

**Transfemoral TAVI versus non-transfemoral approaches:** Non-transfemoral approaches, in most cases the transapical route, have been associated with an increased risk of deaths, strokes and acute kidney injury relative to SAVR; therefore, we provide a strong recommendation for SAVR rather than non-transfemoral TAVI. The transfemoral approach is the least invasive approach, and many centres perform TAVI as a fully-percutaneous procedure using local anesthesia along with conscious sedation. Patients undergoing transfemoral TAVI spend their acute recovery period in the coronary care unit. Transfemoral TAVI patients experience limited post-procedural pain, allowing early ambulation and a shorter length of stay in the hospital. The transfemoral approach has therefore become the access of choice for TAVI centres following a “minimalist” invasive strategy.

Non-transfemoral accesses are often used in patients presenting with special anatomical characteristics that preclude the femoral access. Patients with previous coronary artery bypass grafting presenting with a graft adherent to the sternum and/or close to the mid-line, re-do sternotomy for SAVR would be at prohibitive risk, even if the STS-PROM calculation is low-intermediate. In this special subset of patients, a non-transfemoral (i.e. transapical) approach for TAVI would be of potential utility.

### Key Info

**Benefits and harms**

Transapical TAVI reduces major bleeds, new onset atrial fibrillations and days in hospital while increasing deaths, strokes, heart failure, need for pacemaker insertions and aortic reinterventions in the short term and perhaps even more so in the long term.

**Quality of evidence**

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

**Preference and values**

Patients are likely to place a high value on avoiding the increased risk of deaths and stroke with transapical TAVI despite its benefits on other outcomes. Patients who place a very high value on avoiding initial open heart surgery are likely to choose transapical TAVI.

**Resources and other considerations**

Important issues, or potential issues not investigated
Rationale

We issue a strong recommendation against TAVI performed by non-transfemoral approaches because we consider the harms to clearly outweigh the benefits. Harms of transapical TAVI include increased risk of mortality, strokes, pacemaker insertions, heart failure and aortic valve reinterventions short term which - despite reduced risk of atrial fibrillation, life-threatening bleeds - this leaves SAVR a clearly preferred alternative for all or nearly all patients. Patients who are ineligible for a transfemoral approach (for example due to peripheral arterial disease) but who place a high value on avoiding initial open heart surgery and are willing to accept an increased risk for aortic valve reintervention may opt to choose TAVR via a transapical approach.

Clinical Question/ PICO

Population: Patients with severe symptomatic aortic stenosis who are at low or intermediate perioperative risk who can not undergo transfemoral TAVR

Intervention: Transapical Transcatheter aortic valve insertion (TAVI)

Comparator: Surgical aortic valve replacement (SAVR)

Summary

Comments to the Evidence profile

- Effect-estimates come from a linked systematic review of trials comparing TAVI and SAVR, except for pain and recovery time (not reported in trials) which come from two observational studies [15]/[16].
- Baseline risk estimates come from linked systematic reviews of observational studies (for mortality, stroke, long term aortic valve reintervention, atrial fibrillation) and trials (for the other outcomes). [5]/[3] Baseline risks are age-stratified only for mortality.
- Aortic valve reintervention long term (at 10 years) was not reported in observational studies identified in the systematic review. Studies report structural valve deterioration which we used as an intermediate outcome reflecting need for aortic valve reintervention. Therefore we rated down for very serious indirectness both for baseline risk and for effect-estimates, the latter coming from trials reporting short term aortic valve reintervention. We also rated down for imprecision, resulting in very low certainty in the absolute effect estimates.

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</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality</strong></td>
<td>Hazard Ratio 1.34 (CI 95% 0.91 - 1.97) Based on data from 552 patients in 2 studies. (Randomized controlled) Follow up 2 years</td>
<td>Surgical aortic valve replacement (SAVR) 196 per 1000 Transapical Transcatheter aortic valve insertion (TAVI) 253 per 1000 Difference: 57 more (CI 95% 16 fewer - 153 more)</td>
<td>Moderate Due to borderline inconsistency and imprecision</td>
<td>Transapical TAVI might increase the risk of death.</td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td>Relative risk 1.67 (CI 95% 0.97 - 2.87) Based on data from 552 patients in 2 studies. (Randomized controlled)</td>
<td>Surgical aortic valve replacement (SAVR) 67 per 1000 Transapical Transcatheter aortic valve insertion (TAVI) 112 per 1000 Difference: 45 more</td>
<td>Moderate Due to serious imprecision</td>
<td>Transapical TAVI probably increases the risk of stroke.</td>
</tr>
<tr>
<td>Condition</td>
<td>Follow up</td>
<td>Relative Risk</td>
<td>CI 95%</td>
<td>Difference</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>-----------</td>
<td>---------------</td>
<td>--------</td>
<td>------------</td>
</tr>
<tr>
<td>Aortic valve reintervention</td>
<td>2 years</td>
<td>3.25</td>
<td>1.29 - 8.14</td>
<td>7 more per 1000</td>
</tr>
<tr>
<td>Permanent pacemaker insertion</td>
<td>2 years</td>
<td>2.46</td>
<td>1.17 - 5.15</td>
<td>134 more per 1000</td>
</tr>
<tr>
<td>Moderate/severe heart failure symptoms (NYHA ≥III)</td>
<td>2 years</td>
<td>1.29</td>
<td>1.08 - 1.55</td>
<td>18 more per 1000</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2 years</td>
<td>0.87</td>
<td>0.59 - 1.29</td>
<td>5 fewer per 1000</td>
</tr>
<tr>
<td>Aortic valve reintervention - long term</td>
<td>10 years</td>
<td>3.25</td>
<td>1.29 - 8.14</td>
<td>137 more per 1000</td>
</tr>
<tr>
<td>Life threatening bleeding</td>
<td>2 years</td>
<td>0.53</td>
<td>0.42 - 0.67</td>
<td>194 fewer per 1000</td>
</tr>
</tbody>
</table>
### Atrial fibrillation (includes transient postoperative) 2 years

Relative risk 0.43 (CI 95% 0.35 - 0.56) Based on data from 3,058 patients in 3 studies. (Randomized controlled) Follow up 2 years

<table>
<thead>
<tr>
<th>312 per 1000</th>
<th>134 per 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference: 178 fewer per 1000 (CI 95% 137 fewer - 203 fewer)</td>
<td>Moderate Due to serious indirectness</td>
</tr>
</tbody>
</table>

TAVI reduces the risk of new onset atrial fibrillation.

### Acute kidney injury 2 years

Relative risk 1.54 (CI 95% 0.77 - 3.07) Based on data from 552 patients in 2 studies. (Randomized controlled) Follow up 2 years

<table>
<thead>
<tr>
<th>43 per 1000</th>
<th>66 per 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference: 23 more per 1000 (CI 95% 89 more - 10 fewer)</td>
<td>Low Due to serious imprecision and inconsistency</td>
</tr>
</tbody>
</table>

Transapical TAVI might increase the risk of AKI.

### Aortic valve reintervention - short term 2 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

<table>
<thead>
<tr>
<th>4 per 1000</th>
<th>13 per 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference: 9 more per 1000 (CI 95% 29 more - 1 more)</td>
<td>Low Due to borderline risk of bias and imprecision; serious indirectness</td>
</tr>
</tbody>
</table>

TAVI might increase the risk of aortic valve reintervention.

### Health-related quality of life 2 years

Measured by: Difference from baseline in KCCQ Score. Minimal important difference is 5 points. Scale: 0-100 High better Based on data from 797 patients in 1 studies. (Randomized controlled) Follow up 2 years

<table>
<thead>
<tr>
<th>18.7 points (Mean)</th>
<th>22.2 points (Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference: MD 3.5 more (CI 95% 1.9 fewer - 8.9 more)</td>
<td>Very Low Due to serious risk of bias, imprecision, and indirectness</td>
</tr>
</tbody>
</table>

TAVI may have little or no impact compared to SAVR on HRQoL.

### Length of index hospitalization

Lower better Based on data from: 2,032 patients in 1 studies. (Randomized controlled)

<table>
<thead>
<tr>
<th>12 days (Median)</th>
<th>8 days (Median)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difference: MD 4 fewer (CI 95% 3 fewer - 5 fewer)</td>
<td>Moderate Due to serious indirectness</td>
</tr>
</tbody>
</table>

TAVI probably reduces the length of hospital stay.

### Pain

Based on data from 397 patients in 2 studies

A large prospective observational study showed that ~28% have chronic post-sternotomy pain at 1 year and ~13% have pain >3/10 on visual analog scale. One smaller unadjusted observational study showed no difference in pain scores between TAVI and SAVR at 3 months.

TAVI was associated with significantly less shortness of breath at one month (2 RCTs). Patients in the TAVI group had a shorter index

### Recovery time

Based on data from 3,058 patients in 3 studies

TAVI may reduce recovery time
<table>
<thead>
<tr>
<th>Practical issues</th>
<th>Surgical aortic valve replacement (SAVR)</th>
<th>Transapical Transcatheter aortic valve insertion (TAVI)</th>
<th>Both</th>
</tr>
</thead>
</table>
| Medication routine | - Antiplatelet or anticoagulation medication after procedure, as needed  
- Pain medication after procedure, as needed  
- Resume medications for concomitant cardiac conditions, as needed | | |
| Tests and visits | - Dental care may be needed before the intervention, and is not recommended for 3-6 months afterwards  
- Post operative visits are typically within 1-2 months, and then yearly to check that the valve is working | | |
| Procedure and device | - The doctor will make a small puncture (opening) in the groin for the catheter (long, thin tube), which carries the new valve into the heart, where it is put inside the unhealthy valve - The new heart valve is made of natural tissue (from the heart of a cow or pig) attached to a flexible, metallic mesh frame - This procedure allows one to be awake (conscious sedation) - The procedure takes under 2 hours - TAVI valves are durable for 3 to 5 years but longer term durability data is not yet available | - The doctors will make a cut in the middle of the chest, divide the breastbone, and surgically replace the unhealthy heart valve - The new heart valve is made of tissue (from the heart of a cow or pig) - The heart may be stopped and supported by a machine - One is asleep during the procedure (general anesthesia) - The procedure takes 3-5 hours - TAVI valves are durable for 10 to 20 years with long term data in large numbers of patients | |
| Recovery and adaptation | - After the procedure, in-hospital stay will usually last 2-5 days  
- It could take about a month to recover  
- Pain from the insertion site usually resolves within a few weeks | - After the procedure, in-hospital stay will usually last 5-10 days  
- It could take about 2-3 months to recover  
- About 1 patient in 4 report persisting pain in the sternum at after 1 year, with 1 in 10 with more serious pain | |
<table>
<thead>
<tr>
<th>Topic</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coordination of care</td>
<td>-It is useful to have someone to help with activities during recovery as one regains their strength</td>
</tr>
<tr>
<td>Adverse effects, interactions and antidote</td>
<td>-Long-term effects of TAVI are less well known than surgery</td>
</tr>
<tr>
<td>Physical well-being</td>
<td>-Some patients report less appetite and constipation as they recover</td>
</tr>
<tr>
<td>Emotional well-being</td>
<td>-Some patients report poor sleep as they recover</td>
</tr>
<tr>
<td>-Data on emotional well-being after TAVI is scant</td>
<td></td>
</tr>
<tr>
<td>-Some patients report mood swings, irritability, anxiety, and depression as they recover, although these symptoms may also have been present before surgery</td>
<td></td>
</tr>
<tr>
<td>Costs and access</td>
<td>-Travel costs if intervention happens far from home -Insurance plans may or may not cover some or all aspects of the procedure</td>
</tr>
<tr>
<td>Food and drinks</td>
<td>-Dietary restrictions apply if blood thinners are needed</td>
</tr>
<tr>
<td>Exercise and activities</td>
<td>-Need to avoid strenuous activity during recovery -Rehabilitation may help recovery -If blood thinners are needed, may limit activities with high risk injury</td>
</tr>
</tbody>
</table>
**Details about studies used and certainty down- and upgrading**

<table>
<thead>
<tr>
<th>Study Area</th>
<th>Intervention</th>
<th>Baseline/comparator</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Publication bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>No serious</td>
<td>Serious</td>
<td>No serious</td>
<td>Serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Stroke</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Aortic valve reintervention</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>No serious</td>
<td>No serious</td>
<td>Serious</td>
<td>No serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Permanent pacemaker insertion</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Moderate/severe heart failure symptoms (NYHA ≥III)</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Myocardial</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>Serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
</tr>
</tbody>
</table>

**Work and education**
- May be 2-6 weeks
- May be 6-8 weeks
- Time until return to work depends on speed of recovery

**Travel and driving**
- Driving may be limited during recovery
- Driving is limited for 6 weeks until the sternal bone heals

**Mortality**
- Risk of bias: No serious
- Inconsistency: Serious
  The magnitude of statistical heterogeneity was high, with I^2: 45.3%.
- Indirectness: No serious
- Imprecision: Serious
  Wide confidence intervals
- Publication bias: No serious

**Stroke**
- Risk of bias: No serious
- Inconsistency: No serious
  We found subgroup analyses of transfemoral versus transapical approach to be credible so did not rate down for inconsistency. I^2=0% in each subgroup.
- Indirectness: No serious
- Imprecision: Serious
  Wide confidence intervals
- Publication bias: No serious

**Aortic valve reintervention**
- Risk of bias: No serious
  We considered rating down for unblinded healthcare providers.
- Indirectness: Serious
  We do not have RCT data specifically from transapical patients.
- Imprecision: Serious
  Very few total events. Confidence interval includes no difference and harm with TAVI.
- Publication bias: No serious

**Permanent pacemaker insertion**
- Risk of bias: No serious
  The magnitude of statistical heterogeneity was high, with I^2: 87.8%.
  However, we chose not to rate down for inconsistency because all RCTs suggested an increase in permanent pacemaker insertion.
- Indirectness: No serious
- Imprecision: No serious
- Publication bias: No serious

**Moderate/severe heart failure symptoms (NYHA ≥III)**
- Risk of bias: No serious
- Inconsistency: No serious
- Indirectness: No serious
- Imprecision: Serious
  Confidence intervals include important harm and no harm with TAVR.
- Publication bias: No serious

**Myocardial**
- Risk of bias: Serious
  Inadequate/lack of blinding of outcome assessors, resulting in potential
<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Baseline/comparator: Control arm of reference used for intervention</th>
<th>Risk of bias: No serious</th>
<th>Inconsistency: No serious</th>
<th>Indirectness: No serious</th>
<th>Imprecision: No serious</th>
<th>Publication bias: No serious</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infarction</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>We considered rating down for unblinded healthcare providers.</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Aortic valve reintervention - long term</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>Relative effects on aortic reintervention at 2 years (from trials) applied to 10 years time frame. We do not have RCT data specifically from transapical patients.</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Life threatening bleeding</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>Unclear whether outcome adjudicators were blinded.</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Atrial fibrillation (includes transient postoperative)</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>Unable to perform subgroup analysis by TAVI approach.</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>Clinical heterogeneity - STACCATO study only reported AKI severe enough to require dialysis (1 of 70 patients).</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Aortic valve reintervention - short term</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>We considered rating down for unblinded healthcare providers.</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Health-related quality of life</td>
<td>Systematic review</td>
<td>Control arm of reference used for intervention</td>
<td>Inadequate concealment of allocation during randomization process, resulting in potential for selection bias, Selective outcome reporting</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
</tr>
<tr>
<td>Length of index hospitalization</td>
<td>Primary study</td>
<td>Control arm of reference used for intervention</td>
<td>We do not have RCT data specifically from transapical patients.</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
<td>No serious</td>
</tr>
</tbody>
</table>
References


[6] Thyregod HGH Two-Year Outcomes in Patients With Severe Aortic Valve Stenosis Randomized to Transcatheter Versus Surgical Aortic Valve Replacement: The All-Comers Nordic Aortic Valve Intervention Randomized Clinical Trial.. Circulation. Cardiovascular interventions 2016;9(6): Pubmed

[7] Thyregod HGH, Steinbruchel DA, Ihlemann N, Nissen H, Kjeldsen BJ, Petursson P, Ngo AT, Olsen NT, Chang Y, Franzen OW, Engstrom T, Clemmensen P, Olsen PS, Thyregod HGH Two-Year Outcomes in Patients With Severe Aortic Valve Stenosis Randomized to Transcatheter Versus Surgical Aortic Valve Replacement in Patients With Severe Aortic Valve Stenosis: 1-Year Results From the All-Comers NOTION Randomized Clinical Trial.. Journal of
2 - Flow chart of management alternatives for severe aortic stenosis

Below we provide a flow chart of overall management of patients with severe symptomatic aortic stenosis (AS) to put our recommendations in context with other alternative care and treatment options.

Severe symptomatic AS

- Life expectancy > 1 year if AVR performed
  - No: Palliative therapy *
  - Yes: Bioprosthetic AVR planned

- Mechanical SAVR *
  - No: Mechanical SAVR *
  - Yes: Transfemoral AVR approach possible

Low to intermediate surgical risk
- Transfemoral TAVI *
  - < 65 years: SAVR
    - Strong recommendation
  - 65-74 years: SAVR
    - Weak recommendation
  - 75-84 years: Transfemoral TAVI
    - Weak recommendation
  - 85+ years: Transfemoral TAVI
    - Strong recommendation

High or prohibitive surgical risk
- Transfemoral TAVI *
  - SAVR over transapical TAVI
    - Strong recommendation
  - Consider transapical TAVI *

* Not based on evidence in this review
BMJ Rapidrecs for Transcatheter aortic valve implantation versus surgical aortic valve replacement for severe aortic stenosis in low-intermediate risk

Flow chart

Info Box

Severe symptomatic AS

Life expectancy >1 year if AVR performed

Palliative therapy *

No

Bioprosthetic AVR planned

Yes

Transfemoral AVR approach possible

No

Surgical AVR possible

Yes

Low to intermediate surgical risk

High or prohibitive surgical risk

Transfemoral TAVI *

SAVR over transapical TAVI
Strong recommendation

< 65 years

SAVR
Strong recommendation

65-74 years

SAVR
Weak recommendation

75-84 years

Transfemoral TAVI
Weak recommendation

85+

Transfemoral TAVI
Strong recommendation

* Not based on data
3 - Background and methods for BMJ-Rapidrecs

BACKGROUND

From MAGIC to WikiRecs and the BMJ Rapidrecs project

Translating research for clinical practice is challenging. Systematic reviews of all available evidence and trustworthy clinical practice
guidelines with recommendations for clinicians constitute key vehicles for knowledge translation and information resources for decision
makers and clinicians. Organisations creating systematic reviews and guidelines often struggle with barriers, often not resulting in
appropriate and timely evidence synthesis and dissemination, in particular in the face of potentially practice-changing evidence.

Making GRADE the Irresistible Choice (MAGIC) - a research and innovation program (www.magicproject.org) and non-profit organisation
based in Oslo, Norway - was created to solve key problems with authoring, publication and updating of clinical practice guidelines. Through their online authoring and publication platform (http://www.magicapp.org) clinicians may access digitally structured and multilayered evidence summaries, trustworthy recommendations and consultation decision aids on all devices for use in their clinical practice.

Whereas an increasing number of organisations use MAGICapp to create guidelines challenges remain that go beyond dissemination.
There is a need for more overarching solutions to make sure the loop from evidence production, through synthesis, dissemination and
implementation is closed, ultimately resulting in documented improved care, increased value and reduced waste of health care resources. This
realisation has resulted in the "Digital and Trustworthy Evidence Ecosystem project" where currently siloed actors are linked together using
digitally structured data in platforms such as MAGICapp.

MAGIC has - as part of the Evidence Ecosystem project - launched the WikiRecs (Rapid Recommendations and Evidence summaries
Composed as Synopses) project to circumvent organisational barriers and provide clinicians with guidance for practice-changing evidence
through an international collaborative network of people getting the work done, synthesizing and disseminating evidence and
recommendations in MAGICapp within 90 days of the publication of potentially practice changing evidence. MAGICapp is not sufficient to
disseminate evidence and recommendations to a worldwide audience which makes scientific journals attractive partners in the WikiRecs
project.

In the BMJ-Rapidrecs project the MAGIC WikiRecs group has partnered with the British Medical Journal (BMJ) to publish rapid
recommendations as a synopsis paper in their journal, along with systematic reviews linked to the recommendations. The clinical practice
guideline with recommendations here in MAGICapp is as such one of a package which includes recommendations and one or more systematic
reviews also published in the BMJ. Below we outline the processes and methods used to translate evidence into evidence
summaries, recommendation/s and consultation decision aids for clinical practice in a timely and transparent way that minimises bias and
incorporates the experience of patients. For these rapid recommendations the Rapidrecs group will consider both new and old evidence that
might alter the balance of clinical practice either towards or against current practice.

PROCESS

Process overview
The BMJ Rapidrecs follows a predefined protocol with the following steps, developed in collaboration between the WikiRecs group and the
BMJ:
1. We monitor the literature for practice-changing evidence through
   - Formal monitoring with McMaster Premium LiteratUre Service (PLUS)
2. The RapidRecs executive and The BMJ choose among the identified potentially-practice changing evidence which clinical questions to pursue, based on relevance to a wide audience, widespread interest, and likelihood to change practice.

3. We incorporate the evidence into the existing body of evidence, and broader context of clinical practice via:
   - a rapid and high quality systematic review and meta-analysis on the benefits and harms of this approach with a focus on the outcomes that matter to patients
   - Parallel rapid recommendation/s made in accordance with standards for trustworthy guidelines by an international panel including patients with relevant lived experience as well as front-line clinicians, researchers and methodologists.[20]
   - The systematic review group and the recommendation panel will apply standards for trustworthy guidelines. They will use the GRADE approach, which has developed a transparent process to rate the quality (or certainty) of evidence and grade the strength of recommendations (refs).
     - Further research may be conducted including:
       - A systematic review of observational studies to identify baseline risk estimates that most closely represent the population at the heart of the clinical question, a key component when calculating the estimates of absolute effect of the intervention.
       - A systematic review on the preferences and values of patients on the topic.

4. Disseminate the rapid recommendation/s through
   - publication of the research in BMJ journals
   - short summary of recommendations for clinicians published in The BMJ as well as through press releases and/or marketing to media outlets and relevant parties such as patient groups
   - Links to BMJ Group’s Best Practice point of care resource
   - MAGICapp which provides recommendations and all underlying content in digitally structured multilayered formats for clinicians and others who wish to re-examine or consider national or local adaptation of the recommendations.

Informal monitoring literature by BMJ-Rapidrecs expert groups, including clinician specialists and patients
Who is involved?
Researchers, systematic review and guideline authors, clinicians, and patients often work in silos. Academic journals may publish work from any one or combinations of these groups of people and findings may also be published in the media. But it is rare that these groups work together to produce a comprehensive package of content. We represent a collaborative and international network of people aiming to circumvent organisational barriers in order to provide clinicians with guidance for potentially practice-changing evidence.

Our collaboration involves:
1. The WikiRecs group of researchers who coordinate the systematic review group and the recommendation panels within BMJ Rapidrecs. The WikiRecs group is part of MAGIC (http://www.magicproject.org) as outlined above.
2. The BMJ, which helps identifying practice-changing evidence on key clinical questions, coordinates the editorial process and publishes the package of content linking to the MAGICapp that is presented in a user friendly and journalistic way.

METHODS FOR THE RAPID RECOMMENDATIONS

The formation of these recommendations adheres to standards for trustworthy guidelines with an emphasis on patient involvement, strict management of conflicts of interests as well as transparent and systematic processes for assessing the quality of evidence and for moving from evidence to recommendations.

Guidance on how the panel is picked and how they contribute

Panel members are sought and screened through an informal process with a particular emphasis on the following elements:
- At least one but no more than three authors of the systematic reviews will serve on the recommendation panel.
- At least one patient representative with lived experience as a community panel member. This person receives patient oriented documents to explain the process and is allocated a link panel member to empower their contribution.
- A full spectrum of practicing clinicians involved in the management of the clinical problem and patients it affects, including front-line clinicians with generalist experience and those with deep content clinical and research expertise in the particular topic.
- Methodological experts in health research methodology and guideline development.

Any potential conflicts of interest are managed with extreme prudence:
- No panel member may have a financial interest that is judged by the panel or The BMJ team as relevant to the topic.
- No more than two panel members with an intellectual interest on the topic.

Illustrative example: For the BMJ Rapidrecs on TAVI versus SAVR for patients with severe aortic stenosis the panel recruitment of content experts and community panel members was challenging. Content experts in this area are cardiologists and cardiac surgeons, many of whom have financial conflicts of interests through interactions with the device providers through advisory boards and participation in industry-funded trials. The Chair of the panel was able, with considerable effort and ingenuity, to recruit 3 excellent and unconflicted content experts. Another challenge was to find patient representatives who were able to contribute, as severe aortic stenosis typically affects older and frail people. Two community members were ultimately
recruited, and they both contributed effectively throughout the process.

How the panel meets and works throughout the process
The international panel communicates via teleconferences and e-mail exchange of written documents throughout the process. Minutes from teleconferences are audiorecorded, transcribed, and stored for later documentation (available for peer-reviewers at request).

Teleconferences typically occur at three timepoints, with circulated documents by e-mail in advance:
1. At the initiation of the process to provide feedback on the systematic review protocol (e.g., selection of patient-important outcomes and appropriate prespecified analysis of results) before it is performed.
2. At the evidence summary stage with discussion, feedback and agreement on draft evidence GRADE evidence profile) prepared by the Chair and the methods editor based on the systematic review.
3. At the recommendation formulation phase with discussion, feedback and agreement on draft recommendations and other content underlying the recommendation (e.g., GRADE SoF-table, key information, rationale, practical advice)

Following the last teleconference the final version of the recommendations and all underlying content is circulated by e-mail specifically requesting feedback from all panel members to document agreement before submission to the BMJ. Additional teleconferences are arranged as needed.

Illustrative example: For the development of the TAVI versus SAVR recommendations five teleconferences were arranged. Through two separate teleconferences (needed to let all attend with their busy schedules) for the evidence summary stage content experts provided crucial input to evidence assessment (e.g., type of TAVI devices used in trials). For the recommendation formulation phase the panel needed two teleconferences to discuss all elements in detail, followed by more than 100 e-mails with specific issues to be sorted out. All panel members agreed on final recommendations.

How we move from research findings to recommendations

What information will be considered?
The panel will consider best current evidence from available research. Beyond systematic reviews - performed in the context of the BMJ Rapidrecs - the panel may also include a number of other research papers to further inform the recommendations, and refer to these accordingly.

How is a trustworthy guideline made in BMJ WikiRecs?
The Institute of Medicine laid out how trustworthy guidelines should be made and created key standards as outlined in the table below. The standards are similar to those developed by the Guideline International Network (G-I-N). These standards have been widely adopted by the international guideline community. Peer reviewers of the recommendation article are asked whether their found the guideline trustworthy.

The table below lays out how we hope to meet the standards for our rapid recommendations:

<table>
<thead>
<tr>
<th>Table 1: Summary of Institute of Medicine 8 standards for trustworthy guidelines [20] and how the BMJ Rapidrecs responds to the standards</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Establishing transparency</strong></td>
</tr>
<tr>
<td><em>The processes by which a CPG is developed and funded should be detailed explicitly and publicly accessible</em></td>
</tr>
<tr>
<td>• This method is available and published as a supplementary file as well as in MAGICapp where all recommendations and underlying content is available.</td>
</tr>
<tr>
<td>• We ask the peer-reviewers to judge whether the guidance is trustworthy and will respond to concerns raised.</td>
</tr>
<tr>
<td><strong>2. Managing conflicts of interest</strong></td>
</tr>
<tr>
<td><em>Prior to selection of the guideline development group, individuals being considered for membership should declare all interests and activities potentially resulting in COI with development group activity...</em></td>
</tr>
<tr>
<td>• Interests of each panel member are declared and published with the rapid recommendations</td>
</tr>
<tr>
<td>• No one with financial interests in the past three years, or forthcoming 12 months will participate - as judged by the panel chair and the BMJ</td>
</tr>
<tr>
<td>• No more than two panel members have declared an intellectual conflict of interest. Such conflicts include having taken a position on the issue for example by a written editorial, commentary, or conflicts related to performing a primary research study or systematic review on the topic.</td>
</tr>
<tr>
<td>• The chair must have methods expertise, a clinical background and no financial or intellectual interests declared.</td>
</tr>
<tr>
<td>• Funders and pharmaceutical companies have no role in these recommendations.</td>
</tr>
</tbody>
</table>
3. Guideline Development Group Composition
"The guideline development group should be multidisciplinary and balanced, comprising a variety of methodological experts and clinicians, and populations expected to be affected by the CPG"

- aim to include representation from most or every major geographic region in the world, with specific efforts made to achieve gender-balance.
- We will facilitate patient and public involvement by including patient experience, via patient-representatives and systematic reviews on values and preferences to guide outcome choices and relative weights of each outcome, where available
- Patient-representatives will be given priority during panel meetings and will have an explicit role in vetting final values and preferences judgements.

"CPG developers should use systematic reviews that meet standards set by the IOM. Guideline development group and systematic review team should interact regarding the scope, approach, and output of both processes"

- Each rapid recommendation will be based on one or more high-quality SRs either developed and published in parallel with our BMJ Rapidrecs or after the publication by such a SR by other groups.
- The recommendation panel and SR teams will interact, with up to three members participating in both teams to facilitate communication and continuity in the process.

5. Establishing Evidence Foundations for and Rating Strength of Recommendations
"For each recommendation: explain underlying reasoning, including a clear description of potential benefits and harms, a summary of relevant available evidence and description of the quality, explain the part played by values, opinion, theory, and clinical experience in deriving the recommendation, “provide rating of strength of recommendations”

- The GRADE approach will provide the framework for establishing evidence foundations and rating strength of recommendations.[22][23] For each recommendation systematic and transparent assessments are made across the following key factors:
  ◦ Absolute benefit and harms for all patient-important outcomes of a particular action through structured evidence summaries (e.g. GRADE Summary of Findings tables) [23]
  ◦ Quality of the evidence
  ◦ Values and preferences of patients
  ◦ Resources and other considerations (e.g. feasibility, applicability, equity)

- Each outcome will - if data are available through systematic reviews - include an effect estimate and confidence interval, with a measure of certainty in the evidence, as presented in SoF-tables. If such data are not available narrative summaries will be provided.
- A summary of the underlying reasoning and all additional information (e.g. key factors, practical advice, references) is available online in an interactive format at www.magicapp.org. This summary includes descriptions of how theory (e.g. patophysiology) and clinical experience played into the evidence assessment and recommendation development.
- Recommendations will be rated either weak or strong, as defined by GRADE. [22]
- If the panel disagree on evidence assessment or strength of recommendations, we will follow a structured consensus process customized to the GRADE system and report any final differences in opinion, with their rationale, in the online supplement and online at www.magicapp.org.

6. Articulation of recommendations
"Recommendations should be articulated in a standardized form detailing precisely what the recommended action is, and under what circumstances it should be performed, and so that compliance with the recommendation(s) can be evaluated"

- Each recommendation will appear at the top of the infographic in the BMJ and are available in standardised formats in MAGICapp, articulated to be actionable based on best current evidence on presentation formats of guidelines. [18]
- There is a statement included in each summary article in The BMJ and in the MagicApp that these are recommendations to provide clinicians with guidance. They do not form a mandate of action and should be contextualised in the healthcare system a clinician’s works in, and or with an individual patient.
7. External review
“External reviewers should comprise a full spectrum of relevant stakeholders, authorship should be kept confidential, all reviewer comments should be considered, a rationale for modifying or not should be recorded in writing, a draft of the recommendation should be made available to general public for comment.”

- At least two external peer-reviewers and one patient reviewer will review the article for The BMJ and provide open peer review. Each will have access to all the information in the package. They will be asked for general feedback as well as to make an overall judgement on whether they view the guidelines as trustworthy.
- A BMJ series adviser with methodological and, or statistical expertise will review the BMJ Rapidrecs publication and the systematic reviews.
- The Rapidrecs panel will be asked to read and respond to the peer review comments and make amendments where they judge reasonable.
- The BMJ and WikiRecs team may, on a case-by-case basis, choose to invite key organizations, agencies, or patient/public representatives to provide and submit public peer-review.
- There will be post-publication public review process where people can provide comments and feedback through MAGICapp (or through the BMJ). The Chair will on behalf of panel authors aim to respond to each publicly-available peer-review within 30 days, for a period of six months after publication.

8. Updating
“The date for publication, systematic review and proposed date for future review should be documented, the literature should be monitored regularly and the recommendation should be updated when warranted by new evidence.”

- The Rapidrecs panel will through monitoring of new research evidence for published BMJ Rapidrecs aim to provide updates of the recommendations in situations where the evidence suggest a change in practice. These updates will be initially performed in MAGICapp and submitted to the BMJ for consideration of publication of a new Rapidrecs.
References


[8]


