Supervised exercise for intermittent claudication

Main editor
Ton Kuijpers, Trudy bekkering, Mieke Vermandere, Bert Aertgeerts, and the RapidRecs guideline panel

Publishing and version history
v0.1 published on 03.12.2019
Summary of recommendations

1 - Supervised exercise (SE) versus revascularisation (and revascularisation combined with SE)

**Weak Recommendation**

We suggest supervised exercise over revascularisation.

*This recommendation is for patients with intermittent claudication due to peripheral arterial disease.*

**Weak Recommendation**

We suggest supervised exercise over revascularisation combined with supervised exercise.

*This recommendation is for patients with intermittent claudication due to peripheral arterial disease.*

2 - Primary Care Rapid Recommendations: Background and methods

3 - Supervised exercise for intermittent claudication: a clinical practice guideline
### 1 - Supervised exercise (SE) versus revascularisation (and revascularisation combined with SE)

**Weak Recommendation**

We suggest supervised exercise over revascularisation.

*This recommendation is for patients with intermittent claudication due to peripheral arterial disease.*

**Key Info**

**Benefits and harms**

Small net benefit, or little difference between alternatives

At six months, the panel agreed that there is probably little or no difference for disease-specific quality of life, possibly a small increase in maximum walking distance and possibly little or no difference in pain free walking distance.

At 12 months, there is probably little or no difference for disease-specific quality of life and there is possibly a small decrease in maximum walking distance and in pain-free walking distance. There is possibly little or no difference for major cardiovascular events, serious adverse events and additional interventions.

At 5 and 7 years, there is probably little or no difference for disease-specific quality of life, and possibly little or no difference for major cardiovascular events and additional surgical interventions.

**Certainty of the Evidence**

Low

There is low certainty that there is a small benefit in maximum walking distance and in pain free walking distance at 12 months. There is moderate certainty that there is little or no difference for disease specific quality of life and serious adverse events. There is low to moderate certainty that there is little or no difference for receiving additional surgical interventions and low certainty that there is little or no difference for major cardiovascular events.

**Preference and values**

Substantial variability is expected or uncertain

Patients can perceive small increases in walking distance as very important, depending on their personal situation. Thus, although at 6 and 12 months follow-up the possible benefit in walking distance in favor of SE is only small, this may matter to patients.

In general, there possibly is little to no difference in effects between SE and revascularisation. But revascularisation involves risks, such as postsurgical bleeding, wound infection or thromboembolism. However, in the era of minimally invasive endovascular revascularization techniques, the risk associated with revascularization remains limited. Although we believe there is moderate to high variability between patients in how they weigh the benefits and harms of SE compared to revascularisation we expect the majority of patients will choose SE, but some patients would not.

**Resources and other considerations**

Important issues, or potential issues not investigated

From a societal perspective, SE seems to be more cost-effective than revascularisation. This is based on a study that assessed the costs of the stepped care model (primary SE treatment followed by revascularization in case of SE failure). This pragmatic study, reflecting daily practice, suggested that implementation of a stepped care model for patients with IC may lead to significant savings of health care resources. [2]

The panel believes most patients feel SE is an acceptable option. Some patients are highly motivated to start a SE program, others with less motivation, or those with practical constraints - may prefer revascularisation.

SE is not an easy solution, which is illustrated by the low compliance of patients following such a program. [3] Patients need to be motivated to start and continue SE as it takes a lot of time and perseverance. Pre-exercise patient education and personalised exercise prescriptions may result in improvements in both function and compliance. [4] New techniques, including smart-phone apps, are evolving and might help to decrease barriers of adherence and motivation. [5,6] Also, SE may have additional health benefits, including engagement in an active and healthy lifestyle. The frequent contacts with a health professional may possibly reinforce such changes.
Rationale
In general, there is possibly little to no difference in effects and adverse events between SE and revascularization. We expect the majority of patients will choose SE because revascularization is an invasive procedure, which comes with certain risks. There might nevertheless be a substantial proportion of patients that will choose revascularization, therefore we issue a weak recommendation. This means both options need to be discussed with the patient, ideally in a process of shared decision-making.

Clinical Question/ PICO

| Population: | Patients with intermittent claudication due to peripheral arterial disease |
| Intervention: | Revascularisation |
| Comparator: | Supervised Exercise Therapy |

Summary
The panel agreed that, comparing revascularisation with supervised exercise at 12 months:
- there is probably little or no difference for disease-specific quality of life (moderate quality evidence);
- there is possibly a small decrease in maximum walking distance (175m lower, low quality evidence);
- there is possibly a small decrease in pain-free walking distance (86m lower, low quality evidence); and
- there is possibly little or no difference for major cardiovascular events, serious adverse events and additional interventions (low quality evidence).

<table>
<thead>
<tr>
<th>Outcome Timeframe</th>
<th>Study results and measurements</th>
<th>Absolute effect estimates</th>
<th>Certainty of the Evidence (Quality of evidence)</th>
<th>Plain text summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major cardiovascular events (&lt;1 year)</td>
<td>Relative risk 0.97 (CI 95% 0.24 - 3.86) Based on data from 236 patients in 3 studies. (Randomized controlled)</td>
<td>34 per 1000 Supervised Exercise Therapy 33 per 1000 Revascularisation</td>
<td>Low Due to very serious imprecision</td>
<td>May have little or no difference</td>
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<tr>
<td>Up to 1 year</td>
<td>Difference: 1 fewer per 1000 (CI 95% 26 fewer - 97 more)</td>
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<tr>
<td>7 Critical</td>
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<tr>
<td>Major cardiovascular events (long term)</td>
<td>Relative risk 2.53 (CI 95% 0.79 - 8.15) Based on data from 224 patients in 2 studies. (Randomized controlled)</td>
<td>27 per 1000 Supervised Exercise Therapy 68 per 1000 Revascularisation</td>
<td>Low Due to very serious imprecision</td>
<td>May have little or no difference</td>
</tr>
<tr>
<td>Range 5-7 years</td>
<td>Difference: 41 more per 1000 (CI 95% 6 fewer - 193 more)</td>
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<tr>
<td>7 Critical</td>
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<tr>
<td>Serious adverse events</td>
<td>Relative risk 1.62 (CI 95% 0.7 - 3.72) Based on data from 500 patients in 5 studies. (Randomized controlled)</td>
<td>32 per 1000 Supervised Exercise Therapy 52 per 1000 Revascularisation</td>
<td>Moderate Due to serious imprecision</td>
<td>Probably little or no difference</td>
</tr>
<tr>
<td>Up to 1 year</td>
<td>Difference: 20 more per 1000 (CI 95% 10 fewer - 87 more)</td>
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<tr>
<td>8 Critical</td>
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</tr>
<tr>
<td>Variable</td>
<td>Description</td>
<td>Relative Risk (CI)</td>
<td>Difference (CI)</td>
<td>Risk of Bias/Imprecision</td>
</tr>
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<td>-----------------------------------------</td>
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<td>---------------------------------------------</td>
</tr>
<tr>
<td>Receiving additional interventions (&lt;1 year)</td>
<td>Based on data from 306 patients in 3 studies. (Randomized controlled)</td>
<td>1.14 (0.63 - 2.06)</td>
<td>17 more per 1000 (44 fewer - 126 more)</td>
<td>Moderate Due to serious imprecision</td>
</tr>
<tr>
<td>Receiving additional interventions (long term) Range 5-7 years</td>
<td>Based on data from 261 patients in 3 studies. (Randomized controlled)</td>
<td>0.75 (0.44 - 1.28)</td>
<td>98 fewer per 1000 (220 fewer - 110 more)</td>
<td>Low Due to serious risk of bias and imprecision</td>
</tr>
<tr>
<td>Maximum Walking Distance (6 mo) 6 months</td>
<td>Based on data from: 391 patients in 4 studies. (Randomized controlled)</td>
<td></td>
<td>MD 125 lower (227 lower - 23 higher)</td>
<td>Low Due to serious risk of bias and indirectness</td>
</tr>
<tr>
<td>Maximum Walking Distance (1 year) 1 year</td>
<td>Based on data from: 206 patients in 2 studies. (Randomized controlled)</td>
<td></td>
<td>MD 175 lower (288 lower - 61 higher)</td>
<td>Low Due to serious risk of bias and indirectness</td>
</tr>
<tr>
<td>Pain Free Walking Distance (6 mo) 6 months</td>
<td>Based on data from: 383 patients in 4 studies. (Randomized controlled)</td>
<td></td>
<td>MD 35 lower (80 lower - 10 higher)</td>
<td>Low Due to serious risk of bias and indirectness</td>
</tr>
<tr>
<td>Pain Free Walking Distance (1 year) 1 year</td>
<td>Based on data from: 304 patients in 3 studies. (Randomized controlled)</td>
<td></td>
<td>MD 86 lower (169 lower - 3 higher)</td>
<td>Low Due to serious risk of bias and indirectness</td>
</tr>
<tr>
<td>Disease specific Quality of life (6 mo)</td>
<td>Based on data from: 270</td>
<td></td>
<td>5 5.05</td>
<td>Moderate Due to serious risk of bias</td>
</tr>
</tbody>
</table>
### Practical issues

<table>
<thead>
<tr>
<th></th>
<th>Supervised Exercise Therapy</th>
<th>Revascularisation</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure and device</td>
<td><img src="image" alt="Diagram" /></td>
<td></td>
<td></td>
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<tr>
<td>Tests and visits</td>
<td><img src="image" alt="Diagram" /></td>
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<tr>
<td>Adverse effects, interactions and antidote</td>
<td><img src="image" alt="Diagram" /></td>
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<tr>
<td>Costs and access</td>
<td><img src="image" alt="Diagram" /></td>
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</tr>
</tbody>
</table>

1. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Very Serious.** Confidence intervals include benefit and potential harm. Low number of events.; **Publication bias: No serious.**
2. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Very Serious.** Confidence intervals include benefit and potential harm. Low number of events.; **Publication bias: No serious.**
3. **Inconsistency: No serious. Indirectness: No serious. Imprecision: Serious.** Confidence intervals include benefit and potential harm. Low number of events.; **Publication bias: No serious.**
potential harm. ; Publication bias: No serious.

4. Inconsistency: No serious. Indirectness: No serious. Imprecision: Serious. Confidence intervals include benefit and potential harm. ; Publication bias: No serious.

5. Risk of bias: Serious. Incomplete data and/or selective follow up; Inconsistency: No serious. Indirectness: No serious. Imprecision: Serious. Confidence intervals include benefit and potential harm. ; Publication bias: No serious.

6. Risk of bias: Serious. Patients, clinicians and in 8/10 studies the assessors were not blinded to treatment. ; Inconsistency: No serious. Indirectness: Serious. Walking distance on treadmill correlates poorly with walking distance in daily life. ; Imprecision: No serious. Publication bias: No serious.

7. Risk of bias: Serious. Patients, clinicians and in 8/10 studies the assessors were not blinded to treatment. ; Inconsistency: No serious. Indirectness: Serious. Walking distance on treadmill correlates poorly with walking distance in daily life. ; Imprecision: No serious. Publication bias: No serious.

8. Risk of bias: Serious. Patients, clinicians and in 8/10 studies the assessors were not blinded to treatment. ; Inconsistency: No serious. Indirectness: Serious. Walking distance on treadmill correlates poorly with walking distance in daily life. ; Imprecision: No serious. Publication bias: No serious.

9. Risk of bias: Serious. Patients, clinicians and in 8/10 studies the assessors were not blinded to treatment. ; Inconsistency: No serious. Indirectness: Serious. Walking distance on treadmill correlates poorly with walking distance in daily life. ; Imprecision: No serious. Publication bias: No serious.

10. Risk of bias: Serious. Patients, clinicians and in 8/10 studies the assessors were not blinded to treatment. ; Inconsistency: No serious. Indirectness: No serious. Imprecision: No serious. Publication bias: No serious.

11. Risk of bias: Serious. Patients, clinicians and in 8/10 studies the assessors were not blinded to treatment. ; Inconsistency: No serious. Indirectness: No serious. Imprecision: No serious. Publication bias: No serious.

12. Risk of bias: Serious. Patients, clinicians and in 8/10 studies the assessors were not blinded to treatment. ; Inconsistency: No serious. Indirectness: No serious. Imprecision: No serious. Publication bias: No serious.

References


Clinical Question/ PICO

Population: Patients with intermittent claudication due to peripheral arterial disease
Intervention: Supervised Exercise Therapy + Revascularisation
Comparator: Supervised Exercise Therapy

Summary

The panel agreed that, comparing supervised exercise plus revascularisation with supervised exercise at 12 months:
- there is probably little or no difference for disease-specific quality of life (moderate quality evidence);
- there is possibly a small increase in maximum walking distance (145m more, low quality evidence);
- there is possibly a small increase in pain-free walking distance (169m more, low quality evidence);
- there is probably a small decrease for additional interventions (117 fewer per 1000, moderate quality evidence); and
- there is possibly little or no difference for major cardiovascular events and serious adverse events (low quality evidence).
<table>
<thead>
<tr>
<th>Event Description</th>
<th>Relative Risk</th>
<th>95% CI</th>
<th>Evidence</th>
<th>Difference</th>
<th>Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Major cardiovascular events (&lt; 1 year)</strong></td>
<td>Relative risk 0.4 (CI 95% 0.08 - 2.02)</td>
<td>(Randomized controlled)</td>
<td>38 per 1000</td>
<td>15 per 1000</td>
<td>Low Due to very serious imprecision 1</td>
</tr>
<tr>
<td>up to 1 year</td>
<td></td>
<td></td>
<td></td>
<td>Difference: 23 fewer per 1000 (CI 95% 35 fewer - 39 more)</td>
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<td></td>
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<td></td>
<td></td>
<td>8 Critical</td>
<td></td>
</tr>
<tr>
<td><strong>Major cardiovascular events (5 yrs)</strong></td>
<td>Relative risk 2.52 (CI 95% 0.73 - 8.75)</td>
<td>(Randomized controlled)</td>
<td>86 per 1000</td>
<td>217 per 1000</td>
<td>Low Due to very serious imprecision 2</td>
</tr>
<tr>
<td>at 5 years</td>
<td></td>
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<td>Difference: 131 more per 1000 (CI 95% 23 fewer - 667 more)</td>
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<td></td>
<td>8 Critical</td>
<td></td>
</tr>
<tr>
<td><strong>Receiving additional interventions (&lt;1 yr) &lt; 1 year</strong></td>
<td>Relative risk 0.31 (CI 95% 0.15 - 0.67)</td>
<td>(Randomized controlled)</td>
<td>169 per 1000</td>
<td>52 per 1000</td>
<td>Moderate Due to serious imprecision 3</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>Difference: 117 fewer per 1000 (CI 95% 144 fewer - 56 fewer)</td>
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<td></td>
<td>6 Important</td>
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</tr>
<tr>
<td><strong>Receiving additional interventions (5 yrs) at 5 years</strong></td>
<td>Relative risk 0.57 (CI 95% 0.23 - 1.4)</td>
<td>(Randomized controlled)</td>
<td>286 per 1000</td>
<td>163 per 1000</td>
<td>Low Due to serious risk of bias and imprecision 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Difference: 123 fewer per 1000 (CI 95% 220 fewer - 114 more)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>6 Important</td>
<td></td>
</tr>
<tr>
<td><strong>Serious adverse events (&lt;1 yr)</strong> up to 1 year</td>
<td>Relative risk 3 (CI 95% 0.13 - 70.3)</td>
<td>(Randomized controlled)</td>
<td>0 per 1000</td>
<td>0 per 1000</td>
<td>Low Due to very serious imprecision 5</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Difference: 0 fewer per 1000 0 fewer - 0 fewer</td>
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<td></td>
<td></td>
<td>8 Critical</td>
<td></td>
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<tr>
<td><strong>Serious adverse events (2 yrs) at 2 years</strong></td>
<td>Relative risk 0.89 (CI 95% 0.22 - 3.55)</td>
<td>(Randomized controlled)</td>
<td>67 per 1000</td>
<td>60 per 1000</td>
<td>Low Due to very serious imprecision 6</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Difference: 7 fewer per 1000 52 fewer - 171 more</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>8 Critical</td>
<td></td>
</tr>
<tr>
<td><strong>Maximum walking distance (6 mo)</strong></td>
<td>Measured by: Treadmill High better</td>
<td>Based on data from: 305 patients in 2 studies.</td>
<td>509 meters (Mean)</td>
<td>684 meters (Mean)</td>
<td>Low Due to serious risk of bias and</td>
</tr>
</tbody>
</table>

Serious adverse events

**General**

- Up to 1 year
  - 8 Critical
- At 5 years
  - 8 Critical
- At 2 years
  - 8 Critical

**Maximum walking distance (6 mo)**

- Measured by: Treadmill High better
- Based on data from: 305 patients in 2 studies.
## Practical issues

<table>
<thead>
<tr>
<th>Procedure and device</th>
<th>Supervised Exercise Therapy</th>
<th>Supervised Exercise Therapy + Revascularisation</th>
<th>Both</th>
</tr>
</thead>
</table>

### Supervised Exercise Therapy

<table>
<thead>
<tr>
<th>6 months</th>
<th>Difference: <strong>MD 175 higher</strong> (CI 95% 57 higher - 288 higher)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 Critical</td>
<td>276 meters (Mean) - 421 meters (Mean)</td>
</tr>
<tr>
<td>Maximum Walking Distance (1 year)</td>
<td>276 meters (Mean) - 421 meters (Mean)</td>
</tr>
<tr>
<td>1 year</td>
<td>8 Critical</td>
</tr>
<tr>
<td>Difference: <strong>MD 145 higher</strong> (CI 95% 72 higher - 217 higher)</td>
<td></td>
</tr>
<tr>
<td>8 Critical</td>
<td>322 meters (Mean) - 534 meters (Mean)</td>
</tr>
<tr>
<td>Pain Free Walking Distance (6 mo)</td>
<td>322 meters (Mean) - 534 meters (Mean)</td>
</tr>
<tr>
<td>6 months</td>
<td>8 Critical</td>
</tr>
<tr>
<td>Difference: <strong>MD 212 higher</strong> (CI 95% 223 lower - 646 higher)</td>
<td></td>
</tr>
<tr>
<td>8 Critical</td>
<td>405 meters (Mean) - 574 meters (Mean)</td>
</tr>
<tr>
<td>Pain Free Walking Distance (1 year)</td>
<td>405 meters (Mean) - 574 meters (Mean)</td>
</tr>
<tr>
<td>1 year</td>
<td>8 Critical</td>
</tr>
<tr>
<td>Difference: <strong>MD 169 higher</strong> (CI 95% 137 lower - 480 higher)</td>
<td></td>
</tr>
<tr>
<td>8 Critical</td>
<td>5.1 points (Mean) - 5.69 points (Mean)</td>
</tr>
<tr>
<td>Disease specific Quality of life (6 mo)</td>
<td>5.1 points (Mean) - 5.69 points (Mean)</td>
</tr>
<tr>
<td>6 months</td>
<td>8 Critical</td>
</tr>
<tr>
<td>Difference: <strong>MD 0.59 higher</strong> (CI 95% 0.13 higher - 1.04 higher)</td>
<td></td>
</tr>
<tr>
<td>8 Critical</td>
<td>5.15 points (Mean) - 5.6 points (Mean)</td>
</tr>
<tr>
<td>Disease specific Quality of life (1 year)</td>
<td>5.15 points (Mean) - 5.6 points (Mean)</td>
</tr>
<tr>
<td>1 year</td>
<td>8 Critical</td>
</tr>
<tr>
<td>Difference: <strong>MD 0.45 higher</strong> (CI 95% 0.1 higher - 0.79 higher)</td>
<td></td>
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</tbody>
</table>

### Indirectness

- Difference: MD 175 higher
- Difference: MD 145 higher
- Difference: MD 212 higher
- Difference: MD 169 higher
- Difference: MD 0.59 higher
- Difference: MD 0.45 higher

- Due to serious risk of bias and indirectness 7
- Due to serious risk of bias and indirectness 8
- Due to serious risk of bias and indirectness 9
- Due to serious risk of bias and indirectness 10
- Due to serious risk of bias 11
- Due to serious risk of bias 12

- Possibly small increase
- Possibly small increase
- Possibly small increase
- Probably little or no difference (effect smaller than MID of 1.19)
- Probably little or no difference (effect smaller than MID of 1.19)
References

Weak Recommendation

We suggest supervised exercise over revascularisation combined with supervised exercise.

This recommendation is for patients with intermittent claudication due to peripheral arterial disease.

Key Info

Benefits and harms

At 6 months, the panel agreed that there is probably little or no difference for disease-specific quality of life and possibly a small increase in maximum and pain free walking distance in favor of revascularisation combined with SE.

At 12 months, there is probably little or no difference for disease-specific quality of life and there is possibly a small increase in maximum walking distance and in pain-free walking distance. There is probably a small decrease for additional interventions and there is possibly little or no difference for major cardiovascular events and serious adverse events.

At longer follow-up, there is possibly little or no difference for serious adverse events at 2 years follow-up, major cardiovascular events (at 5 years follow-up) and receiving additional interventions (at 5 years follow-up).

Certainty of the Evidence

There is low certainty that supervised exercise combined with revascularization results in a small increase in (maximum or pain free) walking distance and low certainty that there are little or no differences for major cardiovascular events and serious adverse events. There is moderate certainty that there is little or no difference for disease specific quality of life and low to moderate certainty that there is little or no difference for receiving additional interventions.

Preference and values

Patients might value the possibly small benefit in walking distance in the combined treatment group not important enough to outweigh the possible risks involved with revascularisation, such as postsurgical bleeding, wound infection or thromboembolism. However, in the era of minimally invasive endovascular revascularization techniques, the risk associated with revascularization remains limited.

The panel believes that there is large variability between patients in how they weigh the expected desirable and undesirable consequences of SE compared to SE and revascularisation. The panel expects the majority of patients to choose SE alone, but a substantial proportion may not.

Resources and other considerations

From a societal perspective, SE seems to be more cost-effective than revascularisation and therefore also compared to revascularization and SE. This is based on a study that assessed the costs of the stepped care model (primary SE treatment followed by revascularization in case of SE failure). This pragmatic study, reflecting daily practice, suggested that implementation of a stepped care model for patients with IC may lead to significant savings of health care resources. [2]

Revascularization immediately improves blood flow in the affected artery, but does not affect the underlying disease. All patients undergoing revascularisation should therefore combine such treatment with SE and lifestyle changes despite any potential reduction in ischaemic pain.

SE is not an easy solution, which is illustrated by the low compliance of patients following such a program.[3] Patients need to be motivated to start and continue SE as it takes a lot of time and perseverance. Pre-exercise patient education and personalised exercise prescriptions may result in improvements in both function and compliance. [4] New techniques, including smart-phone apps, are evolving and might help to decrease barriers of adherence and motivation. [5,6]

Rationale

In general, there is possibly little or no differences in effects and adverse events between SE and revascularization combined with
SE. This may indicate that not all patients need a revascularization. The uncertain and small benefit in walking distance and probably small reduction in additional interventions for SE plus revascularization may not outweigh the risks that come with the invasive procedure revascularization. We expect the majority of patients will choose not to have revascularization on top of SE.

We believe that there is some variability in how patients weigh the expected desirable and undesirable consequences of SE compared to SE and revascularization. We expect the majority of patients will choose SE alone, but a substantial proportion may not. Therefore we issue a weak recommendation, which means both options need to be discussed with the patient, ideally in a process of shared decision-making.

Clinical Question/ PICO

**Population:** Patients with intermittent claudication due to peripheral arterial disease

**Intervention:** Supervised Exercise Therapy + Revascularisation

**Comparator:** Supervised Exercise Therapy

Summary

The panel agreed that, comparing supervised exercise plus revascularisation with supervised exercise at 12 months:

- there is probably little or no difference for disease-specific quality of life (moderate quality evidence);
- there is possibly a small increase in maximum walking distance (145m more, low quality evidence);
- there is possibly a small increase in pain-free walking distance (169m more, low quality evidence);
- there is probably a small decrease for additional interventions (117 fewer per 1000, moderate quality evidence); and
- there is possibly little or no difference for major cardiovascular events and serious adverse events (low quality evidence).

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<tr>
<td>Up to 1 year</td>
<td>Difference: 23 fewer per 1000 (CI 95% 35 fewer - 39 more)</td>
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<td></td>
</tr>
<tr>
<td>8 Critical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major cardiovascular events (5 yrs)</td>
<td>Relative risk 2.52 (CI 95% 0.73 - 8.75) Based on data from 72 patients in 1 studies. (Randomized controlled)</td>
<td>86 per 1000 217 per 1000</td>
<td>Low Due to very serious imprecision 2</td>
<td>May have little or no difference</td>
</tr>
<tr>
<td>At 5 years</td>
<td>Difference: 131 more per 1000 (CI 95% 23 fewer - 667 more)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 Critical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Receiving additional interventions (&lt;1 yr)</td>
<td>Relative risk 0.31 (CI 95% 0.15 - 0.67) Based on data from 330 patients in 2 studies. (Randomized controlled)</td>
<td>169 per 1000 52 per 1000</td>
<td>Moderate Due to serious imprecision 3</td>
<td>Probably slight decrease</td>
</tr>
<tr>
<td>&lt; 1 year</td>
<td>Difference: 117 fewer per 1000 (CI 95% 144 fewer - 56 fewer)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Event</td>
<td>Risk Relative</td>
<td>CI 95%</td>
<td>Difference</td>
<td>Level</td>
</tr>
<tr>
<td>-----------------------------------</td>
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<td>-------------------------</td>
</tr>
<tr>
<td>Receiving additional interventions (5 yrs) at 5 years</td>
<td>0.57</td>
<td>0.23 - 1.4</td>
<td>123 fewer per 1000</td>
<td>Low</td>
</tr>
<tr>
<td>Serious adverse events (&lt;1 yr) up to 1 year</td>
<td>3</td>
<td>0.13 - 70.3</td>
<td>0 fewer per 1000</td>
<td>Low</td>
</tr>
<tr>
<td>Serious adverse events (2 yrs) at 2 years</td>
<td>0.89</td>
<td>0.22 - 3.55</td>
<td>7 fewer per 1000</td>
<td>Low</td>
</tr>
<tr>
<td>Maximum Walking Distance (6 mo) at 6 months</td>
<td></td>
<td></td>
<td>175 higher</td>
<td>Low</td>
</tr>
<tr>
<td>Maximum Walking Distance (1 year) at 1 year</td>
<td></td>
<td></td>
<td>145 higher</td>
<td>Low</td>
</tr>
<tr>
<td>Pain Free Walking Distance (6 mo) at 6 months</td>
<td></td>
<td></td>
<td>212 higher</td>
<td>Low</td>
</tr>
</tbody>
</table>
### Practical issues

<table>
<thead>
<tr>
<th></th>
<th>Supervised Exercise Therapy</th>
<th>Supervised Exercise Therapy + Revascularisation</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure and device</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tests and visits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse effects, interactions and antidote</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Costs and access</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. **Inconsistency:** No serious. **Indirectness:** No serious. **Imprecision:** Very Serious. Confidence interval includes benefit and
potential harm. Low number of events; Publication bias: No serious.

2. Inconsistency: No serious. Indirectness: No serious. Imprecision: Very Serious. Confidence intervals includes benefit and potential harm. Low number of events; Publication bias: No serious.

3. Inconsistency: No serious. Indirectness: No serious. Imprecision: Serious. Low number of patients; Publication bias: No serious.

4. Risk of bias: Serious. Incomplete data and/or large loss to follow up; Inconsistency: No serious. Indirectness: No serious. Imprecision: Serious. Low number of events; Publication bias: No serious.


6. Inconsistency: No serious. Indirectness: No serious. Imprecision: Very Serious. Confidence interval includes benefit and potential harm; Low number of events; Publication bias: No serious.

7. Risk of bias: Serious. Patients, clinicians and in 8/10 studies the assessors were not blinded to treatment.; Inconsistency: No serious. Indirectness: Serious. Walking distance on treadmill correlates poorly with walking distance in daily life.; Imprecision: No serious. Publication bias: No serious.

8. Risk of bias: Serious. Patients, clinicians and in 8/10 studies the assessors were not blinded to treatment.; Inconsistency: No serious. Indirectness: Serious. Walking distance on treadmill correlates poorly with walking distance in daily life.; Imprecision: No serious. Publication bias: No serious.

9. Risk of bias: Serious. Patients, clinicians and in 8/10 studies the assessors were not blinded to treatment.; Inconsistency: No serious. Indirectness: Serious. Walking distance on treadmill correlates poorly with walking distance in daily life.; Imprecision: No serious. Publication bias: No serious.

10. Risk of bias: Serious. Patients, clinicians and in 8/10 studies the assessors were not blinded to treatment.; Inconsistency: No serious. Indirectness: Serious. Walking distance on treadmill correlates poorly with walking distance in daily life.; Imprecision: No serious. Publication bias: No serious.

11. Risk of bias: Serious. Patients, clinicians and in 8/10 studies the assessors were not blinded to treatment.; Inconsistency: No serious. Indirectness: No serious. Imprecision: No serious. Publication bias: No serious.

12. Risk of bias: Serious. Patients, clinicians and in 8/10 studies the assessors were not blinded to treatment.; Inconsistency: No serious. Indirectness: No serious. Imprecision: No serious. Publication bias: No serious.

References

2 - Primary Care Rapid Recommendations: Background and methods

BACKGROUND

From MAGIC to WikiRecs, BMJ Rapid Recommendations and the Primary Care Rapid Recommendations 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 to support evidence translation. In a parallel rapid recommendation process like the BMJ Rapid Recommendations project, MAGIC was instrumental in creating the WikiRecs (Rapid Recommendations and Evidence summaries Composed as Synopses) project to support evidence-based practice. MAGIC and the British Medical Journal (BMJ) have collaborated to develop a comprehensive process to translate evidence into the existing body of evidence, and broader context of clinical practice via publication of the research in high-impact journals and systematic reviews also published in The BJGP. 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 Primary Care 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 Primary Care RapidRecs follows a predefined protocol with the following steps:

1. On a regular basis, we monitor the literature for practice-changing evidence via multiple sources:
   a. Screening results of McMaster Premium LiteraturUre Service (PLUS), a continuously updated database, that filters new records based on quality and relevance for certain disciplines, among which primary care. This database provides us an overview of high quality and highly relevant records for primary care.
   b. Informal monitoring the literature by experts on the field of primary care, including clinician specialists and patients

2. The Primary Care RapidRecs executive team chooses which clinical questions to pursue among the identified potentially-practice-changing evidence, based on priority ratings that evaluate both the impact of the topic (including prevalence, net benefit and the newsworthiness) and availability of evidence

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.
   - The recommendation panel will apply the GRADE approach, which has developed a transparent process to rate the quality (or certainty) of evidence and grade the strength of recommendations.

4. Disseminate the rapid recommendations through
   - publication of the research in high-impact journals
   - short summary of recommendations for clinicians published in high-impact journals

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 Rapid Recommendations project the MAGIC WikiRecs group has partnered with The British Medical Journal (The BMJ) to publish rapid recommendations as a synopsis paper in their journal, along with one or more systematic reviews linked to the recommendations. [16]

Using largely the same methods as the BMJ Rapid Recommendations project, we launched a similar group focusing on primary care, the Primary Care Rapid Recommendations. The clinical practice guideline with recommendations here in MAGICapp is as such one of a package which includes recommendations and systematic reviews also published in The BJGP. 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 Primary Care 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.
• press release and/or marketing to media outlets and relevant parties such as patient groups
• 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.

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. Primary Care RapidRecs circumvents organisational barriers in order to provide clinicians with guidance for potentially practice-changing evidence.

Our collaboration involves
• The Primary Care RapidRecs group with a designated Executive team responsible for recruiting and coordinating the network of researchers who perform the systematic reviews and the recommendation panels. The Primary Care RapidRecs group is part of MAGIC (www.magicproject.org), a non for profit organization that provides MAGICapp (www.magicapp.org) an authoring and publication platform for evidence summaries, guidelines and decision aids, which are disseminated online for all devices.[6]

METHODS FOR THE PRIMARY CARE 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.[2,3,7]

Guidance on how the panel is picked and how they contribute
Panel members are sought and screened through an informal process.
The following panel members are important
• At least one author of the individual systematic reviews
• At least one patient representative with lived experience of the disease or condition. This person receives patient-oriented documents to explain the process and is allocated a linked 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 can have a financial interest – as assessed by the panel chair or the Primary Care Rapidrecs executive team as relevant to the topic
• No more than two panel members with an intellectual interest on the topic (typically having published statements favouring one of the interventions).

How the panel meets and works
The international panel communicates via teleconferences and e-mail exchange of written documents throughout the process. Teleconferences are audiorecorded, transcribed, and stored for later documentation (available for peer-reviewers on 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 (for example, on 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 is circulated by e-mail specifically requesting feedback from all panel members to document agreement before submission. Additional teleconferences are arranged as needed.

How we move from research findings to recommendations
What information is considered?
The panel considers best current evidence from available research. Beyond systematic reviews - performed in the context of the Primary Care Rapid Recommendations - the panel may also include a number of other research papers to further inform the recommendations.

How is a trustworthy guideline made?
The Institute of Medicine (IOM)’s guidance on how trustworthy guidelines should be developed and articulated key standards is outlined in the table below.[2] The standards are similar to those developed by the Guideline International Network (G-I-N).[3] These standards have been widely adopted by the international guideline community. Peer reviewers of the recommendation article are asked whether they found the guideline trustworthy (in accordance with IOM standards). Below, we lay out how we hope to meet the standards for our rapid recommendations:
1. Establishing transparency

"The processes by which a CPG is developed and funded should be detailed explicitly and publicly accessible"*

- This method is available and published as a supplementary file as well as in MAGICapp where all recommendations and underlining content is available.
- We ask the peer-reviewers to judge whether the guidance is trustworthy and will respond to concerns raised.

2. Managing conflicts of interest

"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...".

- Interests of each panel member are declared prior to involvement and published with the rapid recommendations.
- No one with any potential financial interests in the past three years, or forthcoming 12 months will participate - as judged by the panel chair and the Executive Committee of the Primary Care RapidRecs.
- 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 an editorial, commentary, or conflicts related to performing a primary research study or written a prior systematic review on the topic.
- The Chair must have methods expertise, a clinical background and no financial or intellectual interests.
- Funders and pharmaceutical companies have no role in these recommendations.

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"*

- The Primary Care RapidRecs group will 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 addressing 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 when discussing the panel's judgements of values and preferences.


"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 Primary Care Rapid Recommendations or produced by other authors and available at the time of making the recommendation.
- 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.[7] For each recommendation systematic and transparent assessments are made across the following key factors:
  - Absolute benefit and harms for all patient-important outcomes through structured evidence summaries (e.g. GRADE Summary of Findings tables)[5]
  - Quality of the evidence[8]
  - 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 Summary of Findings 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) will be available online in an interactive format at www.magicapp.org. This summary will include 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.[9]
- If the panel members disagree regarding 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 guideline infographic, published in a high impact journal and will be available in standardised formats in MAGICapp, articulated to be actionable based on best current evidence on presentation formats of guidelines.[10]
There will be a statement included in each summary article in the journal 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 will review the article for the high-impact journal 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.
- The RapidRecs primary care panel will be asked to read and respond to the peer review comments and make amendments where they judge reasonable.
- The RapidRecs primary care executive 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 through which people can provide comments and feedback through MAGICapp. 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 Primary Care RapidRecs panel will, through monitoring of new research evidence on published Rapid Recommendations, aim to provide updates of the recommendations in situations in which the evidence suggests a change in practice. These updates will be initially performed in MAGICapp. Results will be discussed with the Primary Care RapidRecs executive committee for consideration of updating the Rapid Recommendation.

References:

3 - Supervised exercise for intermittent claudication: a clinical practice guideline

Bekkering GE1, Kuijpers T2, Adegas A3, Burgers J4, Crockett K5, Forjaz C6, Forneau J7, Giesen H8, Kunnamo I9, Leicht A10, Nordansti
J11, Siemieniuk R12, Spurling G13, Valkenburg W18, Van Reijen H14, Zwaenepoel B15, Aertgeerts B16, Vermandere M17

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2. Methods editor, Dutch College of General Practitioners, Utrecht, The Netherlands
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6. Exercise physiologist. Exercise Hemodynamic Laboratory, School of Physical Education and Sport, University of Sã£o Paulo, Brazil
7. Vascular surgeon. Department of Vascular Surgery, University Hospitals Leuven, Leuven, Belgium; Department of Cardiovascular
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8. Patient, The Netherlands
9. Methodologist, GP. Editor in Chief, EBM Guidelines @ EBMeDS at Duodecim Medical Publications Ltd. University of Helsinki
University of Helsinki University of Helsinki
10. Exercise specialist/physiologist. Sport and Exercise Science, James Cool University, Australia
11. Vascular surgeon. Department of Vascular Surgery, Sahlgrenska University Hospital and Institute of Medicine at The Sahlgrenska
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16. Chair, GP. Academic Centre for General Practice, Department of Public Health and Primary Care, KU Leuven, Belgium; President
Belgium Centre for Evidence Based Medicine and Cochrane Belgium
17. GP. Academic Centre for General Practice, Department of Public Health and Primary Care, KU Leuven, Belgium; Coordinator of
EBMPracticeNet (non-profit association, Belgium)

Introduction
A recent trial reported that supervised exercise and percutaneous transluminal angioplasty were equally effective for intermittent
claudication over a period of approximately five years.1 Triggered by these results, a review team updated a previous systematic
review.2 Based on this review and using the GRADE approach, an expert panel formulated a weak recommendation in favour of
supervised exercise rather than revascularisation alone or supervised exercise combined with revascularisation.

Box 1. What you need to know
- Intermittent claudication is not prevalent but may be underdiagnosed in primary care.
- This recommendation applies to patients with intermittent claudication due to peripheral arterial disease.
- We make a weak recommendation in favour of supervised exercise (SE) rather than revascularisation alone.
- We make a weak recommendation in favour of SE rather than SE combined with revascularisation.
- The recommendations are weak because there is little or no difference between the treatments, and revascularisation is an
invasive treatment involving certain risks.
- Both options need to be discussed with the patient, ideally in a process of shared decision-making.
- We take an individual patient perspective in creating our recommendations. However, from a societal perspective, SE is
probably more cost-effective than revascularization.

How the recommendation was created
Methodology was in accordance of the BMJ RapidRecs series.3 An international guideline panel, including patients with personal
experience of claudication, general practitioners, physiotherapists, exercise specialists, vascular surgeons, exercise physiologists,
epidemiologists and methodologists, prepared the recommendation. No panel member had financial conflicts of interest; intellectual and
professional conflicts of interests were minimised and described (Appendix 1). The panel met online three times to discuss the evidence
and to formulate recommendations. The panel defined the scope of the recommendation and subsequently selected six patient-
important outcomes: maximum walking distance, pain-free walking distance, health-related quality of life (HRQoL), risk of additional
surgical interventions, risk of major cardiovascular events and risk of serious adverse events. Box 2 illustrates the role of patients in this
process.
Box 2. How patients were involved in the creation of this guideline
Two patients with lived experience of claudication were full panel members. They participated in the teleconferences and met all authorship criteria. These panel members identified important outcomes and led the discussion on patient values and preferences. These patient representatives agreed that even small improvements in walking distance were very important to them. The patients also stated that risk of serious events is important. They expected moderate to great variability in how much importance other patients would value a small improvement of walking distance and a small increase of risk of serious adverse events.

The evidence
The recommendations were informed by a linked systematic review (SR) of randomised controlled trials (RCTs) on the effects of SE compared to revascularisation in patients with IC. Table 1 gives an overview of the number and type of patients included.

Table 1. Characteristics of studies included in the systematic review

<table>
<thead>
<tr>
<th>Data sources</th>
<th>10 studies</th>
<th>1176 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comparison:</td>
<td>6 studies compared SE to revascularization</td>
<td>5 studies compared SE+revascularization to SE</td>
</tr>
<tr>
<td>Location of study:</td>
<td>9 studies from Europe</td>
<td>1 from US</td>
</tr>
<tr>
<td>Type of revascularization:</td>
<td>8 studies used endovascular</td>
<td>2 studies used surgical revascularization</td>
</tr>
<tr>
<td>Patient characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (range): 63 to 70 yrs</td>
<td>% female (range): 33 to 81%</td>
<td></td>
</tr>
<tr>
<td>Mean (range) no pts enrolled: 108 (16 to 212)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of CI:</td>
<td>aorto-iliac: 2 studies</td>
<td>femoropopliteal: 3 studies</td>
</tr>
<tr>
<td></td>
<td>both: 4 studies</td>
<td>not reported: 1 study</td>
</tr>
<tr>
<td>Treadmill testing procedure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5 to 3 km/h+incline: 3 studies</td>
<td>3.2 to 3.5 km/h (graded standard protocol): 4 studies</td>
<td></td>
</tr>
<tr>
<td>4 km/h+incline: 2 studies</td>
<td>4 km/h without incline: 1 study</td>
<td></td>
</tr>
<tr>
<td>Exercise procedure</td>
<td></td>
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<tr>
<td>1 to 3 times weekly; 30 to 60 min sessions. No details on workload. 12 weeks to 12 months; mostly walking or exercise circuit.</td>
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</table>

Absolute benefit and harms
The infographic explains the recommendations and provides an overview (GRADE Summary of Findings) of the absolute benefits and harms of SE and revascularisation.

The panel agreed that, comparing revascularisation with supervised exercise at 12 months:
- there is probably little or no difference on disease-specific quality of life (moderate quality evidence)
- there is possibly a small decrease in maximum walking distance (175m lower, low quality evidence)
- there is possibly a small decrease in pain-free walking distance (86m lower, low quality evidence)
- there is possibly little or no difference in risk of major cardiovascular event, risk of serious adverse events and risk of additional interventions (low quality evidence).

The panel agreed that, comparing supervised exercise plus revascularisation with supervised exercise at 12 months:
- there is probably little or no difference on disease-specific quality of life (moderate quality evidence)
- there is possibly a small increase in maximum walking distance (145m more, low quality evidence)
• there is possibly a small increase in pain-free walking distance (169m more, low quality evidence)
• there is possibly a small decrease in risk of additional interventions (117 fewer per 1000, moderate quality evidence)
• there is possibly little or no difference on risk of major cardiovascular events and risk of serious adverse events (low quality evidence).

The panel agreed that there are possibly little or no differences in effects between SE and revascularisation. The panel also concluded that there is possibly little or no difference in risk of additional surgical interventions between SE and revascularisation with a small benefit for the combined treatment. Finally, there is possibly little or no difference between the intervention groups on the risk of major cardiovascular events and serious adverse events (SAE).

Values and Preferences
We are uncertain about the effects on walking distance and harms of the two treatments. Although there may be little or no difference between the different treatments in walking distance, patients can perceive small increases as very important, depending on their personal situation. Compared to SE, revascularisation is an invasive procedure, which involves risks, such as postsurgical bleeding, wound infection or thromboembolism. However, in the era of minimally invasive endovascular revascularization techniques, the risk associated with revascularization remains limited. The panel feels that the advantages do not clearly outweigh the harms for all patients and expects that the majority of patients are likely to choose SE.

Revascularization immediately improves blood flow in the affected artery, but does not affect the underlying disease. All patients undergoing revascularisation should therefore combine such treatment with SE and lifestyle changes. However, they may be less motivated because the pain has disappeared. Revascularisation might therefore be of benefit for patients that do not respond to SE, or are not willing to undergo an exercise intervention. This is the so-called stepped care model, which strives to initially refer all IC patients to an SE program and restrict revascularisation to those who do not respond to SE.

The possible increase in maximum and pain-free walking distance with SE is modest, but the panel anticipates that for the majority of fully informed patients these possible benefits of SE compared to revascularisation outweigh the probable downsides. The panel believes that there is large variability between patients weighing the expected desirable and undesirable consequences of SE. Some patients will be highly motivated to start an SE program, others with less motivation or those with practical constraints, may prefer revascularisation. The panel therefore issues a weak recommendation, which means both options need to be discussed with the patient in a process of shared decision-making.

Practical issues and other considerations
The panel took into account that SE may have additional health benefits: the exercise hopefully facilitates engagement in an active and healthy lifestyle. It may produce other health benefits beyond those included in this investigation, such as cardiovascular function, daily functioning and fitness. The frequent contacts with a health professional will possibly reinforce such changes. SE also covers lifestyle counselling and education about the disease (see Table 3). Well-informed patients are better able to manage their illness and understand that they are at risk of SAE due to their underlying disease.

SE is not an easy solution, which is illustrated by the low compliance of patients following such programs. Patients need to be motivated to start and continue SE as it takes a lot of time and perseverance. Pre-exercise patient education and personalised exercise prescriptions may result in improvements in both function and compliance. New techniques, including smart-phone apps, are evolving and might help to decrease barriers of adherence and motivation.

Box 3. Elements of SE
• Treatment consists of exercise, not restricted to walking.
• Treatment includes also information on disease, to increase and enhance motivation to exercise and facilitate other lifestyle changes, where needed.
• Duration of at least 3 months

Costs and resources
From a societal perspective, SE seems to be more cost-effective than revascularisation. This is based on a study that assessed the costs of the stepped care model (primary SE treatment followed by revascularization in case of SE failure). This pragmatic study, reflecting daily practice, suggested that implementation of a stepped-care model for patients with IC may lead to significant savings of health care resources.

Data supplements
Appendix 1: Full list of panel members and declarations of interests

Competing interests
All authors have completed the ICMJE interests disclosure form and a detailed, contextualised description of all disclosures is reported
in Appendix 1. The chair and methods editor judged that no panel member had any financial conflict of interest. Professional and academic interests are minimised (by including maximal two panel members with intellectual conflicts) as much as possible, while maintaining necessary expertise on the panel to make fully informed decisions.

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**REFERENCES**


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**Appendix 1.**

<table>
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All panel members were pre-screened for conflicts of interest prior to the guideline process that resulted in this WikiRecs. The pre-screening was performed by the chair and methods editors of the WikiRecs primary care group. No financial conflicts of interest were allowed and intellectual and professional conflicts of interest were managed appropriately (see Primary Care Rapid Recommendations: Background and methods).

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**Professional disclosures:** Drs. Forneau and Nordanstig perform revascularizations.

**Intellectual disclosures:** Drs. Bekkering and Van Reijen participated in writing the complementary systematic review that formed the
evidence base for this guideline.
Dr Leicht is co-author of a position statement on exercise and peripheral arterial disease (Askew CD, Parmenter B, Leicht AS, Walker PJ & Golledge J. Exercise prescription for patients with peripheral arterial disease and intermittent claudication: A position statement from Exercise & Sports Science Australia. Journal of Science and Medicine in Sport 2014; 7:623-629.) No other panel member has previously formally made statements favouring either option in CI patients.

No panel member has disclosed any other relationships that could influence the work.
References


