MEDICAL UNIVERSITY OF SOUTH CAROLINA
VALUE INSTITUTE
Evidence-Based Practice Brief
Heart and Vascular Observation Units following Catheterization or Electrophysiology Studies

Author(s): Rebecca Harper, Lean Six Sigma Black Belt; Amanda Davis, MPH, RD, CHES; Emily Brennan, MLIS

ASK THE QUESTION

Question: In patients admitted to a cardiac observation unit following catheterization or electrophysiology studies, what protocols are useful in minimizing patient risk and need for inpatient admission?

SEARCH FOR EVIDENCE

Databases: PubMed, Scopus

PubMed search strategy: ("observation"[Majr] OR "observation unit" OR "observation units" OR "observation status" OR "assessment unit") AND ("Cardiovascular Diseases"[Mesh] OR heart OR cardiac OR cardiovascular OR vascular OR electrophysiology OR "23 hour")

Filters: Humans, English, Published last 10 years

CRITICALLY ANALYZE THE EVIDENCE

<table>
<thead>
<tr>
<th>Title</th>
<th>Organization and Author</th>
<th>Date</th>
<th>Evidence Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay following percutaneous coronary intervention: an expert consensus document update</td>
<td>Society for Cardiovascular Angiography and Interventions (Seto et al.)</td>
<td>2018</td>
<td>No level of evidence provided</td>
</tr>
</tbody>
</table>

This published clinical guideline have been evaluated for this review using the University of Pennsylvania's Center for Evidence-Based Practice Trustworthy Guideline rating scale. The scale is based on the Institute of Medicine’s “Standards for Developing Trustworthy Clinical Practice Guidelines” (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.
There was one guideline found addressing length of stay following percutaneous coronary intervention (PCI) that incorporated recommendations for same day discharge (Seto et al., 2018). The Society for Cardiovascular Angiography and Interventions (SCAI) consensus-based guidelines incorporates the use of a variety of patient status types as follows:

**FIGURE 1** Flowchart of patient status following elective PCI
SCAI (2018) Consensus recommendations for same-day discharge following PCI include:

<table>
<thead>
<tr>
<th>TABLE 4</th>
<th>Consensus recommendations for discharge following PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient</strong></td>
<td>Expedited and same-day discharge requirements and milestones</td>
</tr>
<tr>
<td>Clinically stable</td>
<td>Chronic kidney disease requiring prolonged hydration</td>
</tr>
<tr>
<td>At baseline functional and mental status</td>
<td>Decompensated CHF or fluid overload</td>
</tr>
<tr>
<td>Baseline comorbidities (e.g., diabetes, CHF, COPD, PAD, ESRD) stable</td>
<td>Decompensated COPD</td>
</tr>
<tr>
<td>Continuing angina</td>
<td>Contrast reaction with ongoing symptoms</td>
</tr>
<tr>
<td><strong>Procedure</strong></td>
<td>Successful procedure, including:</td>
</tr>
<tr>
<td>• Single or multivessel PCI, proximal LAD, or bifurcation PCI</td>
<td>Inability to deliver stent/balloon angioplasty only</td>
</tr>
<tr>
<td>• Uncomplicated CTO attempt</td>
<td>Last remaining coronary artery PCI</td>
</tr>
<tr>
<td>• Regardless of number, length of stents used</td>
<td><strong>Adequate hemostasis</strong></td>
</tr>
<tr>
<td>Effective dual-antiplatelet therapy administered</td>
<td>Vascular complication</td>
</tr>
<tr>
<td>• Pretreatment not required</td>
<td>Large contrast volume</td>
</tr>
<tr>
<td><strong>Program</strong></td>
<td>Meets PCI program operational requirements for postprocedure care</td>
</tr>
<tr>
<td>• Adequate caregiver support</td>
<td>Periprocedural MI</td>
</tr>
<tr>
<td>• Patient and caregiver education</td>
<td>Left ventricular support device used</td>
</tr>
<tr>
<td>• Provision of P2Y12 inhibitor and medication instruction</td>
<td>Large-bore (≥ 9 French) or brachial access</td>
</tr>
<tr>
<td>• Contact information and follow-up appointment</td>
<td>Atherectomy</td>
</tr>
<tr>
<td><strong>Inadequate home support</strong></td>
<td><strong>No transportation home</strong></td>
</tr>
<tr>
<td><strong>Discomfort of patient, caregiver, or physician with same-day discharge</strong></td>
<td><strong>Inadequate access to emergency medical care following PCI</strong></td>
</tr>
</tbody>
</table>

Abbreviations per Tables [1-3]: CHF, congestive heart failure; COPD, chronic obstructive lung disease; ESRD, end-stage renal disease.
Six studies were found addressing protocols for minimizing patient risk and the need for inpatient admission following percutaneous coronary intervention (PCI). The majority of the studies focused on patients undergoing an elective PCI with stable coronary heart disease. Two studies (Saad, Y. et al., 2015 and Nascimento, F. O. et al, 2014) included criteria to include or exclude patients for same-day discharge following an elective PCI. Din, J.N. et al. (2017) surveyed interventional cardiologists to get their opinions on what would be a safe and appropriate length of stay after a PCI. Three of the six studies (Abdelaal, E., et al., 2013; Brayton, K.M., et al., 2013; Bundhun, P. K., et al., 2017) were either systematic reviews or meta-analyses. All three concluded that patients undergoing an elective, uncomplicated PCI with same-day discharge appeared to be equally as safe as keeping them overnight in the hospital for observation.

The Harvard Heart Letter (April 2011) provides criteria for same-day discharge for patients undergoing routine, uncomplicated angioplasty based on work done at Mt. Sinai Medical Center in New York and 2009 guidelines from the Society for Cardiovascular Angiography. The criteria include:

- Under 65 years of age
- No diabetes or controlled diabetes
- Good kidney function
- No heart failure
- Good ejection fraction (> 30%)
- Angioplasty not performed for heart attack
- No major complications or minor mishaps during the procedures
- Bleeding stopped quickly at catheter access site in the groin
- Patient can walk 200 meters or more soon after the procedure without any bleeding from the access site
- Social support, including someone to drive the patient home from the hospital and a working home or cell phone for follow-up call after the procedure.

Finally, a letter to the editor in The Journal of Invasive Cardiology (Khouzam, R.N., et al, 2014) also provides criteria on how to select patients for same-day discharge after a PCI. These include medical history, patient’s age, creatinine and ejection fraction score, radial access vs. femoral access, and arterial closure devices vs. manual compression.

<table>
<thead>
<tr>
<th>PICO Question: In patients admitted to a cardiac observation unit following catheterization or electrophysiology studies, what protocols are useful in minimizing patient risk and need for inpatient admission?</th>
<th>GRADE CRITERIA (See Appendix A)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Author/Date/Journal</strong></td>
<td>Purpose of Study</td>
</tr>
<tr>
<td>Abdelaal, E., et al., 2013, JACC: Cardiovascular Interventions</td>
<td>To evaluate outcomes of same-day discharge (SDD) following PCI vs overnight hospitalization (ON)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Lower Quality Rating if:
- High risk of bias (When design limitations for one or more criteria impact the quality of studies sufficiently enough to lower confidence in the estimate of effect)
- Studies inconsistent (When there are
Conducted between 1999 and 2011

12 studies were single-center (n = 4,182 patients)

1 was large US multicenter observational study (n = 107,018 patients)

3 studies in US; 3 in Canada; 5 in Europe; and 2 in Asia

developed an indication for extended observation, and crossed over to an overnight stay -reasons included procedural-related complications, such as major coronary dissection not suitable for stenting, in-lab transient vessel closure with hemodynamic collapse, intracoronary thrombus, pericardial effusion, procedural arrhythmia, wire perforation, chest pain, or issues with the access site (e.g., hematoma, delayed hemostasis)

Average LOS after PCI ranged between 4 and 11 h for SDD, with ≥77% of patients sent home between 4 and 8 h post-procedure, and 1 day for ON

Total number of complications in the SDD group was 67 of 1,023 (6.5%) versus 56 of 1,016 (5.5%) for the ON group (OR: 1.20, 95% CI: 0.82 to 1.74)

At 30 days, the incidence of MACE in the SDD versus the ON group was 13 of 1,023 (1.3%) versus 13 of 1,016 (1.3%) (OR: 0.99, 95% CI: 0.45 to 2.18)

Incidence of re-hospitalizations within 30 days after PCI between the SDD and ON groups was 41 of 1,023 (4.0%) versus 37 of 1,016 (3.6%) (OR: 1.10, 95% CI

Observational Studies:
At 30 days, the incidence of MACE in the SDD versus the ON group was 10 of 1,817 (0.6%) versus 11 of 950 (1.2%) (OR:

inconsistent across studies

differences in the direction of the effect, populations, interventions or outcomes between studies)

☐ Studies are indirect
(Your PICO question is quite different from the available evidence in regard to population, intervention, comparison, or outcome)

☐ Studies are imprecise
(When studies include few patients and few events and thus have wide confidence intervals and the results are uncertain)

☐ Publication Bias
(e.g. pharmaceutical company sponsors study on effectiveness of drug)

Increase Quality Rating if:
☐ Large effect
(When the relative risk of association between two factors is large or very large)

☐ Dose response
(When the dose-response relationship increases the confidence than an effect is real and substantial)

☐ Plausible confounders
(When plausible residual confounding is directly impacting the magnitude of effect)
<table>
<thead>
<tr>
<th>Study Limitations</th>
<th>None</th>
<th>Systematic Review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review did not address focused clinical question</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Search was not detailed or exhaustive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quality of the studies was not appraised or studies were of low quality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methods and/or results were inconsistent across studies</td>
<td></td>
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</tbody>
</table>

Brayton, K.M., et al., 2013, *Journal of the American College of Cardiology*

To evaluate safety of same-day discharge (SDD) after PCI

37 studies included

7 RCTs (n = 2,738)
1,256 randomized to SDD and 1,482 to overnight observation

30 observational studies (n = 14,032)
10,065 (71.7%) actually discharged on same day

RCTs:
- 87.3% of SDD successfully discharged on same day as PCI
- Almost half of cases deferred occurred in one trial that performed randomization prior to the PCI procedure
- Remaining cases deferred:
  - 33% for access site complications
  - 30% physician preference
  - 17% patient preference
  - 11% recurrent chest pain
  - 4.9% non-cardiac reasons
  - 2.4% orthostasis

Study Limitations = None

<table>
<thead>
<tr>
<th>Level of evidence for studies as a whole:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

Level of evidence for studies as a whole:

- High
- Moderate
- Low
- Very Low

Incidence of re-hospitalizations within 30 days after PCI between the SDD and ON groups was 131 of 1,645 (8.0%) versus 10,147 of 105,827 (9.6%) (OR: 0.62, 95% CI: 0.10 to 3.98), respectively.

Total number of complications reported in the SDD group were 148 of 3,156 (4.7%) versus 10,272 of 106,629 (9.6%) for the ON group, (OR: 0.67, 95% CI: 0.27 to 1.66).

A sensitivity analysis was performed by removing the largest study:
- total complications in the remaining SDD group was 19 of 1,817 (1.0%) versus 23 of 950 (2.4%) in the ON group (OR: 0.4, 95% CI: 0.07 to 2.14)
- incidence of re-hospitalization was 3 of 306 (1.0%) in the SDD versus 2 of 148 (1.4%) in the ON group (OR: 0.34, 95% CI: 0.01 to 22.57)
• 1.2% arrhythmias
• No difference observed between the 2 groups for primary composite endpoints of death/MI/TLR (7.17% vs. 6.07%; OR: 0.90; 95% CI: 0.43 to 1.87; P = 0.78)
• No difference in major bleeding/vascular complications (1.88% vs 1.29%; OR: 1.69; 95% CI: 0.84 to 3.40; P = 0.15)

Observational studies:
• Primary composite endpoint of death/MI/TLR occurred at pooled rate of 1.00% (95%CI: 0.58 to 1.68)
• Major bleeding/vascular complications occurred at pooled rate of 0.68% (95% CI: 0.35 to 1.32)
• 15 deaths in SDD group (11 occurred after 24 h; timing was unclear in remaining 4)

Bundhun, P. K., et al., 2017, PLOSONE
To compare adverse clinical outcomes associated with same day discharge vs. overnight stay in the hospital following PCI
Systematic review and meta-analysis
8 RCTs published between 1996 and 2016
3,081 patients (1,598 patient were discharged on the same day and 1,483 patients stayed overnight)
Stable CAD patients
30-day follow up:
• Mortality, MI and MACEs were not significantly different between same day discharge and overnight stay following PCI with OR: 0.22, 95% CI: 0.04–1.35; P = 0.10, OR: 0.68, 95% CI: 0.33–1.41; P = 0.30 and OR: 0.45, 95% CI: 0.20–1.02; P = 0.06 respectively
• Blood transfusion and re-hospitalization were also not significantly different between these two groups with OR: 0.64, 95% CI: 0.13–3.21; P = 0.59 and OR: 1.53, 95% CI: 0.88–2.65; P = 0.13 respectively
• Any adverse event, major bleeding and repeated revascularization were also not

Study Limitations =
□ None
□ Systematic Review
□ Review did not address focused clinical question
☒ Search was not detailed or exhaustive
□ Quality of the studies was not appraised or studies were of low quality
□ Methods and/or results were inconsistent across studies
<table>
<thead>
<tr>
<th>Study</th>
<th>Objective</th>
<th>Design</th>
<th>Methods</th>
<th>Findings</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saad, Y., et al., 2015, Heart, Lung and Circulation</td>
<td>To assess safety and efficacy of Same Day Discharge (SDD) of patients who underwent elective percutaneous coronary intervention (PCI)</td>
<td>Retrospective cohort</td>
<td>303 patients (mean age 62+/- 9 years, 89% male)</td>
<td>Low risk patients who underwent an elective PCI using mainly a femoral approach can be safely discharged on the same day of the procedure. Average observation time of 4.5 hours post-PCI appeared sufficient for effective triage of low risk patients for the SDD. No events were reported during the first 48 hours after PC.</td>
<td>Study Limitations = None</td>
</tr>
<tr>
<td>Din, J.N., et al., 2017, Catheterization and Cardiovascular Interventions</td>
<td>To study current practices of interventional cardiologists concerning length of stay after PCI</td>
<td>Cross-sectional survey</td>
<td>505 responses to online survey from interventional radiologists</td>
<td>Reported practice for uncomplicated elective PCI: 24% same-day discharge, 70% overnight observation, 6% either extended observation or inpatient stay.</td>
<td>Study Limitations = None</td>
</tr>
<tr>
<td>Nascimento, F. O., et al., 2014, The Journal of Invasive Cardiology</td>
<td>Retrospective cohort</td>
<td>93 consecutive patients discharged on same day after uncomplicated elective PCI</td>
<td>95 consecutive patients stayed overnight in the hospital for routine observation after uncomplicated elective PCI (control group)</td>
<td></td>
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</tbody>
</table>

### Patient Factors:
- 49 +/-1% (US) vs 40 +/-2% (Non-US) (P <=0.05)

### Anatomical Factors:
- 66 +/-2% (US) vs 54 +/-2% (Non-US) (P <=0.001)

### Procedural Factors:
- 63 +/-1% (US) vs 55 +/-2% (Non-US) (P <=0.01)

### Complications:
- 47 +/-1% (US) vs 40 +/-2% (Non-US) (P ns)

Patients undergoing PCI via femoral access had higher rates of same day discharge is vascular closure device used compared with manual hemostasis (31% vs. 13%; P<0.001)

### 48-hour outcomes:
- Overall NACE events occurred in 0 SDD patients an in 2 ONS patients – no statistically significant difference between the two groups (P = .25)
  - No major bleeding occurred in either group
  - No minor bleeding in SDD group and 2 ONS patients (P = .25)
  - No major vascular complications in either group
  - Minor vascular complications occurred in 2 SDD patients and 5 ONS patients (P = .23)
  - No target vessel revascularization or stroke in patients in either group

### 30-day outcomes:
- No statistical difference between both groups in rate of composite NACE or in individual complication rates
  - No deaths in SDD group vs 1

### Study Limitations =
- Non-Experimental/Observational Studies (case-control, cohort, cross sectional, longitudinal, descriptive, epidemiologic, case study/series, survey)
  - Insufficient sample size
  - Sample not representative of patients in the population as a whole
  - Variables (confounders, exposures, predictors) were not described and accounted for
  - Outcome criteria not objective or were not applied in blind fashion
  - Insufficient follow-up, if applicable
  - For prognostic study, sample not defined at common point in course of disease/condition
  - For diagnostic study, gold standard not applied to all patients
  - For diagnostic study, no independent, blind comparison between index test and gold standard
perfusion imaging or stenosis on coronary computerized tomography
- Successful PCI
- No angiographic evidence of untreated intimal dissection
- Absence of vascular complications at completion of PCI
- PCI performed before 3 p.m. to allow 6 hours of observation before discharge on same day

Exclusion criteria:
- Non-ST elevation myocardial infarction or ST-elevation myocardial infarction as indication for PCI
- Complex PCI (unprotected left main intervention, atherectomy, chronic total occlusions or interventions on a last remaining vessel)
- Significant procedural complications (prolonged chest pain, transient closure, no-flow or slow-flow phenomenon, hemodynamic instability, persistent electrocardiographic changes, major side-branch occlusion or an angiographically suboptimal result)
- Unresolved peri-procedural hemodynamic or electrical instability

in ONS group from non-cardiovascular causes (P = .51)
- Overall NACE events occurred in 3 SDD patients and 6 ONS patients with no statistically significant difference between groups (P = .26)
- No major bleeding occurred in either group
- No major vascular complications in either group
- 2 SDD patients and 1 ONS patient underwent target vessel revascularization (P = .18)
- 1 SDD patient and 4 ONS patients had myocardial infarction (P = .19)
- No stroke in either group

See Table 5 below for Inclusion/Exclusion Criteria for Same-Day Discharge
**Saad, Y., et al., 2015, Heart, Lung and Circulation:**

### Table 1

**Criteria for Same-day Discharge.**

<table>
<thead>
<tr>
<th><strong>Inclusion criteria</strong></th>
<th><strong>Exclusion criteria</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Be a non inpatient undergoing a planned, non emergency procedure on Monday – Thursday.</td>
<td>• Temporary vessel closure during PCI</td>
</tr>
<tr>
<td>• Be willing to be discharged on the day of their PCI</td>
<td>• Suboptimal angiographic result</td>
</tr>
<tr>
<td>• Be considered suitable by the proceduralist</td>
<td>• Dissection type C to E</td>
</tr>
<tr>
<td>• Procedures required completion and a &gt; 4 hours observation period prior to 18:30 (latest time for discharge)</td>
<td>• Residual dissection after successful stent implantation</td>
</tr>
<tr>
<td>• Have a 6F or 7F sheath used</td>
<td>• Occlusion of major side branch</td>
</tr>
<tr>
<td>• Have an uncomplicated procedure (does not meet any angiographic exclusion criteria below)</td>
<td>• Angiographic thrombus</td>
</tr>
<tr>
<td>• Have a suitable social environment (does not meet any social exclusion criteria below)</td>
<td>• No reflow/slow flow phenomenon</td>
</tr>
<tr>
<td>• Have no acute changes on post PCI ECG</td>
<td>• Perforation with guide wire</td>
</tr>
<tr>
<td>• Have adequate puncture site haemostasis (successfully deployed femoral closure device or radial approach preferred but not essential)</td>
<td></td>
</tr>
<tr>
<td>• Be able to ambulate 4 hours post sheath removal without problems</td>
<td></td>
</tr>
</tbody>
</table>

**Exclusion criteria**

- **Angiographic Exclusions**
  - Temporary vessel closure during PCI
  - Suboptimal angiographic result
  - Dissection type C to E
  - Residual dissection after successful stent implantation
  - Occlusion of major side branch
  - Angiographic thrombus
  - No reflow/slow flow phenomenon
  - Perforation with guide wire

- **Clinical Exclusion**
  - Age 80 years or greater
  - Severe renal failure (GFR < 30ml/min)
  - Severe bleeding risk (eg on warfarin/LMWH etc)
  - Severe LV dysfunction (EF <30%) or symptomatic heart failure
  - Severe visual or hearing impairment
• Multi-vessel stenting #
• Use of GP IIb/IIIa inhibitors

Social Exclusions
• Lives alone or has no telephone
• Staying 30 minutes or more, by car, from Liverpool hospital on first night
• Patient or co-habiting relative/friend cannot communicate with nursing/medical staff without the need for an interpreter

# Multi-vessel disease was stenosis ≥ 50% in ≥ 2 major coronary arteries or a left main stenosis of ≥ 50%. Patients with MVD not undergoing multi-vessel PCI, were not excluded.

Nascimento, F. O., et al., 2014, The Journal of Invasive Cardiology:

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Elective PCI for stable or crescendo angina, or asymptomatic but positive stress test or stenosis on coronary computerized tomography</td>
<td>1. Non-ST elevation myocardial infarction or ST-elevation myocardial infarction as indication for PCI</td>
</tr>
<tr>
<td>2. Successful PCI</td>
<td>2. Complex PCI (unprotected left main intervention, atherectomy, chronic total occlusions, or interventions on a last remaining vessel)</td>
</tr>
<tr>
<td>3. No angiographic evidence of untreated intimal coronary dissection</td>
<td>3. Significant procedural complications (prolonged chest pain, transient closure, no-flow or slow-flow phenomenon, hemodynamic instability, persistent electrocardiographic changes, major side-branch occlusion, or an angiographically suboptimal result)</td>
</tr>
<tr>
<td>4. Absence of unresolved postprocedural chest pain</td>
<td>4. Unresolved periprocedural hemodynamic or electrical instability</td>
</tr>
<tr>
<td>5. Systolic blood pressure lower than 160 mm Hg at the time of discharge</td>
<td>5. Serum creatinine greater than 2.0 mg/dL</td>
</tr>
<tr>
<td>6. Absence of vascular complications at completion of PCI</td>
<td></td>
</tr>
<tr>
<td>7. PCI performed before 3 pm to allow 6 hours of observation before discharge on the same day</td>
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</tr>
</tbody>
</table>

Note: all inclusion and exclusion criteria should be met. PCI = percutaneous coronary intervention.
REFERENCES


### Appendix A: GRADE criteria for rating a body of evidence on an intervention

Developed by the GRADE Working Group

#### Grades and interpretations:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Further research is very unlikely to change our confidence in the estimate of effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.</td>
</tr>
<tr>
<td>Low</td>
<td>Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.</td>
</tr>
<tr>
<td>Very low</td>
<td>Any estimate of effect is very uncertain.</td>
</tr>
</tbody>
</table>

#### Type of evidence and starting level

<table>
<thead>
<tr>
<th>Type of Evidence</th>
<th>Starting Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized trial</td>
<td>high</td>
</tr>
<tr>
<td>Observational study</td>
<td>low</td>
</tr>
<tr>
<td>Any other evidence</td>
<td>very low</td>
</tr>
</tbody>
</table>

#### Criteria for increasing or decreasing level

**Reductions**
- Study quality has serious (–1) or very serious (–2) problems
- Important inconsistency in evidence (–1)
- Directness is somewhat (–1) or seriously (–2) uncertain
- Sparse or imprecise data (–1)
- Reporting bias highly probable (–1)

**Increases**
- Evidence of association† strong (+1) or very strong (+2)
- Dose-response gradient evident (+1)
- All plausible confounders would reduce the effect (+1)

†Strong association defined as significant relative risk (RR 2-5 or 0.5-0.2) based on consistent evidence from two or more studies with no plausible confounders; Very strong association defined as significant relative risk (RR >5 or <0.2) based on direct evidence with no threats to validity
Appendix B. Trustworthy Guideline rating scale

The University of Pennsylvania’s Center for Evidence-Based Practice Trustworthy Guideline rating scale is based on the Institute of Medicine’s “Standards for Developing Trustworthy Clinical Practice Guidelines” (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.

The purpose of this scale is to focus on the weaknesses of a guideline that may reduce the trust a clinical user can have in the guideline, and distinguish weaknesses in documentation (e.g. guideline does not have a documented updating process) from weaknesses in the guidance itself (e.g. recommendations are outdated). Current quality scales like AGREE emphasize documentation. They are important checklists for developers of new guidelines, but are less useful for grading existing guidelines. These scales also are harder for clinicians and other persons who are not methodology experts to apply, and their length discourages their use outside formal technology assessment reports. This new scale is brief, balanced, and easy and consistent to apply.

We do not attempt to convert the results of this assessment into a numeric score. Instead we present a table listing the guidelines and how they are rated on each standard. This facilitates qualitative understanding by the reader, who can see for what areas the guideline base as a whole is weak or strong as well as which guidelines are weaker or stronger.

1. Transparency

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Guideline development methods are fully disclosed.</td>
</tr>
<tr>
<td>B</td>
<td>Guideline development methods are partially disclosed.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline development methods are not disclosed.</td>
</tr>
</tbody>
</table>

The grader must refer to any cited methods supplements or other supporting material when evaluating the guideline. Methods should include:

- Who wrote the initial draft
- How the committee voted on or otherwise approved recommendations

Evidence review, external review and methods used for updating are not addressed in this standard.

2. Conflict of interest

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Funding of the guideline project is disclosed, disclosures are made for each individual panelist, and financial or other conflicts do not apply to key authors of the guideline or to more than 1 in 10 panel members.</td>
</tr>
<tr>
<td>B</td>
<td>Guideline states that there were no conflicts (or fewer than 1 in 10 panel members), but does not disclose funding source.</td>
</tr>
<tr>
<td>C</td>
<td>Lead author, senior author, or guideline panel members (at least 1 in 10) have conflict of interest, or guideline project was funded by industry sponsor with no assurance of independence.</td>
</tr>
<tr>
<td>NR</td>
<td>Guideline does not report on potential conflict of interests.</td>
</tr>
</tbody>
</table>

For purposes of this checklist, conflicts of interest include employment by, consulting for, or holding stock in companies doing business in fields affected by the guideline, as well as related financial conflicts. This definition should not be considered exclusive. As much as anything, this is a surrogate marker for thorough reporting, since it may be assumed that guideline projects are funded by the sponsoring organization and many authors think it unnecessary to report a non-conflict.

3. Guideline development group

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Guideline development group includes 1) methodological experts and clinicians and 2) representatives of multiple specialties.</td>
</tr>
<tr>
<td>B</td>
<td>Guideline development group includes one of the above, but not both.</td>
</tr>
</tbody>
</table>
Guideline developers all from one specialty or organization, and no methodologists.

Affiliations of guideline developers not reported

The purpose of this standard is to ensure that supporters of competing procedures, or clinicians with no vested interest in utilization of one procedure or another, are involved in development of the guideline. Both AGREE II and IOM call for patient or public involvement: very few guideline panels have done so to date, so this is not necessary for guidelines to be rated A. Involvement of methodologists or HTA specialists in the systematic review is sufficient involvement in the guideline development group for our purposes. In the absence of any description of the guideline group, assume the named authors are the guideline group.

4. Systematic review

A Guideline includes a systematic review of the evidence or links to a current review.
B Guideline is based on a review which may or may not meet systematic review criteria.
C Guideline is not based on a review of the evidence.

In order to qualify as a systematic review, the review must do all of the following:
- Describe itself as systematic or report search strategies using multiple databases
- Define the scope of the review (including key questions and the applicable population)
- Either include quantitative or qualitative synthesis of the data or explain why it is not indicated

Note: this element does not address the quality of the systematic review: simply whether or not it exists. Concerns about quality or bias of the review will be discussed in text, where the analyst will explain whether the weaknesses of the review weaken the validity or reliability of the guideline.

Note: a guideline may be rated B on this domain even if the review on which it is based is not available to us. This potential weakness of the guideline should be discussed in text of the report.

5. Grading the supporting evidence

A Specific supporting evidence (or lack thereof) for each recommendation is cited and graded
B Specific supporting evidence (or lack thereof) for each recommendation is cited but the recommendation is not graded.
C Recommendations are not supported by specific evidence.

To score a B on this domain there should be specific citations to evidence tables or individual references for each relevant recommendation in the guideline, or an indication that no evidence was available. Any standardized grading system is acceptable for purposes of this rating. If a guideline reports that there is no evidence available despite a thorough literature search, it may be scored B on this domain, or even A if evidence for other recommendations is cited and graded.

6. Recommendations

A Considerations for each recommendation are documented (i.e. benefits and harms of a particular action, and/or strength of the evidence); and recommendations are presented in an actionable form.
B Either one or the other of the above criteria is met.
C Neither of the above criteria are met

In order to be actionable, the guideline should specify the specific population to which the guideline applies, the specific intervention in question, and the circumstances under which it should be carried out (or not carried out). The language used in the recommendations should also be consistent with the strength of the recommendation (e.g. directive and active language like “should” or “should not” for strong recommendations, and passive language like “consider” for weak recommendations). A figure or algorithm is considered actionable as long as it is complete enough to incorporate all the applicable patients and interventions. Please see the forthcoming NICE manual (24) for a good discussion of actionability in guidelines.
7. External review

<table>
<thead>
<tr>
<th></th>
<th>Guideline was made available to external groups for review.</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Guideline was reviewed by members of the sponsoring body only.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline was not externally reviewed.</td>
</tr>
<tr>
<td>NR</td>
<td>No external review process is described.</td>
</tr>
</tbody>
</table>

8. Updating and currency of guideline

<table>
<thead>
<tr>
<th></th>
<th>Guideline is current and an expiration date or update process is specified.</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>Guideline is current but no expiration date or update process is specified.</td>
</tr>
<tr>
<td>C</td>
<td>Guideline is outdated.</td>
</tr>
</tbody>
</table>

A guideline is considered current if it is within the developers’ stated validity period, or if no period or expiration data is stated, the guideline was published in the past three years (NOTE: the specific period may be changed at the analyst’s discretion, based on whether the technology is mature and whether there is a significant amount of recent evidence). A guideline must address new evidence when it is updated. A guideline which is simply re-endorsed by the panel without searching for new evidence must be considered outdated.