

**Critical Review Form
Meta-Analysis**

PGY-2

[Cabello JB, Burls A, Empananza JI, Bayliss SE, Quinn T. Oxygen therapy for acute myocardial infarction. Cochrane Database Syst Rev. 2016 Dec 19;12:CD007160.](#)

Objective: “To assess the effects of routine use of inhaled oxygen for acute myocardial infarction (AMI).” (p. 9)

Methods: The authors sought to identify any randomized controlled trial (RCT) in which adults of any age with suspected or proven AMI (either STEMI or NSTEMI) were enrolled within 24 hours of symptom onset and were randomized to receive either inhaled oxygen administered by any device (at normal pressure) for one hour or more within 24 hours of symptom onset or to receive air (or titrated oxygen in the event of desaturation). The authors used a nine-point scale suggested by GRADE to classify outcomes into three levels of importance; they only included studies with type 1 (“critical for decision-making”) or type 2 (“important but not critical for decision-making) outcomes reported. Mortality was prespecified as the primary outcome.

Numerous bibliographic databases were searched, including the Cochrane Central Register of Controlled Trials, MEDLINE In-Process, Embase, PubMed, CINAHL, and Web of Science. Clinical trial registers were also searched, as were the proceedings of several relevant annual meetings and conferences. The authors also contacted experts in the field to identify additional unpublished research.

Study quality was assessed using the two-part tool described in section 8.5 of the Cochrane Handbook ([Higgins 2011](#)), which looks at six specific domains: sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other potential threats to validity. Studies were classified as having low, high, or unclear risk of bias based on the results of the assessment.

The authors performed two sets of meta-analyses. In the first, they pooled data as reported for those patients with confirmed AMI in four of the studies. In the second, they analysed patients on a strict intention-to-treat fashion, including those patients initially enrolled in the studies with presumed AMI, who were later excluded when deemed not to have AMI. A subgroup analysis of studies conducted during the reperfusion era was also performed (excluding one study performed in the 1970s).

A [previous Cochrane review on this topic](#), conducted in 2013 identified four relevant studies. During this updated search, conducted in June 2016, 204 new records were identified, of which only one new RCT was eligible for inclusion. The 5 studies included in this meta-analysis comprised a total of 1173 participants, of whom 75.3% were men.

Guide	Question	Comments
I	<i>Are the results valid?</i>	
1.	Did the review explicitly address a sensible question?	Yes. Oxygen has long been touted as a key in the treatment of patients with suspected MI, albeit based on little evidence. More recently, evidence has come to light regarding the dangers of hyperoxemia in many conditions, including following cardiac arrest , in traumatic brain injury , and following stroke . An assessment of the risks and benefits of supplemental oxygen in otherwise normoxic patients would therefore help guide management of these cases.
2.	Was the search for relevant studies detailed and exhaustive?	Yes. The authors searched all of the major bibliographic databases, several registries of controlled trials to find ongoing studies, and proceedings of annual meetings and conferences. They also contacted experts to identify additional unpublished studies. Their search was conducted without language or date restriction. This is an impressively broad search.
3.	Were the primary studies of high methodological quality?	No. Overall, the risk of bias associated with the primary outcome, and for the main outcomes across studies, was rated as high. This was primarily due to lack of blinding in all but one of the studies and inadequate reporting of methods in almost all of the studies.
4.	Were the assessments of the included studies reproducible?	Yes. The authors assessed study quality using the two-part tool described in section 8.5 of the Cochrane Handbook (Higgins 2011). This tool has been used for years by the Cochrane collaborative.
II.	<i>What are the results?</i>	
1.	What are the overall results of the study?	<ul style="list-style-type: none"> • The pooled risk of mortality in patients with confirmed AMI was similar between the groups (RR 1.02, 95% CI 0.52 to 1.98; $I^2 = 49\%$), as it was for the ITT analysis (RR 0.99, 95% CI 0.50 to 1.95; $I^2 = 46\%$). • Pooled risk of mortality in the 3 studies performed in the reperfusion era yielded a RR of 0.58 (95% CI 0.24 to 1.39; $I^2 = 0\%$). • Cardiac failure was measured in 2 studies, with a pooled RR of 0.88 (95% CI 0.50 to 1.55; $I^2 = 27\%$). • Recurrent infarction or ischemia was measured in 2 trials, with a pooled RR of 1.67 (95% CI 0.94 to 1.99; $I^2 = 80\%$). • Opiate use was measured in 2 trials, with a RR 0.99 (95% CI 0.83 to 1.18; $I^2 = 54\%$). • Measures of infarct size (cardiac enzymes and cardiac MRI) varied between studies and hence could not be pooled, but overall did not suggest any

		statistically significant benefit or harm from oxygen therapy.
2.	How precise are the results?	See above. For the primary outcome, mortality, the pooled results did not find a statistically significant difference between the groups. The confidence intervals were fairly narrow, given that ~800-1000 patients were included in each pooled result.
3.	Were the results similar from study to study?	See above. Overall, there was at least moderate heterogeneity (I^2 values of 25% to 50%) for most of the outcomes, including mortality. Much of this is likely due to methodological and clinical differences between the studies. For the 3 studies conducted in the reperfusion era, there very little heterogeneity ($I^2 = 0\%$).
III.	<i>Will the results help me in caring for my patients?</i>	
1.	How can I best interpret the results to apply them to the care of my patients?	Overall, the current evidence does not suggest any significant benefit to providing oxygen in the setting of suspected or confirmed AMI in normoxic patients. While this data is limited by significant heterogeneity and poor study quality, the lack of benefit observed was fairly consistent.
2.	Were all patient important outcomes considered?	Yes. The authors of the meta-analysis at least attempted to consider most important outcomes, including mortality, cardiac failure, and dysrhythmias. There ability to provide meaningful estimates of effect size was limited by the studies themselves, which did not all report on these outcomes, and which used variables measures of these outcomes in some instances. The authors did not include any patient-centered measures of long-term outcomes, such as quality of life (e.g. via the Chronic Heart Failure Questionnaire).
3.	Are the benefits worth the costs and potential risks?	Likely no. Given the lack of clear benefit across all the studies, and in the pooled analysis, it seems that there is no benefit to giving oxygen to normoxic patients with suspected or confirmed AMI.

Limitations:

- 1. Quality of evidence was overall low, with high risk of bias Three of the five studies provided no description of [random sequence generation](#), only one study was [double-blinded](#) (and used a questionable method to achieve this), and all studies had issues with incomplete outcome data.**
- 2. Overall, there was at least moderate [heterogeneity](#) (I^2 values of 25% to 50%) for most of the outcomes, including mortality.**

3. Given the concern that oxygen therapy may decrease infarction size and preserve cardiac function, it would have been helpful to see some [patient-centered](#) measure of long-term outcomes, such as quality of life (e.g. via the [Chronic Heart Failure Questionnaire](#)).

Bottom Line:

This systematic review and meta-analysis looking at the effects of oxygen in patients with confirmed or suspect AMI involved an extensive literature search and rigorous assessment of study quality. Overall, the risk of bias in the 5 included studies was high. Meta-analysis revealed no significant effect on mortality, cardiac failure, recurrent infarction or ischemia, or infarct size measured by cardiac enzymes. These results are limited by the poor quality of the included studies, but overall suggest that routine administration of oxygen in patients with suspected AMI is not necessary, though it seems unlikely to cause significant harm.