**Clinical question.**
In patients with suspected ACS/STEMI in the ED and prehospital settings (P), does the use of nitroglycerin (I), compared with no nitroglycerin (C), improve diagnosis of ACS/MI (O)?

- **Is this question addressing an intervention/therapy, prognosis or diagnosis?** Diagnosis

- **State if this is a proposed new topic or revision of existing worksheet:**

- **Conflict of interest specific to this question:**
Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? No

### Search strategy (including electronic databases searched).

- **Key words:**
  - Nitroglycerin
  - Acute coronary syndrome
  - Myocardial infarction
  - Acute myocardial infarction
  - Emergency Department
  - Pre-hospital

- **Databases Searched**
  - PubMed: 
    - (“nitroglycerin”[MeSH Terms] OR “nitroglycerin”[All Fields]) AND acute[All Fields] AND 
    - (“myocardial infarction”[MeSH Terms] OR “myocardial”[All Fields] AND “infarction”[All Fields]) OR 
    - “myocardial infarction”[All Fields]) AND specificity[Title/Abstract] 
    - (“nitroglycerin”[MeSH Terms] OR “nitroglycerin”[All Fields]) AND ST-segment[All Fields] AND 
    - elevation[All Fields] AND (“myocardial infarction”[MeSH Terms] OR “myocardial”[All Fields] AND 
    - “Infarction”[All Fields]) OR “myocardial infarction”[All Fields])
  - Cochrane Database: keywords myocardial infarction and nitroglycerin
  - AHA Endnote Master library

References were reviewed and each article was reviewed for new citations. Primary studies were presented instead of subgroup analyses when available.

- **State inclusion and exclusion criteria**

  - **Inclusion:** All patients treated with an nitroglycerin at the time of presentation in the emergency department or prehospital setting

  - **Exclusion criteria:** Initiation of treatment > 24 hours after symptom onset, initiation of therapy post invasive procedure, initiation of therapy after 24 hours from presentation

- **Number of articles/sources meeting criteria for further review:**

  - 135 articles met criteria based on the primary search. 55 articles were reviewed, 27 included in the analysis. Reason for exclusion: Initiation of nitroglycerin > 24 hours after symptom onset (18), post procedure (7), 24 hrs after admission (3)
Summary of evidence

Evidence Supporting Clinical Question

| Good | | | | | |
|-----|-----|-----|-----|-----|
| Fair | | | | | |
| Poor | | | | | |
| D1 | D2 | D3 | D4 | D5 |

A = Return of spontaneous circulation endpoint  
B = Survival of event studies  
C = Survival to hospital discharge  
D = Intact neurological survival  
E = Other  

*Italics = Animal*
### Evidence Neutral to Clinical question

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**Level of evidence**

A = Return of spontaneous circulation endpoint  
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C = Survival to hospital discharge  
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### Evidence Opposing Clinical Question

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A = Return of spontaneous circulation endpoint  
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REVIEWER’S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

Discussion: It has been well established that nitroglycerin is a useful therapeutic tool, use of relief of pain after administration of nitroglycerin is often viewed as indicative of coronary artery disease. Several studies have utilized the reduction of pain as a criteria for angina and have included it as a component of complex decision rules. This worksheet evaluated the relief of pain as a unique diagnostic tool.

In a conveyance sample of 649 emergency department patients in a LOE D3 trial, the change in pain score before and after nitroglycerin sublingual administration was not associated with a diagnosis of CAD. This study however was limited by lack of routine diagnostic testing and incomplete follow-up. (Diercks 2005, 581). In another LOE D3 study, a convenience sample of 270 patients were studied. The investigators report a LR positive of 1.1 suggesting poor diagnostic accuracy (Steele 2006, 164). Henrikson et al in a LOE D3 trial reported a likelihood ratio positive and negative with a 95% CI that included 1. (Henrikson, 2003, 979). Goodacre in a LOE D3 trial evaluated the relief of pain with nitroglycerin as an independent predictor of AMI or ACS in patients presenting to the emergency department and admitted for chest pain to an inpatient unit or observation unit. The value of pain relief was a dichotomized value and there was no association with the diagnosis of AMI or ACS in an univariate analysis. (Goodacre 2002, 203)

Based on the available studies, relief of pain with nitroglycerin is not a useful diagnostic tool when assessed by percent change, absolute relief, or percent change in visual analog scale in emergency department patients with chest pain.

Acknowledgements:
(Goodacre, Locker et al. 2002; Shry, Dacus et al. 2002; Henrikson, Howell et al. 2003; Diercks, Boghos et al. 2005; Steele, McNaughton et al. 2006)


Level of Evidence 3, fair, against
A change in pain scale after the administration of nitroglycerin was not diagnostic of coronary artery disease. The study used a convienence, sample with no consistent diagnostic strategy.


Level of Evidence 3, fair, against
This is a prospective observational trial to determine features useful for the diagnosis of ACS and AMI. Nitroglycerin was not a univariate predictor of AMI (OR 2.1, 95% CI 0.4-10.9) or ACS (OR 2.0, 95% CI 0.6-4.1).


Level of Evidence 3, fair, against
Using a 1-10 pain scale with a significant reduction defined as a 50% change in pain the authors reported no value of nitroglycerin. The likelihood ration positive was 1.0 and the AUC ROC curve was .48.


Level of Evidence 3, fair, against
This a retrospective review of admitted ED patients with chest pain of sjz\ Steele, R., T. McNaughton, et al. (2006). "Chest pain in emergency department patients: if the pain is relieved by nitroglycerin, is it more likely to be cardiac chest pain?" CJEM 8(3): 164-9.

Level of Evidence 3, fair, against
In this ED patient population 60 patients were identified as having CAD. The LR positive was 1.1 and the LR negative was 1.01. Almost all the patients were admitted therefore the patient population may be relatively high risk for CAD.