NATIONAL TRAINING AND RESEARCH APPRAISAL GROUP

Mortality and prehospital thrombolysis for acute myocardial infarction

Morrison et al. JAMA 283, 2686-2692 2000

1. METHODS	
1.1 Is the question clear? a) What is the population? b) What is the exposure/intervention? c) What is/are the outcome(s)?	Yes. Does prehospital administration of thrombolytics, compared with in hospital , reduce in-hospital mortality? a) Published and unpublished studies of patients being hospitalised for AMI b) Pre-hospital or in-hospital thrombolytic therapy c) All cause hospital mortality
1.2 Is the search thorough? a) Bibliographic database; years covered? b) References in relevant articles? c) Grey literature (unpublished research reports etc.)?	Yes a) 1982-1999 using Medline, Embase, Science Citations – also dissertation abstracts, current contents b) Yes. Texts and journal articles searched c) Yes. Grants, primary authors, thrombolytic agent manufacturers
1.3 Is the validity of included studies adequately assessed? a) Are the inclusion criteria appropriate? b) Has methodological quality been assessed? c) Is assessment reproducible, blind? d) Was missing information obtained from investigators? e) Is publication bias an issue?	Yes a) Yes – they selected for studies were there was a direct comparison of pre and in-hospital treatment in AMI as part of a randomised controlled trial, in which <u>all cause</u> hospital mortality was reported. b) Yes – using the Detsky scale – a reference is provided to this. c) Assessments of study selection and quality were made by two independent people and their agreement measured using the kappa statistic, given as a measure of agreement beyond chance. Assessments of quality were made blind to everything except methods and results. d) Authors were invited to review their data e) Probably not. The authors actively sought unpublished data to include in the data set. There is not enough data or sufficient spread in study numbers to do a funnel plot.

Critical Appraisal of an Overview (continued)

2. RESULTS	
2.1 Effect: a) On what scale is the effect measured? e.g., odds ratio b) How big is the overall effect?	a) Odds ratio – odds of hospital death after pre-hospital thrombolysis compared with odds of death after in hospital thrombolysis b) 0.83 – a 17% reduction in the odds of death
2.2 Consistency: a) Are the results consistent between studies? b) How sensitive are the results to changes in the way the review is done?	a) Measures of heterogeneity were not significant. The authors correctly point out that the power to detect a lack of homogeneity is low, given that there are only 6 studies. They have plotted the data in figure 2. One of them stands out and you can work out from table 3 that this is the GREAT study. The text mentions that this study had different inclusion criteria from the rest. b) Authors assessed whether there were differences in outcome if they only considered high quality studies or mobile ITUs and detected no differences.
2.3 Precision: a) Does the lower confidence limit (closest to 1 or 0, depending on whether ratio of difference) include clinically relevant effects? b) Does the upper confidence limit exclude clinically relevant effects?	OR = 0.83 (0.70 – 0.98) a) 0.98 tells us that we are 95% sure that there is at least a 2% reduction in the odds of death if given thrombolytics prior to coming into hospital. Given that the results are from trials, and the fact that there may be bias because of the lack of reporting of allocation concealment and blind outcomes in most, this is not particularly impressive b) 0.70, a potential 30% reduction in the odds of death is important
3. INTERPRETATION OF RESULTS	
3.1 Are subgroup analyses interpreted cautiously?	No subgroup analyses done
3.2 a) Can the conclusions and data be generalised to other settings? b) Is NNT (numbers needed to treat) stated or able to be calculated?	a) Probably, at least in westernised societies, because the outcome was similar in trials within different healthcare systems and with different providers, and is also similar to that seen in other reviews b) No, but you could calculate the proportion who die in the prehospital group and subtract this from the in-hospital proportion, using the data in table 3. This will give you the actual risk reduction (ARR). The NNT is1/ARR = 63 in this case.
3.3 Are recommendations linked to the strength of the evidence?	The OR suggests that there is a significant reduction in the odds of death – around 17%, but the NNT is high – you need to treat over 60 patients pre-hospital to benefit one more. This high NNT indicates that, despite the efficacy, only a small proportion

	of patients die in hospital on either treatment. The authors do not highlight this but do talk about whether a change in policy can be afforded. They also point out that the benefit is driven by time to needle, with about a one hour benefit in time. They suggest that this may be much less in an urban setting and a different policy might be more cost effective.