

S3-file: MEDLINE database search, flow diagram illustrating the literature selection process, and evidence assessment for the first query.

Query # 3: *“Does hypofibrinogenemia treatment reduce mortality in trauma?”*

PubMed search details: search date December 13 2014

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((("fibrinogen"[MeSH Terms] OR "fibrinogen"[All Fields]) AND ("organization and administration"[MeSH Terms] OR ("organization"[All Fields] AND "administration"[All Fields]) OR "organization and administration"[All Fields] OR "administration"[All Fields])) OR ((("fibrinogen"[MeSH Terms] OR "fibrinogen"[All Fields]) AND ("therapy"[Subheading] OR "therapy"[All Fields] OR "treatment"[All Fields] OR "therapeutics"[MeSH Terms] OR "therapeutics"[All Fields])) OR ("fibrinogen"[MeSH Terms] OR "fibrinogen"[All Fields])) AND ((("injuries"[Subheading] OR "injuries"[All Fields] OR "trauma"[All Fields] OR "wounds and injuries"[MeSH Terms] OR ("wounds"[All Fields] AND "injuries"[All Fields]) OR "wounds and injuries"[All Fields]) OR (traumatic[All Fields] AND ("haemorrhage"[All Fields] OR "hemorrhage"[MeSH Terms] OR "hemorrhage"[All Fields])) OR ("shock, traumatic"[MeSH Terms] OR ("shock"[All Fields] AND "traumatic"[All Fields]) OR "traumatic shock"[All Fields] OR ("traumatic"[All Fields] AND "shock"[All Fields]))) AND ("2000/"[PDAT] : "3000"[PDAT]))
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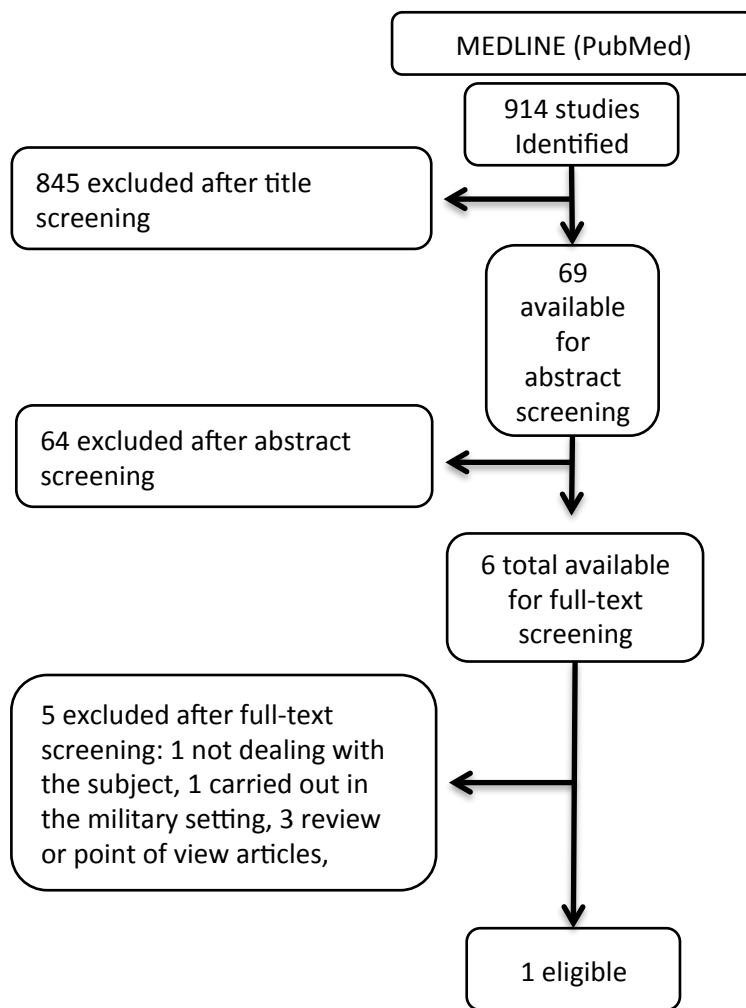


Table S3

Observational study	1	
Year	2012	
Journal	JTH	
First Author	Rourke	
Statistical method	Logistic regression	
Inclusion criteria	Time from injury to arrival within 120 minutes, SBP < 90 at admission, poor responsiveness to initial fluid administration	
Treatment	Fibrinogen administration within the first 12 hours	
Centres	2	Outcome NA
N° patients/centre/year	NA	Variable: OR (95%-CI) Fibrinogen: 0.91 (0.81-1.01)
Study duration (days)	1095	
Total (included in the model)	NR	
GRADE CRITERIA		
	Statistical reporting	Partial
	Statistical quality	Low
Downgrading	Appropriate eligibility criteria	Yes
	Measurement of exposure	Yes
	Measurement of outcome	Yes
	Control for confounding	No
	Bias	very serious
GRADE overall		
Up-grading	Size of effect	Very large
	Residual confounding	Does not indicate upgrading
	Dose /response	Yes
DETAILS		
Downgrading	Control for confounding: Important predictors were not included in the mortality model. Statistical reporting : Subgroup of coagulopathic patients from a sample of 517 patients. Not reported the number of patients and of deaths. Logistic regression. No Statistical support reported. Checking for conformity with linear gradient for continuous variables not reported. Test for interaction not reported. Internal validity assessment not reported. Goodness-of-fit assessment not reported. Collinearity assessment not reported. Statistical tests for models not reported. Variable selection method: Stepwise forward selection. Reporting of variable coding method not performed. Statistical quality: Insufficient statistical reporting. Important covariates are missing in the model (possible underfitting). No propensity score was developed. The analysis does not account for survival bias.	
Up-grading		
External validity	Only two centres participating to the study	
Conclusive evaluation	GRADE rating up/down	Downgraded study
	GRADE rating	Very low evidence
	Statistical reporting	Partial
	Statistical quality	Low
	External validity issues	Yes
Final grading	Downgraded study	