

## Supplementary

### Section 1: Adverse events

**Table I.** The adverse events observed in the five studies

Studies	Total adverse events	Prolonged cholestasis	Fever and rash	Vomiting and dyspepsia	Transient bronchospasm	Infection	Arrhythmia
Nabi <i>et al.</i> 2017 [23]	0%	0	0	0	0	0	0
Darweesh <i>et al.</i> 2017 [24]	NA	82	3	11	0	NA	NA
Singh <i>et al.</i> 2013 [21]	Not measured	NA	NA	NA	NA	NA	NA
Lee <i>et al.</i> 2009 [22]	46/81 (56.8%)	NA	2	11	1	20	9
Mumtaz <i>et al.</i> 2009 [25]	6/47 (12.7%)	NA	2	4	1	NA	NA

## Section 2: Search strategy

PubMed and Medline = 340

#	Searches	Results
1	Acetylcysteine and acute or fulminant liver failure	384
2	Acetylcysteine and viral hepatitis-induced acute liver failure	31
3	Acetylcysteine and drug-induced acute liver failure	204
4	Acetylcysteine and autoimmune hepatitis-induced liver failure	5
5	Acetaminophen and non-acetaminophen acute liver failure OR acetaminophen and non-paracetamol induced acute liver failure	59
6	1 or 2 or 3 or 4 or 5	384

Cochrane Library = 47

#	Searches	Results
1	Acetylcysteine and acute or fulminant liver failure	22
2	Acetylcysteine and viral hepatitis-induced acute liver failure	17
3	Acetylcysteine and drug-induced acute liver failure	8
4	Acetylcysteine and autoimmune hepatitis-induced liver failure	0
5	Acetaminophen and non-acetaminophen acute liver failure OR acetaminophen and non-paracetamol induced acute liver failure	0
6	1 or 2 or 3 or 4 or 5	47

ClinicalTrials.gov = 9

Searches	Results
Acetylcysteine and acute or fulminant liver failure	6
Acetylcysteine and viral hepatitis-induced acute liver failure	2
Acetylcysteine and drug-induced acute liver failure	1
Acetylcysteine and autoimmune hepatitis-induced liver failure	0
Acetaminophen and non-acetaminophen acute liver failure OR acetaminophen and non-paracetamol induced acute liver failure	1
1 or 2 or 3 or 4 or 5	9

Duplicates = 40

Records screened = 352

Clinical trials = 21

Clinical trials excluded = 16

Clinical trials analyzed = 5

### Section 3: Definitions

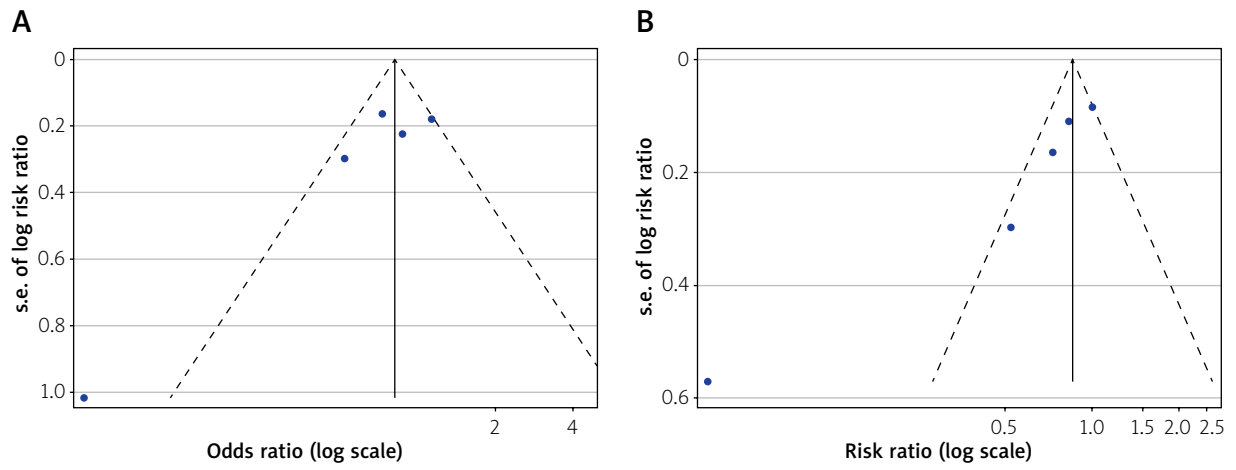
#### Outcome variable definitions

Variable	Common Definition
Acute or fulminant liver failure	Development of coagulopathy (INR > 1.5) and encephalopathy within 8 weeks of the first symptom in the absence of underlying cirrhosis. The ALF patients can have the underlying condition for less than 26 weeks
All-cause mortality	The death rate of the population from all causes of death during the study period
Liver transplant-free survival	The survival during the study period free of liver transplantation or liver related mortality
Length of stay	Length of hospital stay determined by number of nights spent in hospital starting from the day of admission

#### Section 4: Quality assessment

**Table:** showing Newcastle Ottawa Scale<sup>31</sup> for quality assessment of observational studies

Quality assessment criteria	Nabi <i>et al.</i> 2017 [23]	Darweesh <i>et al.</i> 2017 [24]	Singh <i>et al.</i> 2013 [21]	Lee <i>et al.</i> 2009 [22]	Mumtaz <i>et al.</i> 2009 [25]
Representativeness of exposed cohort	*	*	*	*	*
Representativeness of non-exposed cohort	—	—	*	*	*
Ascertainment of exposure	—	—	*	*	—
Outcome of interest was not present at beginning of study	*	*	*	*	*
Study controls for age/sex	*	*	*	*	*
Adjustment for 3 additional risk factors	*	*	*	*	*
Assessment of outcome	*	*	*	*	*
Was follow-up long enough?	—	*	—	—	—
Adequacy of follow-ups of cohorts	*	*	*	*	*
Overall quality score (maximum = 9)	6/9	7/9	8/9	8/9	7/9



**Supplemental Figure S1.** Funnel plot for bias assessment in overall and transplant-free survival