

SUPPORTING INFORMATION:

Supplementary Table 1: Trial inclusion criteria and definition details

Study	Assessment of alcohol use disorder	Treatment of alcohol use disorder	Diagnosis of alcohol-related liver disease	Trial required period of abstinence prior to transplant	Definition of relapse	Assessment of relapse	Accounted for Alcohol-related Hepatitis (N)	Accounted for Severe Alcohol-related Hepatitis (N)
Gish, 1993^[24]	All participants had a diagnosis of alcohol dependence or abuse according to DSM criteria	Alcohol contract documenting requirements of transplant team with rehabilitation and psychiatric care, drug testing, and abstinence commitment	Diagnosis of alcoholism and cirrhosis, included patients with other causes of liver disease	None – though only transplanted patients with 1 to 6 months of sobriety	Any consumption	Random blood or urine testing and interviews	Yes (7 – NS if transplant or no-transplant cohort)	No ¹
Anand, 1997^[22]	Psychiatrists assessed social support and probability of future abstinence	NS	NS	From the time patient medically advised to stop alcohol intake (no fixed period)	NS	Interviews	Yes (20 – no-transplant cohort)**	No
Poynard, 1999^[25]	NS	NS	Alcohol consumption \geq 50 g/day, absence of another cause of cirrhosis, histology	NS	NS	NS	NS	Yes, but no specific definition (1 – transplant and 1 no-transplant- matching criteria included “severe, biopsy proven, alcoholic hepatitis”)
Veldt, 2002^[26]	NS	NS	Alcohol consumption > 3 units per day for men or >2 units per day for women of longer than 5 years duration with diagnosis of cirrhosis based on “classical clinical,	6-month	Broke down into: 1) abstinent (self-declared with agreement of labwork) 2) sober (decreased	Interviews, lab work (alcohol level, GGT, MCV), physician evaluation	NS	Yes, defined as jaundice, elevated labs (white blood cell, aspartate aminotransferase), fever, and Maddrey’s discriminant function > 32 or encephalopathy (13 total, 5

			biological, and imaging criteria and on liver histology when available"		alcohol intake to <3 or <2 units per day for man and women respectively) 3) relapse – sobriety period alternating with "excessive consumption"		spontaneous improvement, 1 transplant)	
DiMartino, 2004 ^[23]	NS	NS	NS	NS	NS	Assessed every 3 months 1) "106 variables related to alcohol consumption" 2) "systematic detection of alcohol in blood and urine"	NS	NS
Immordino, 2009 ^[20]	NS	NS	Grouped patients with cirrhosis into either 1) Alcoholism Alone or 2) Alcoholism + miscellaneous causes	NS	NS	NS	Yes – When 3 of the following 4 findings were present on pathology "(1) polymorphonucl ear infiltrates, (2) centrolobular hepatocyte swelling and degeneration, (3) macrovesicular and	NS

							microvesicular steatosis, (4) Mallory's bodies" – (8 transplant patients)	
Alvarez, 2011^[21]	NS	NS	Alcohol consumption >80g/day in men and 60 g/day in women. Patients with other forms of liver disease were excluded	NS	NS	Interviews, followed by urine testing when "excessive use was suspected"	Yes – biopsy "showing histological cirrhosis with superimposed changes of alcoholic hepatitis"	Yes, severity defined by Maddrey's discriminant function >32 and or the presence of hepatic encephalopathy
Mathurin, 2011^[18]	Excluded candidates predisposed to addiction	NS	Jaundice not attributable to infectious etiology in past 3 months or recent GI bleed and absence of other causes of liver disease, including negative hepatitis B, C, and HIV testing. Additionally biopsy proven in 88% of transplanted patients (23/26)	None	Any alcohol consumption, with documentation of frequency, type, and amount	Interviews performed "at short intervals"	No	Yes, entire study population defined as Maddrey's discriminant function >32
Im, 2016^[19]	Psychosocial evaluations by transplant psychiatrists and social workers	NS	"Histological or clinical evidence of alcoholic hepatitis"	None	Defined 1) alcohol relapse after liver transplant – alcohol consumption of ≥ 4 drinks a day or ≥ 1 drink daily for 4 consecutive days	Assessment of alcohol consumption at "short intervals" by random alcohol testing	No	Yes, entire study population defined as Maddrey's discriminate function >32

					2) slip after liver transplant – brief alcohol consumption followed by abstinence			
Onishi, 2017^[27]	NS	Education and support from a psychiatrist was provided to a patient with a heavy drinking relapse	History of “habitual and excessive alcohol consumption”	NS	NS	Interviews	NS	NS

Diagnostic and Statistical Manual (DSM); Not Specified (NS)

¹Within the cohort, 7 (15%) patients had alcohol-related hepatitis, unclear how this was defined

Supplementary Table 2: Assessment of Risk of Bias

a) Newcastle – Ottawa Quality Assessment Scale Cohort and Case Control Studies

Title	Category (Maximum Stars)*		
	Selection (4)	Comparability (2)	Outcome/Exposure (4)
Gish, 1993 ^[24]	4	2	2
Anand, 1997 ^[22]	4	2	3
Poynard, 1999 ^[25]	3	2	2
Veldt, 2002 ^[26]	4	2	3
Immordino, 2009 ^[20]	4	1	3
Alvarez, 2011 ^[21]	4	0	3
Mathurin, 2011 ^[18]	2	1	2
Im, 2016 ^[19]	2	1	2
Onishi, 2017 ^[27]	4	0	3

¹The number indicated in brackets represents the maximum stars available in a category. If a category reached the maximum stars, the quality was considered high. If there was a deduction from the maximum, the quality was considered impaired.

b) Cochrane

Study	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Random sequence generation (selection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
DiMartino, 2004 ^[23]	U	U	U	U	U	U	L

High risk of bias (H); Low risk of bias (L); Unclear risk of bias (U)

Supplementary Table 3: Presence of relapse in the transplant cohort

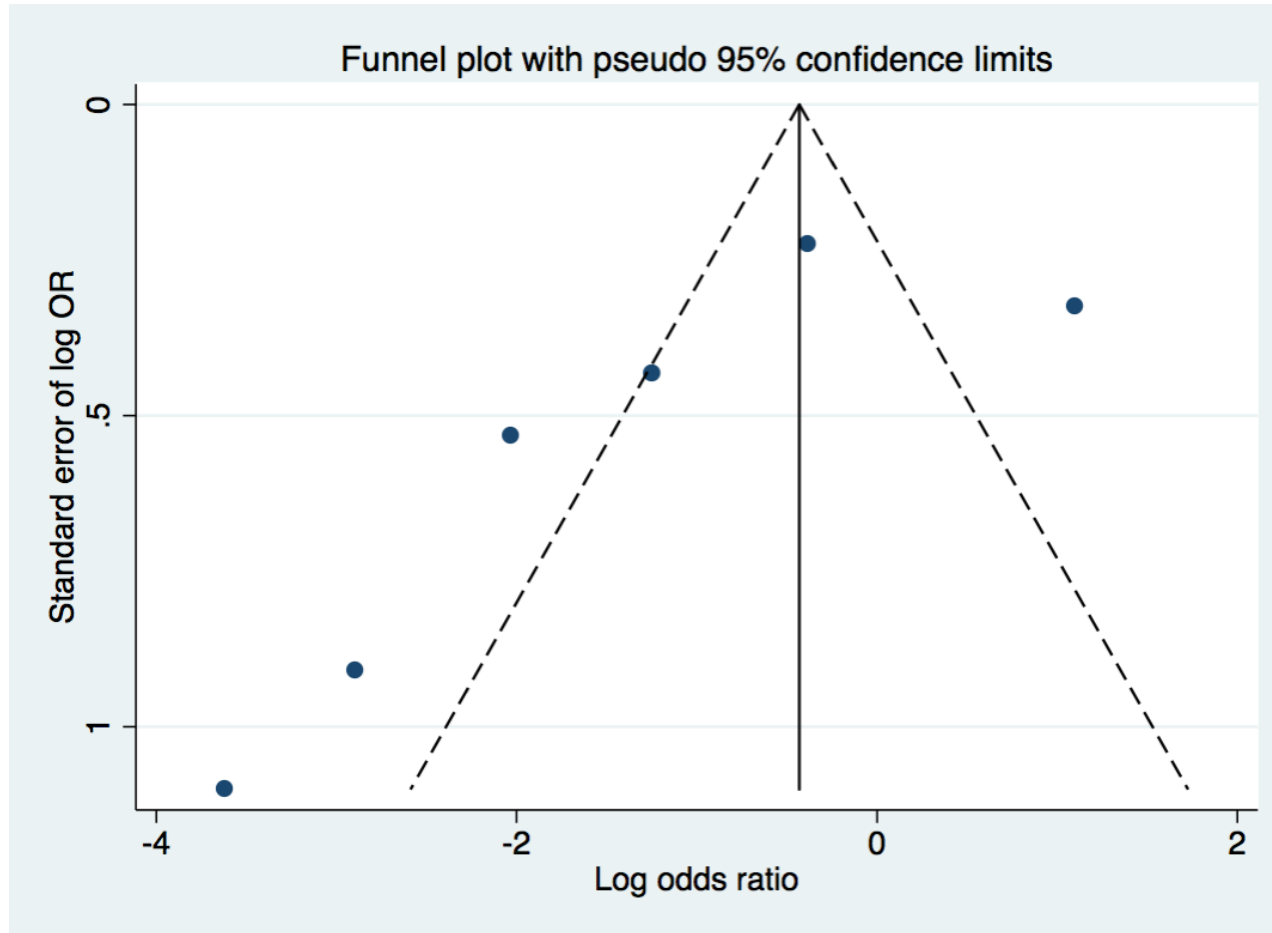
Study	Details of relapse in transplant cohort	Graft dysfunction N (%)	Retransplant N (%)
Gish, 1993^[24]	“drank transiently” “consumed alcohol less than 10 times”	NS	NS
Anand, 1997^[22]	60% (3/5) – “drinking socially” 20% (1/5) – pancreatitis 20% (1/5) – liver biopsy with fatty infiltration	0 (0)	NS
Poynard, 1999^[25]	31 – “drank alcohol”	2 (6)	1 (50)
Velldt, 2002^[26]	NS	NS	NS
DiMartino, 2004^[23]	NS	NS	NS
Immordino, 2009^[20]	NS	NS	NS
Alvarez, 2011^[21]	NS	NS	NS
Mathurin, 2011^[18]	67% (2/3) – daily consumption (30 g/day and >50 g/day) 33% (1/3) – occasional (estimated 10 g/week)	0 (0)	0 (0)
Im, 2016^[19]	50% (1/2) – “slips” of 60 and 15g of alcohol on two separate days followed by abstinence 50% (1/2) – elevated liver enzymes with liver biopsy consistent with alcohol-related hepatitis	0 (0)	0 (0)
Onishi, 2017^[27]	100% (1/1) – “heavy drinking” who was able to “successfully quit drinking”	0 (0)	0 (0)

Supplementary Figures:

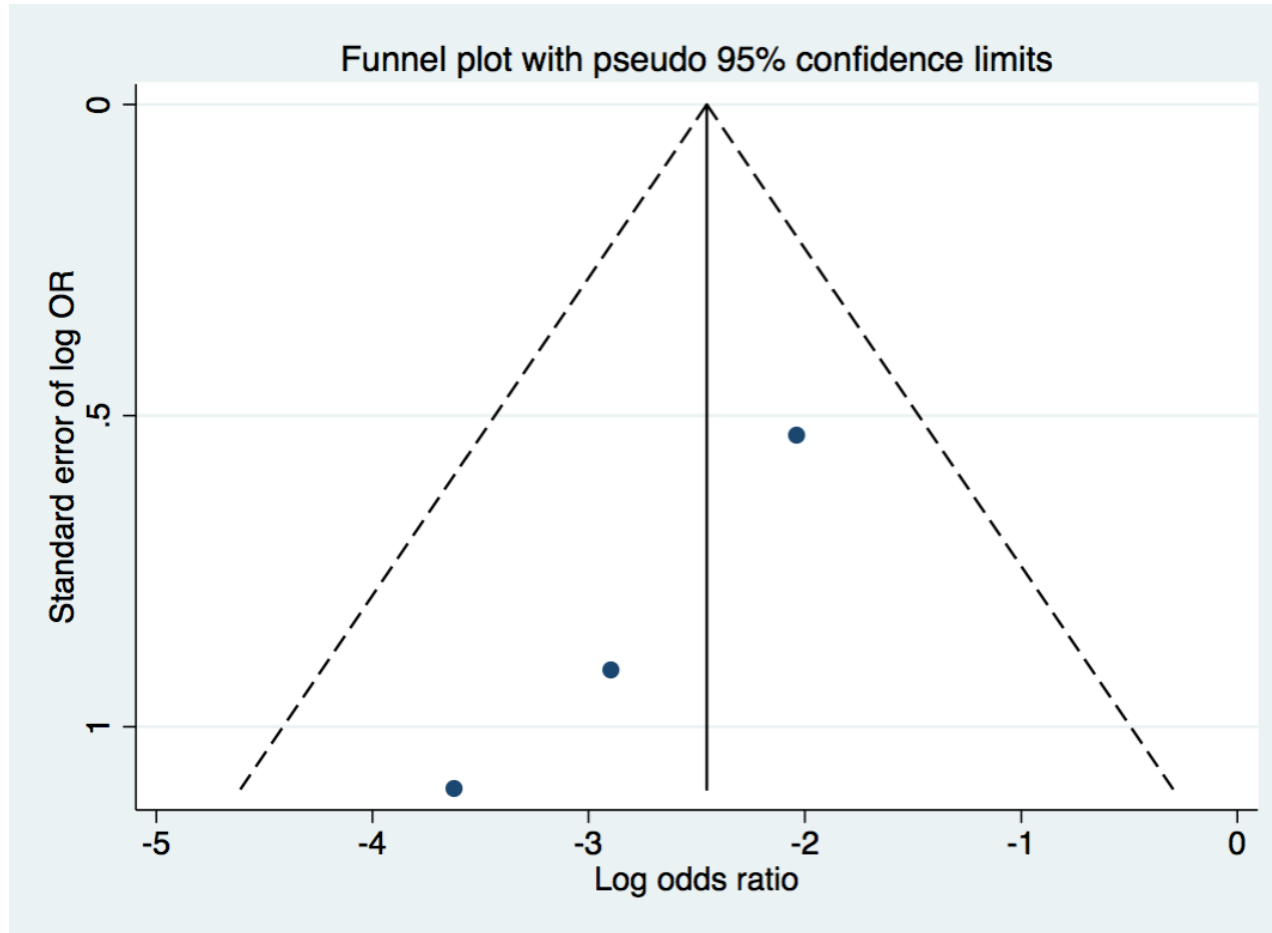
Supplementary Figure 1a-b. Funnel plot suggesting publication bias when assessing the reported outcome of mortality including all studies (a) and only prospective trials (b).

Supplementary Figure 2a-b. Funnel plot suggesting publication bias when assessing the reported outcome of relapse including all studies (a) and only prospective trials (b).

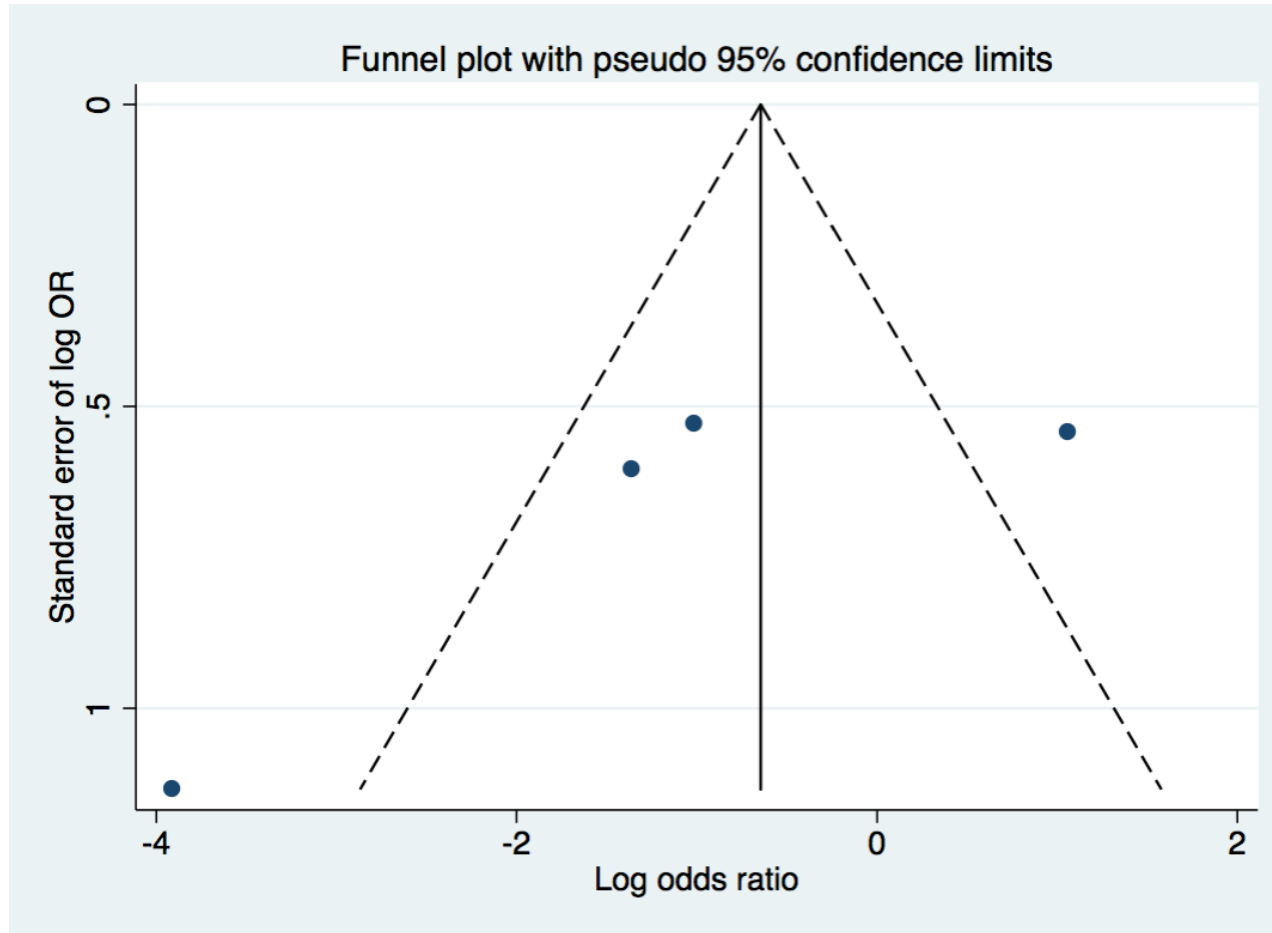
Supplementary Figure 1a. Funnel plot suggesting publication bias when assessing the reported outcome of mortality including all studies.



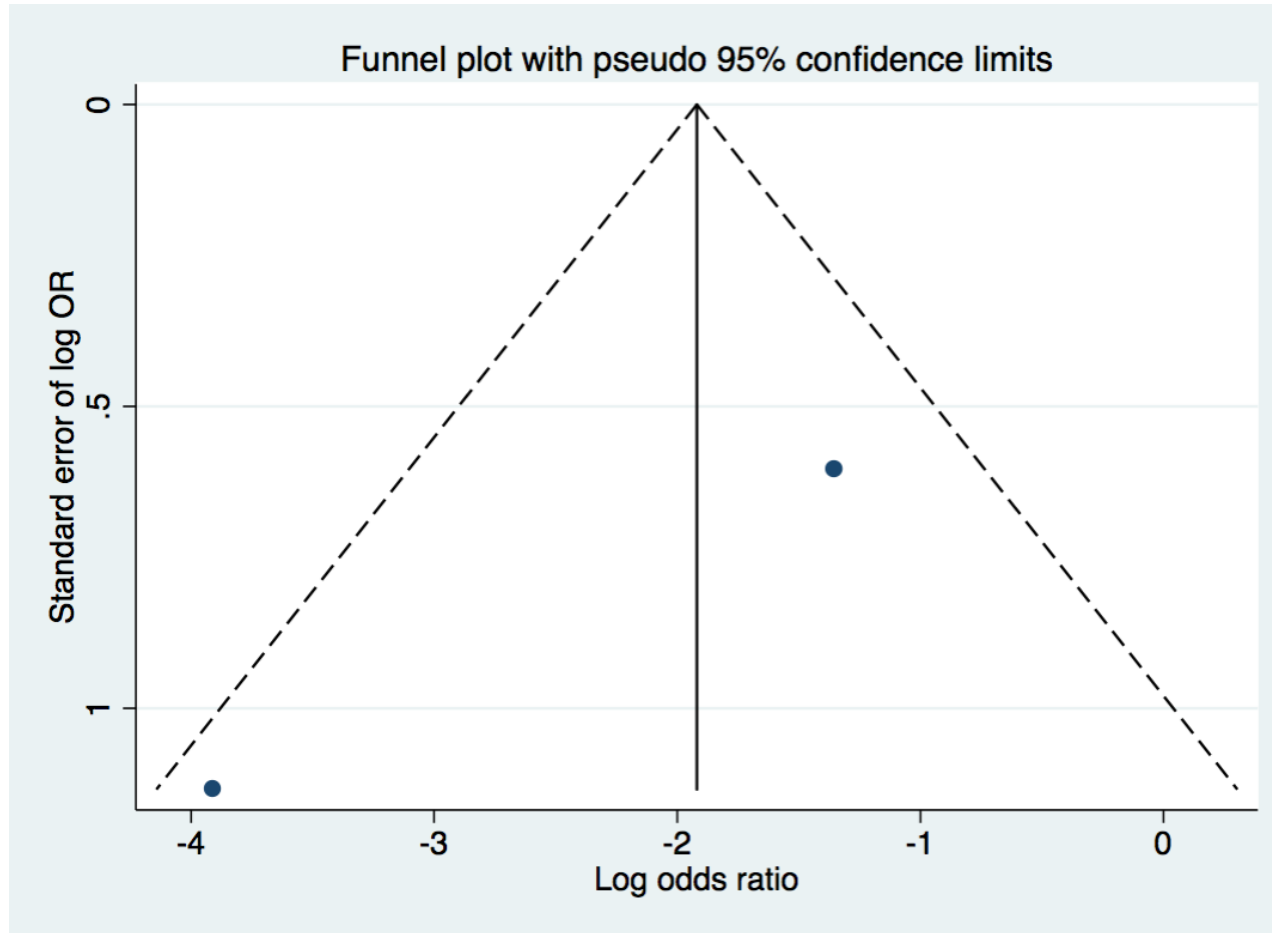
Supplementary Figure 1b. Funnel plot suggesting publication bias when assessing the reported outcome of mortality including only prospective trials.



Supplementary Figure 2a. Funnel plot suggesting publication bias when assessing the reported outcome of relapse including all studies.



Supplementary Figure 2b. Funnel plot suggesting publication bias when assessing the reported outcome of relapse including only prospective trials.



Supplemental text:

Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

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- 1 exp Liver Diseases, Alcoholic/
 - 2 (Alcoholic Liver Disease* or Alcoholic Fatty Liver or Alcoholic Steatohepatitis or Alcoholic Hepatitis or Alcoholic Hepatitides or Alcoholic Liver Cirrhosis or Alcoholic Cirrhosis or Alcoholic Hepatic Cirrhosis or Alcohol-related liver disease or Alcohol-related end-stage liver disease).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
 - 3 1 or 2
 - 4 Liver Transplantation/
 - 5 (Liver Transplant* or Liver Grafting* or Hepatic Transplantation* or Early liver transplantation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
 - 6 4 or 5
 - 7 exp Survival Rate/
 - 8 (Survival Rate* or Survivorship or Mean Survival Time*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

9 7 or 8

10 Mortality/

11 (Mortalit* or Case Fatality Rate* or Death Rate*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

12 10 or 11

13 Treatment Outcome/

14 (Treatment Outcome* or Clinical Effectiveness or Clinical Effectivenesses or Patient Relevant Outcome* or Patient-Relevant Outcome* or Clinical Efficacy or Treatment Effectiveness or Treatment Efficacy or Rehabilitation Outcome*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

15 13 or 14

16 Prognosis/

17 (Prognosis or Prognoses or Prognostic Factor*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

18 16 or 17

19 Recurrence/

20 (Recurrence* or Recrudescence* or Relapse*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

21 19 or 20

22 Relapse.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

23 Alcohol Drinking/

24 (Alcohol Drinking or Alcohol Consumption).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

25 23 or 24

26 Posttransplant short-term results.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

27 Patient Compliance/

28 (Patient Compliance or Patient Adherence or Patient Cooperation or Patient Non-Compliance or Patient Non Compliance or Patient Nonadherence or Patient Noncompliance or Patient Non-Adherence or Patient Non Adherence).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

29 27 or 28

30 Temperance/

31 Temperance*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

32 30 or 31

33 Alcohol Abstinence/

34 (Abstinence or Alcohol Abstinence*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

35 33 or 34

36 Alcohol Cessation.mp.

37 9 or 12 or 15 or 18 or 21 or 22 or 25 or 26 or 29 or 32 or 35 or 36

38 3 and 6 and 37
