Biopsy in ArLD

Does anyone routinely biopsy in ArLD?

Does anyone routinely biopsy in ArLD?

no

Biopsy for research – why?

- Mechanistic

- Stratification

- Outcome

Biopsy *for* research

- Phase II
  - Probably

- Phase III
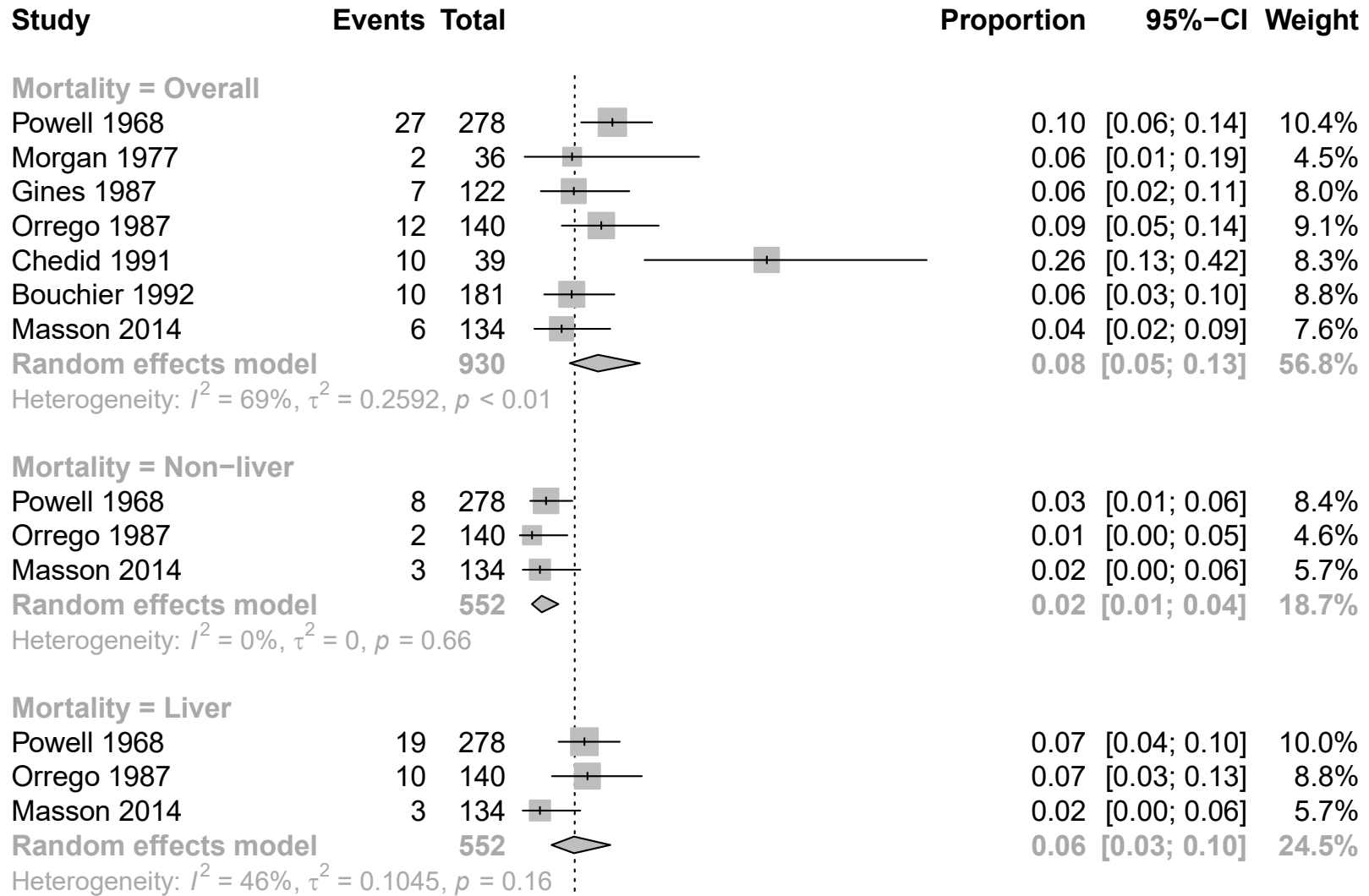 - Probably not

Biopsy *for* research – why not?

- Patients don't like it – affects recruitment

- Not a patient-relevant outcome

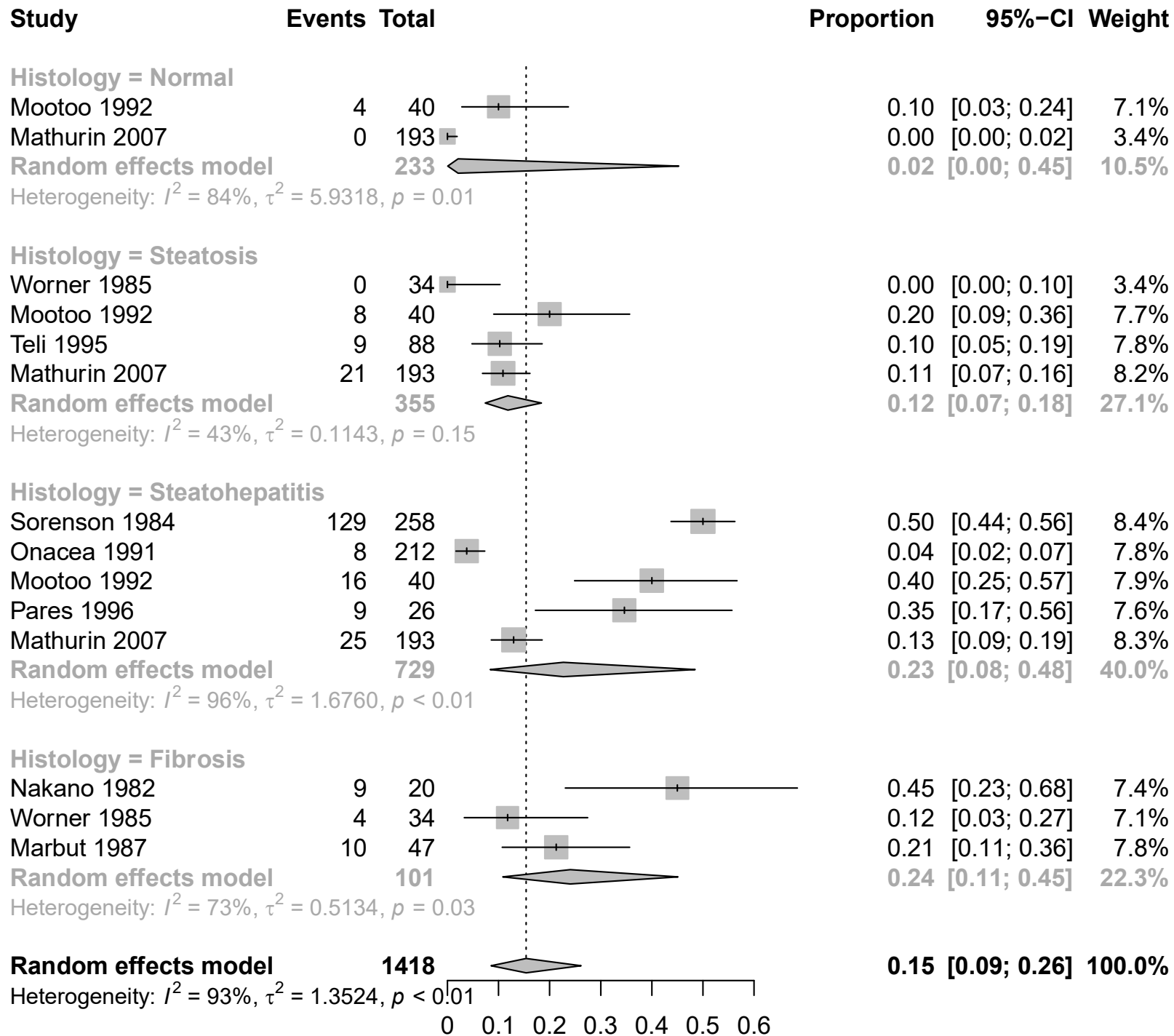- No information (yet) on histology surrogate outcomes

Biopsy *as* research

Worldwide Alcoholic Liver Disease Outcomes Study

WALDO

Biopsy *as* research

Study	Events	Total		Proportion	95%−CI	Weight
Mortality = Overall						
Powell 1968	27	278		0.10	[0.06; 0.14]	10.4%
Morgan 1977	2	36		0.06	[0.01; 0.19]	4.5%
Gines 1987	7	122		0.06	[0.02; 0.11]	8.0%
Orrego 1987	12	140		0.09	[0.05; 0.14]	9.1%
Chedid 1991	10	39		0.26	[0.13; 0.42]	8.3%
Bouchier 1992	10	181		0.06	[0.03; 0.10]	8.8%
Masson 2014	6	134		0.04	[0.02; 0.09]	7.6%
Random effects model		**930**		**0.08**	**[0.05; 0.13]**	**56.8%**
Heterogeneity: $I^2 = 69\%$, $\tau^2 = 0.2592$, $p < 0.01$						
Mortality = Non−liver						
Powell 1968	8	278		0.03	[0.01; 0.06]	8.4%
Orrego 1987	2	140		0.01	[0.00; 0.05]	4.6%
Masson 2014	3	134		0.02	[0.00; 0.06]	5.7%
Random effects model		**552**		**0.02**	**[0.01; 0.04]**	**18.7%**
Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.66$						
Mortality = Liver						
Powell 1968	19	278		0.07	[0.04; 0.10]	10.0%
Orrego 1987	10	140		0.07	[0.03; 0.13]	8.8%
Masson 2014	3	134		0.02	[0.00; 0.06]	5.7%
Random effects model		**552**		**0.06**	**[0.03; 0.10]**	**24.5%**
Heterogeneity: $I^2 = 46\%$, $\tau^2 = 0.1045$, $p = 0.16$						

Study	Events	Total	Proportion	95%−CI	Weight
Histology = Normal					
Mootoo 1992	4	40	0.10	[0.03; 0.24]	7.1%
Mathurin 2007	0	193	0.00	[0.00; 0.02]	3.4%
Random effects model		233	0.02	[0.00; 0.45]	10.5%
Heterogeneity: $I^2 = 84\%$, $\tau^2 = 5.9318$, $p = 0.01$					
Histology = Steatosis					
Worner 1985	0	34	0.00	[0.00; 0.10]	3.4%
Mootoo 1992	8	40	0.20	[0.09; 0.36]	7.7%
Teli 1995	9	88	0.10	[0.05; 0.19]	7.8%
Mathurin 2007	21	193	0.11	[0.07; 0.16]	8.2%
Random effects model		355	0.12	[0.07; 0.18]	27.1%
Heterogeneity: $I^2 = 43\%$, $\tau^2 = 0.1143$, $p = 0.15$					
Histology = Steatohepatitis					
Sorenson 1984	129	258	0.50	[0.44; 0.56]	8.4%
Onacea 1991	8	212	0.04	[0.02; 0.07]	7.8%
Mootoo 1992	16	40	0.40	[0.25; 0.57]	7.9%
Pares 1996	9	26	0.35	[0.17; 0.56]	7.6%
Mathurin 2007	25	193	0.13	[0.09; 0.19]	8.3%
Random effects model		729	0.23	[0.08; 0.48]	40.0%
Heterogeneity: $I^2 = 96\%$, $\tau^2 = 1.6760$, $p < 0.01$					
Histology = Fibrosis					
Nakano 1982	9	20	0.45	[0.23; 0.68]	7.4%
Worner 1985	4	34	0.12	[0.03; 0.27]	7.1%
Marbut 1987	10	47	0.21	[0.11; 0.36]	7.8%
Random effects model		101	0.24	[0.11; 0.45]	22.3%
Heterogeneity: $I^2 = 73\%$, $\tau^2 = 0.5134$, $p = 0.03$					
Random effects model		**1418**	**0.15**	**[0.09; 0.26]**	**100.0%**
Heterogeneity: $I^2 = 93\%$, $\tau^2 = 1.3524$, $p < 0.01$					

0   0.1   0.2   0.3   0.4   0.5   0.6

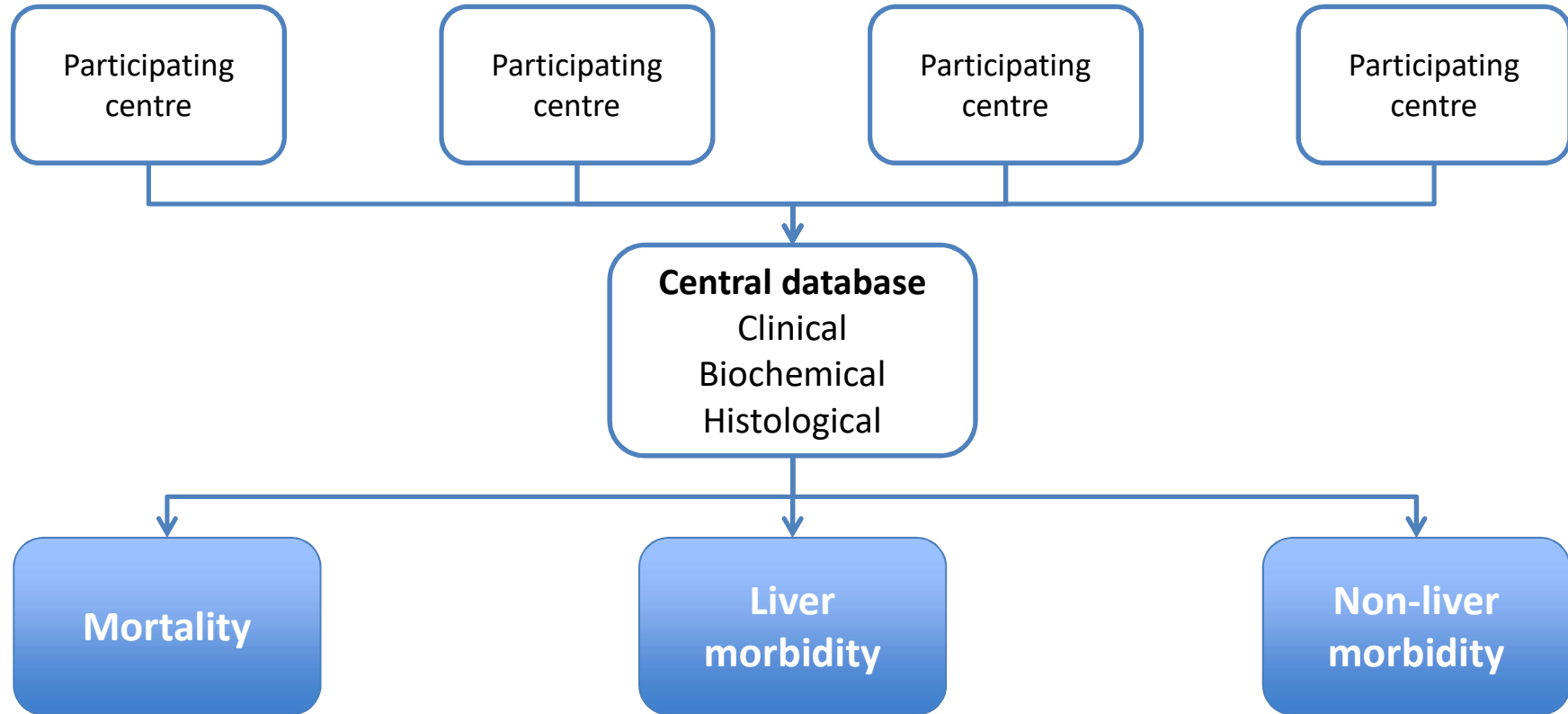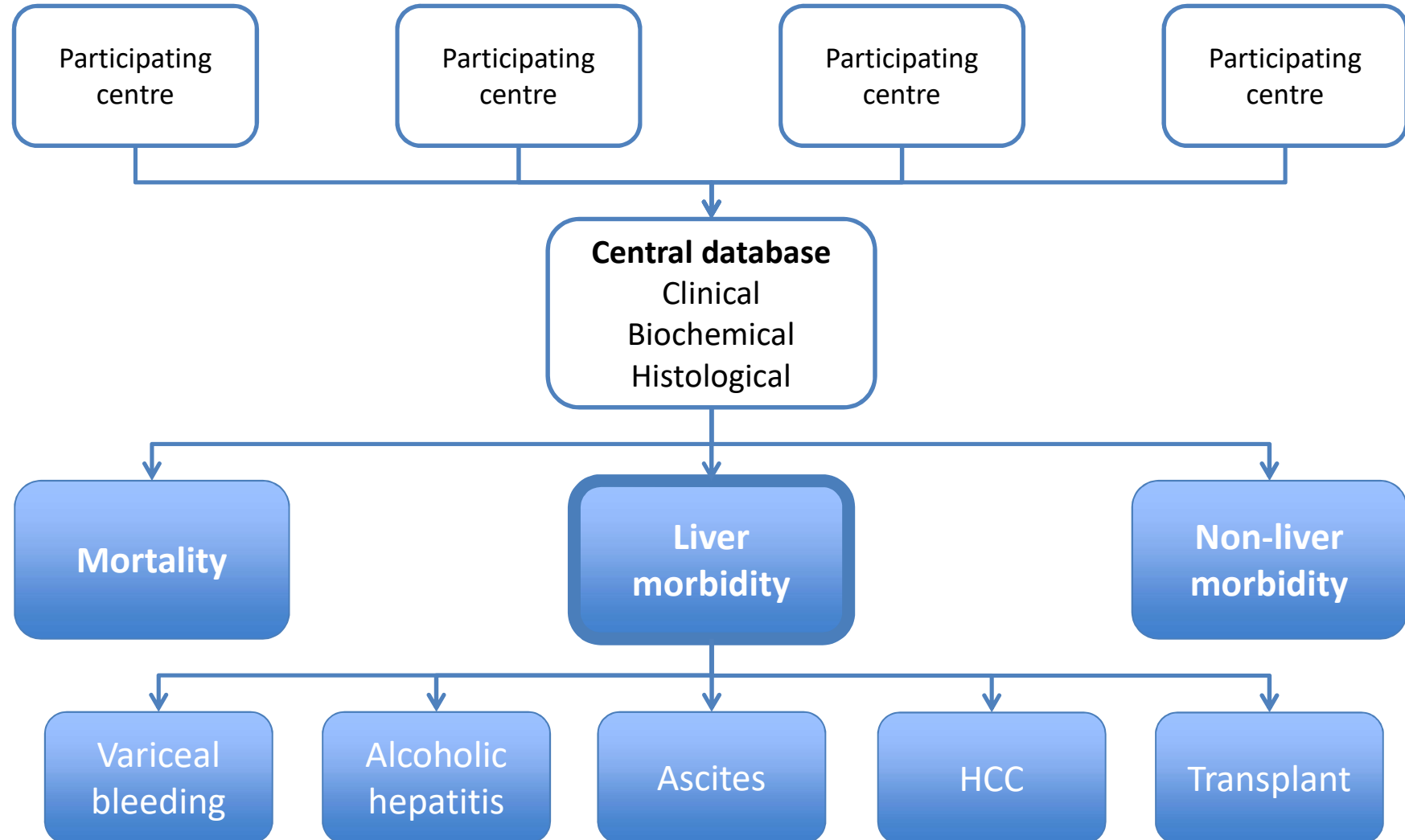WALDO is an international collaboration that will pool outcome data from biopsy-proven cases of ALD

WALDO

WALDO

WALDO

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┌─────────────┐   ┌─────────────┐   ┌─────────────┐   ┌─────────────┐
│Participating│   │Participating│   │Participating│   │Participating│
│   centre    │   │   centre    │   │   centre    │   │   centre    │
└─────────────┘   └─────────────┘   └─────────────┘   └─────────────┘
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Central database
Clinical
Biochemical
Histological

Mortality

Liver morbidity

Non-liver morbidity

Diabetes

Cancer

Cardiovascular disease

NHS
Health Research Authority
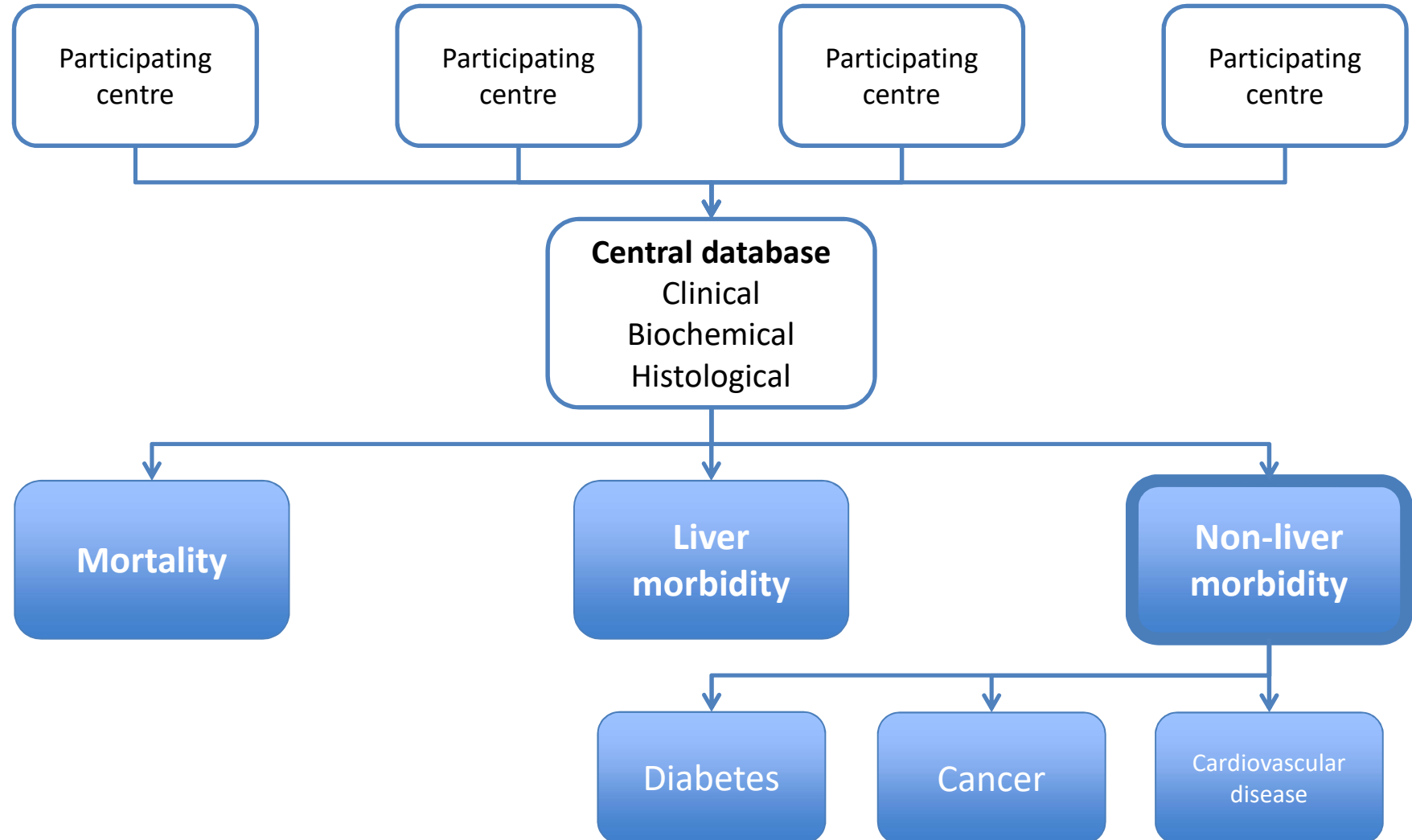
London - London Bridge Research Ethics Committee

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London
SE1 6LH

Telephone: 020 7104 8222
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Please note: **This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval**

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07 December 2018

Dr Richard Parker
Consultant Hepatologist
Leeds Teaching Hospitals NHS Trust
Merville Building
St James's University Hospital
LS9 7TF

Dear Dr Parker

Study title:	**Worldwide Alcohol related Liver Disease Outcomes study**
REC reference:	**18/LO/2132**
Protocol number:	**1**
IRAS project ID:	**254195**