Supplemental Material

Occupational Benzene Exposure and the Risk of Lymphoma Subtypes: a Meta-Analysis of Cohort Studies Incorporating Three Study Quality Dimensions

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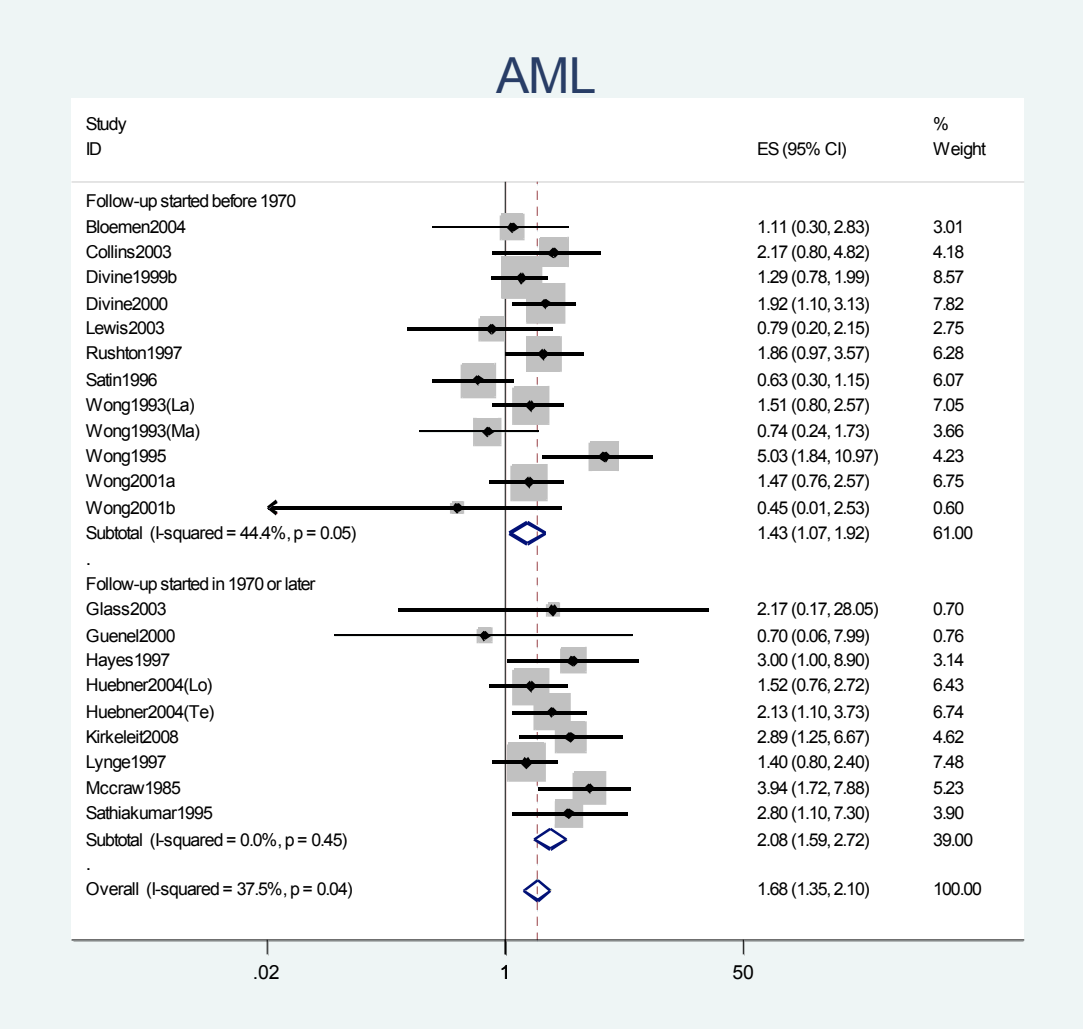
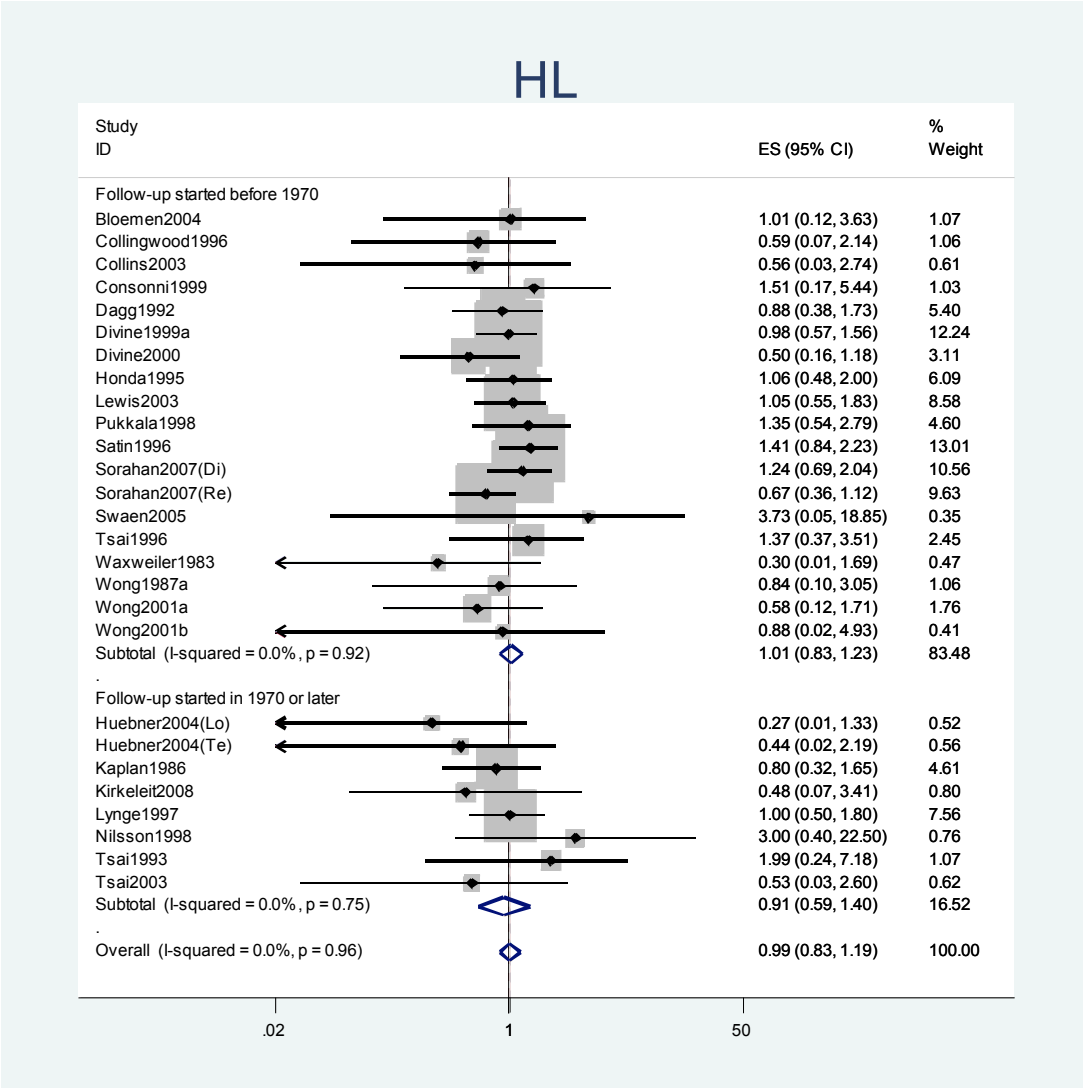
Supplemental Material, Figure 1: Forest plots of all studies for AML and five lymphoma subtypes in cohort studies of workers exposed to benzene, stratified by start of follow-up.



Sub-cohorts were identified with the following codes: Chemical workers cohort (Ch), Distribution cohort (Di), Gasoline workers cohort (Ga), Italian cohort (It), Land-based workers cohort (La), Louisiana cohort (Lo), Marine workers cohort (Ma), Oil and Gas workers cohort (Oi), Refinery cohort (Re), Texas cohort (Te), UK cohort (UK).



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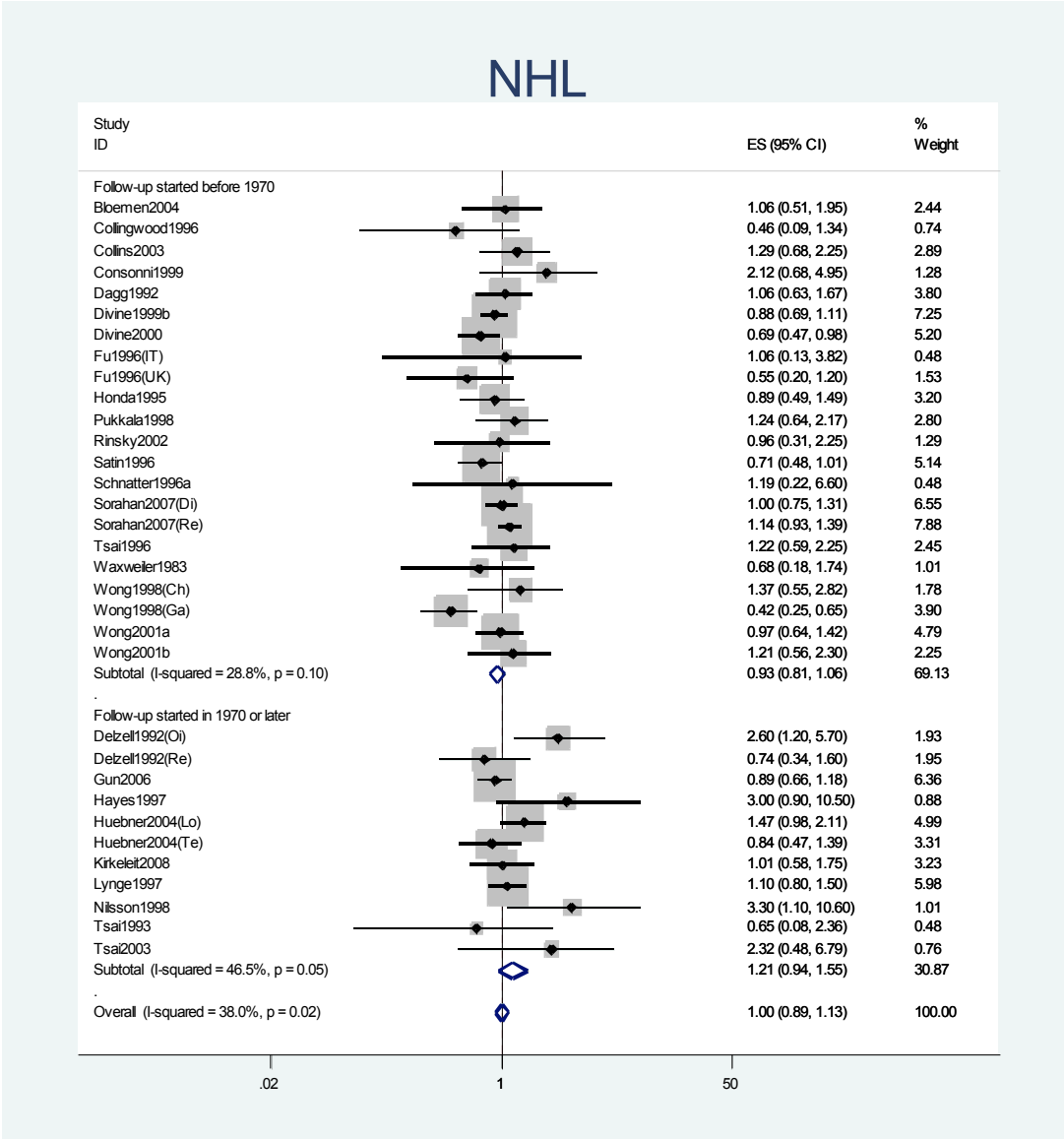

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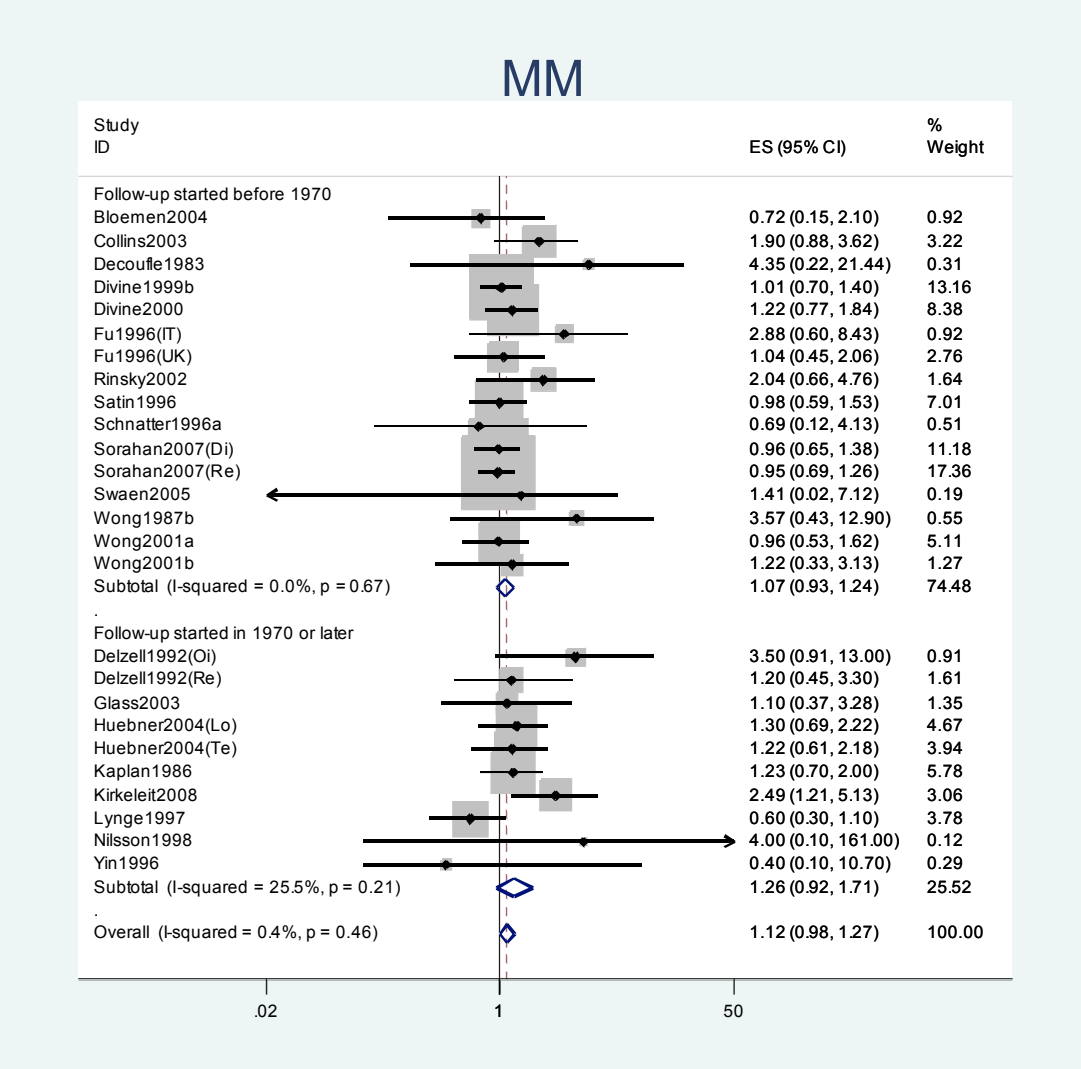

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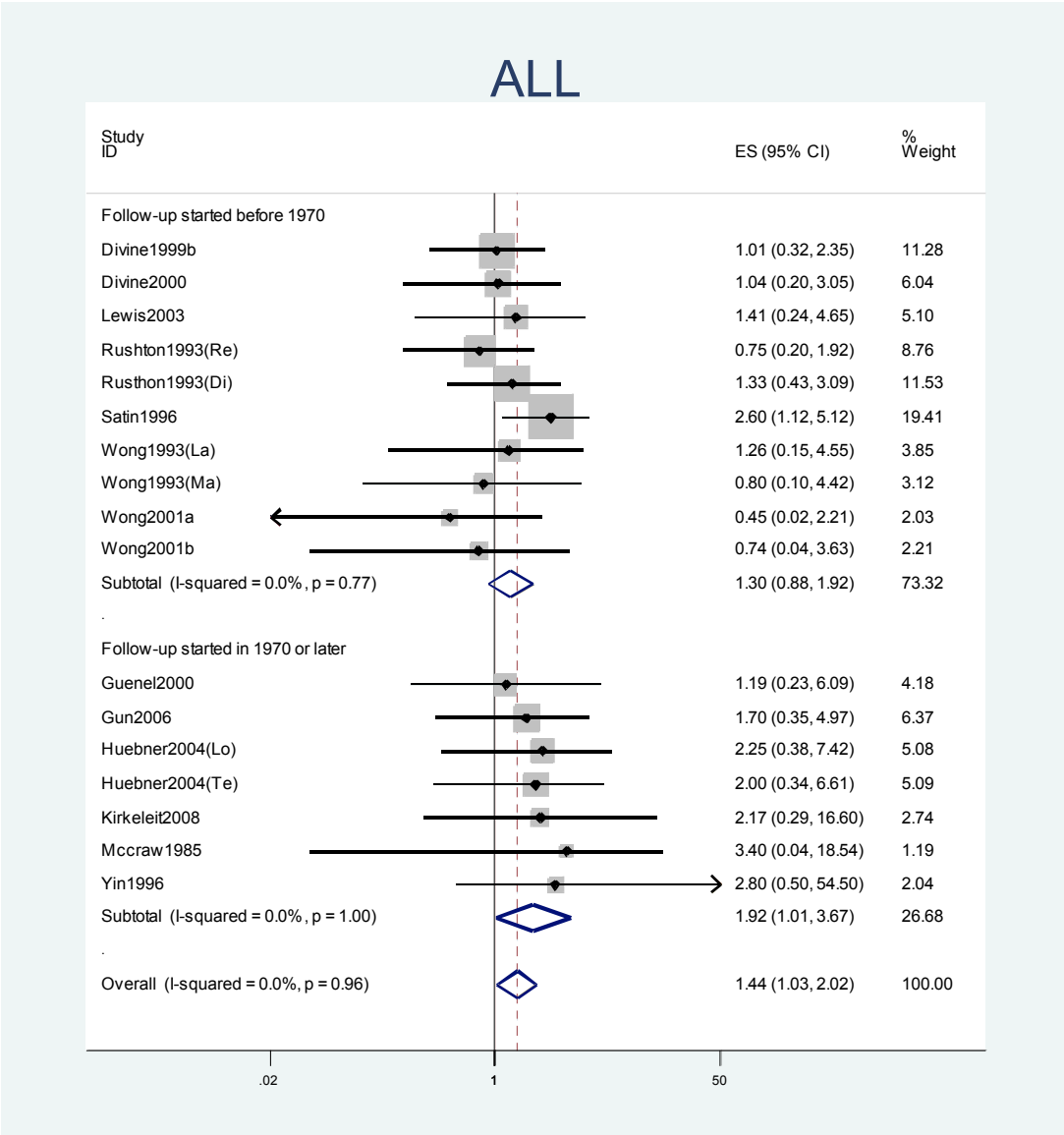

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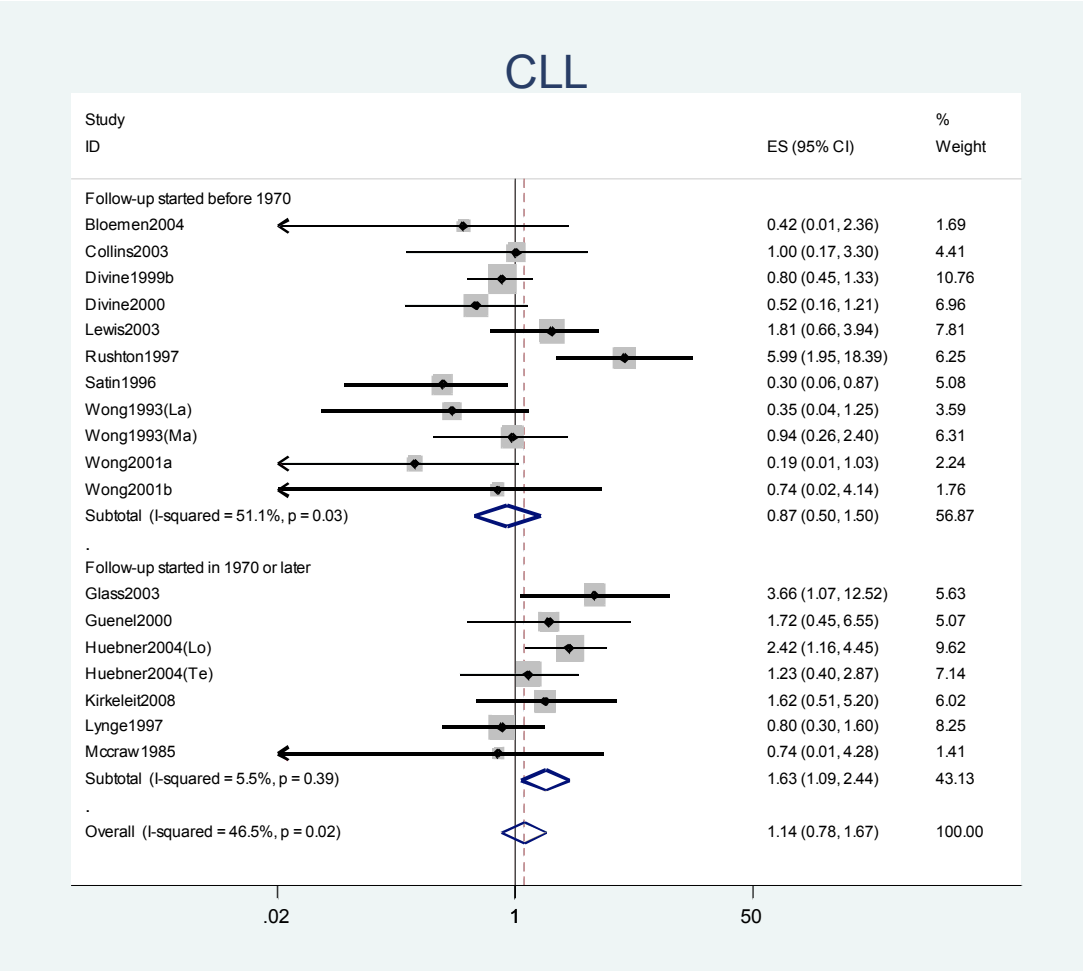

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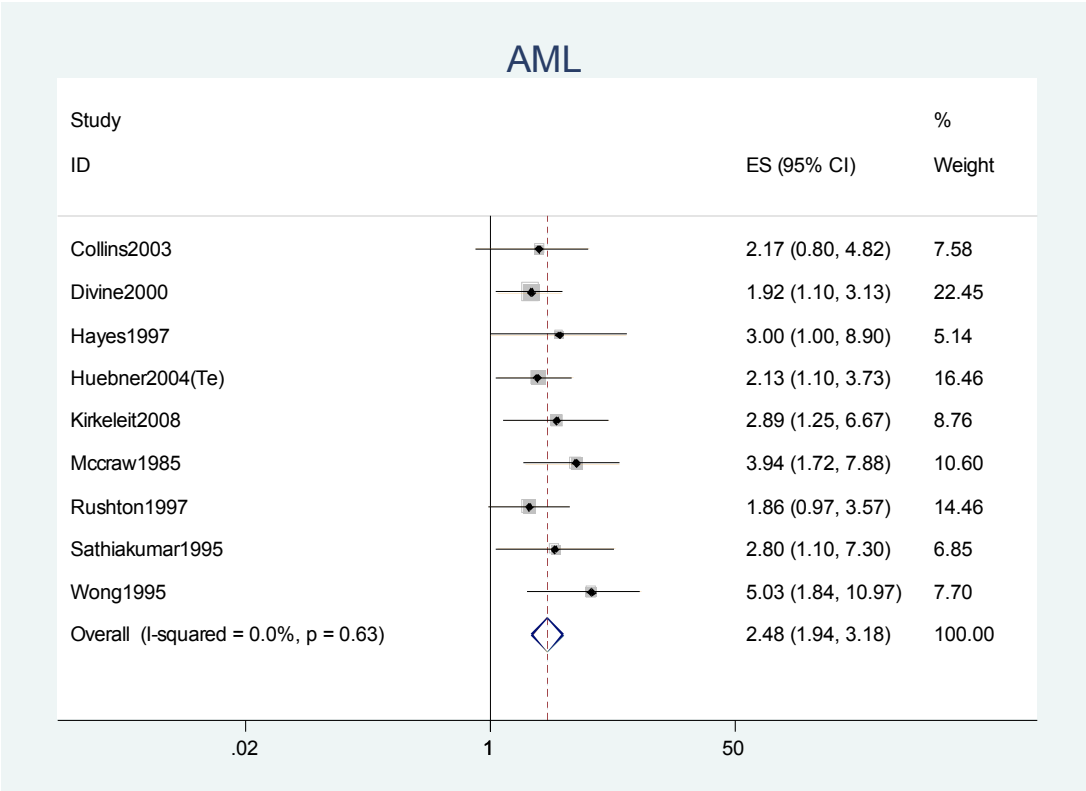

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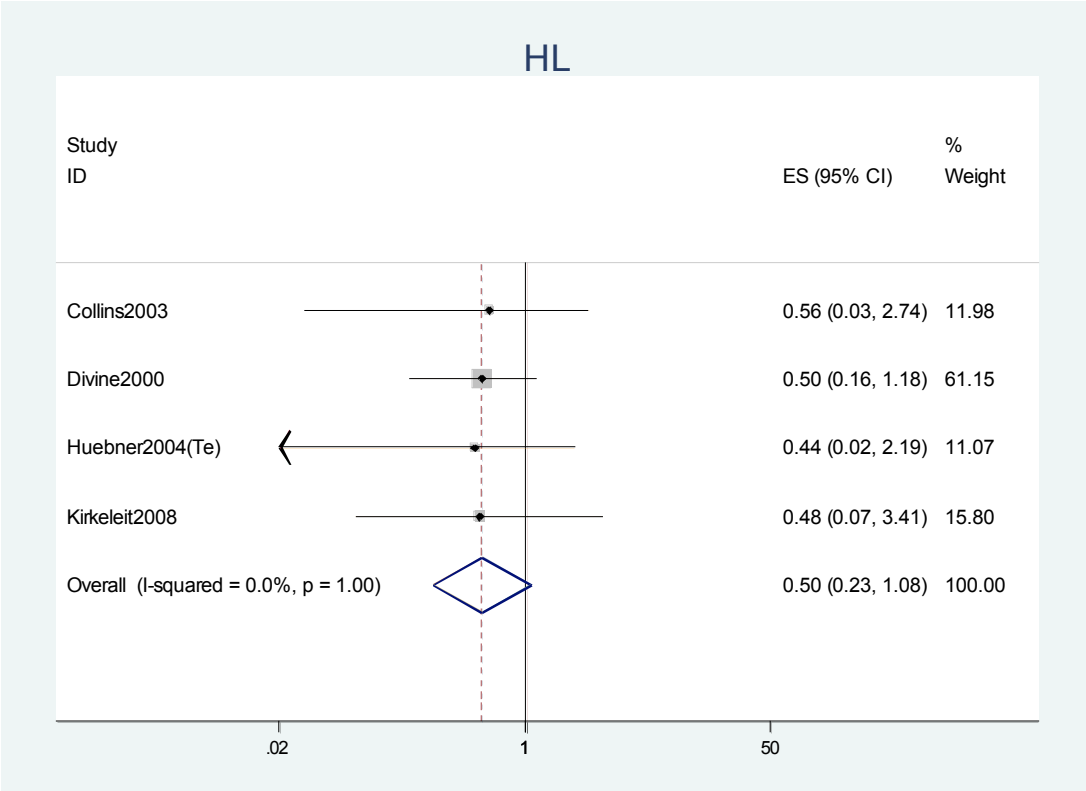
[a] AML RR >1, p<0.1



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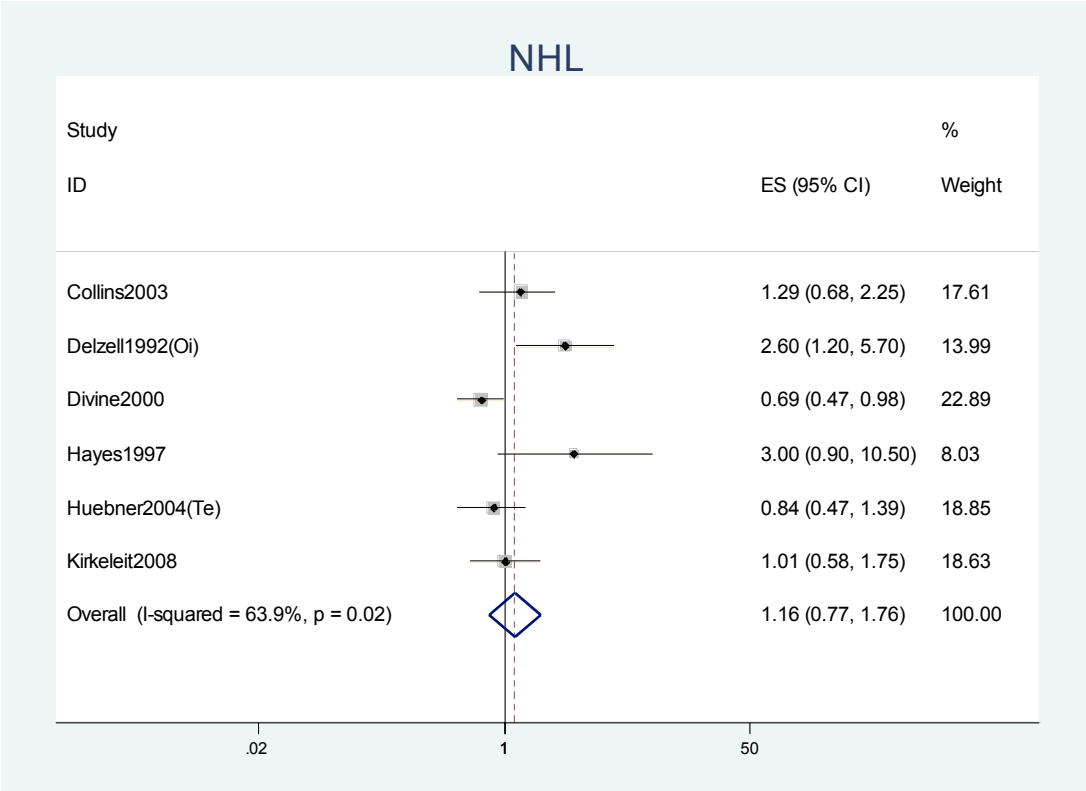

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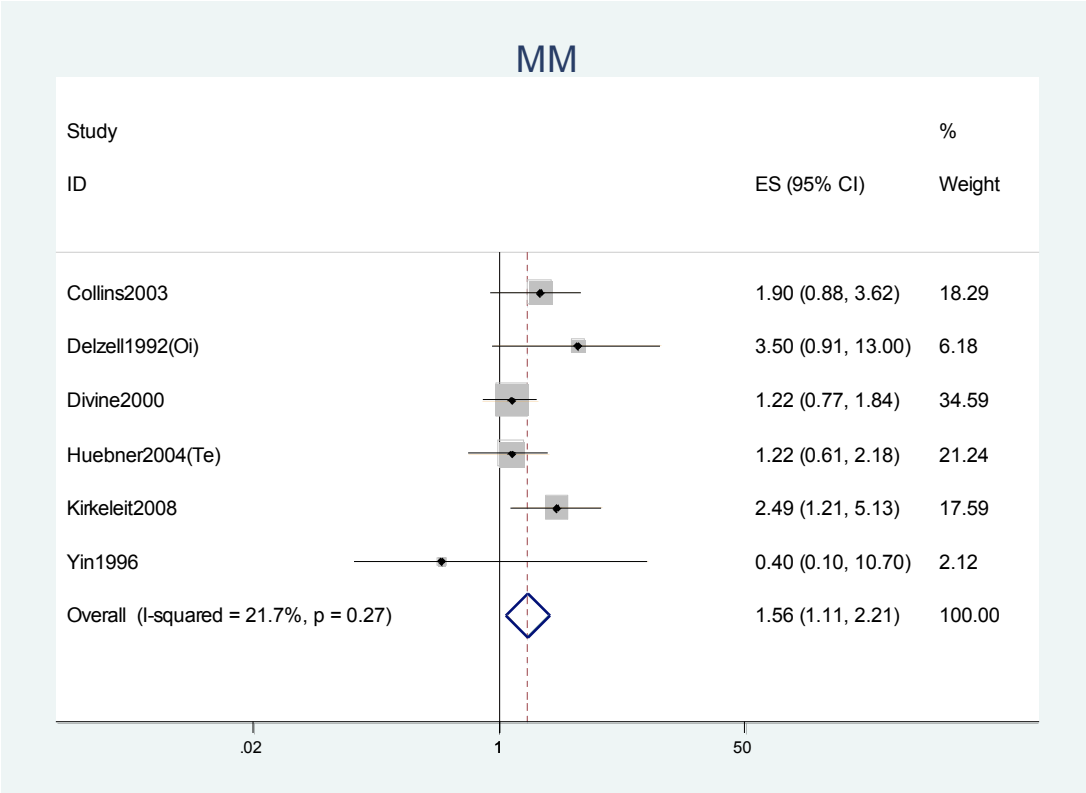

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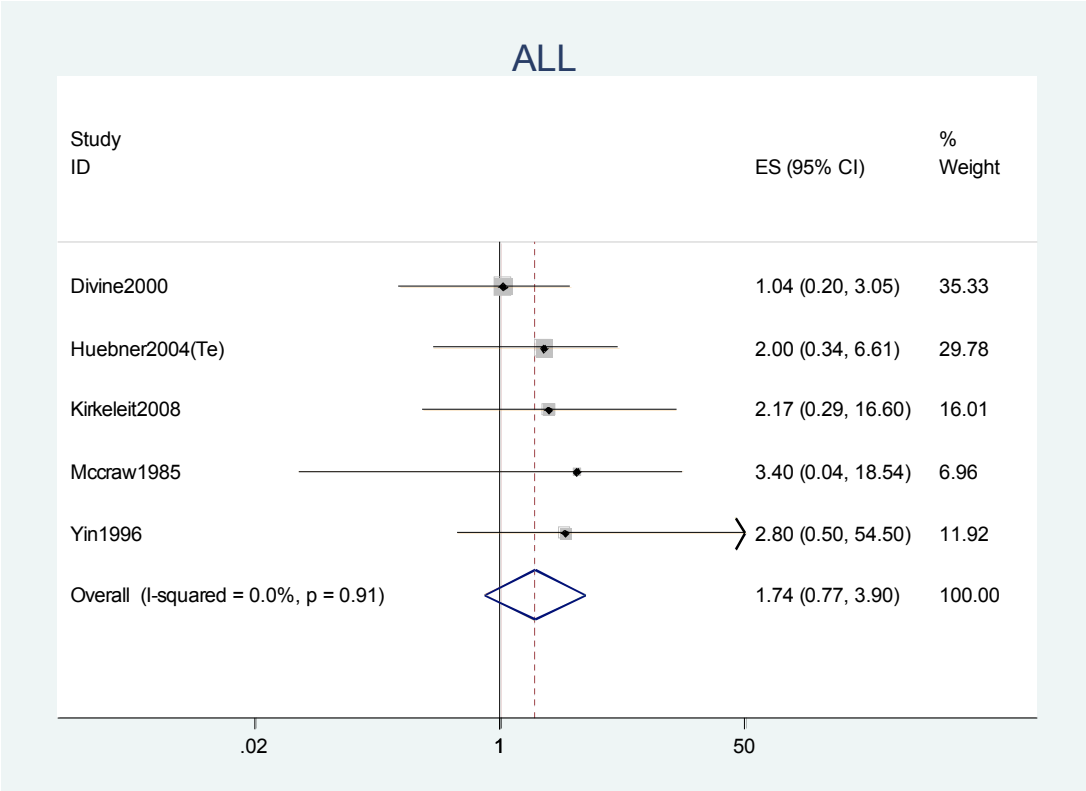

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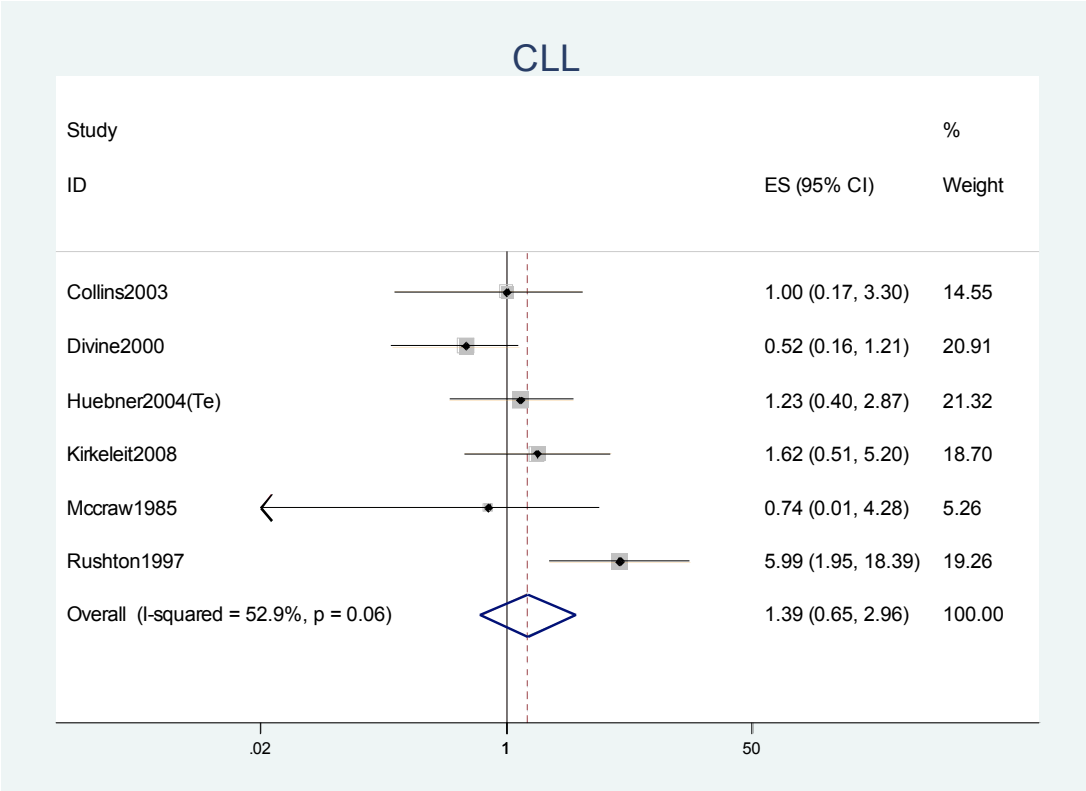

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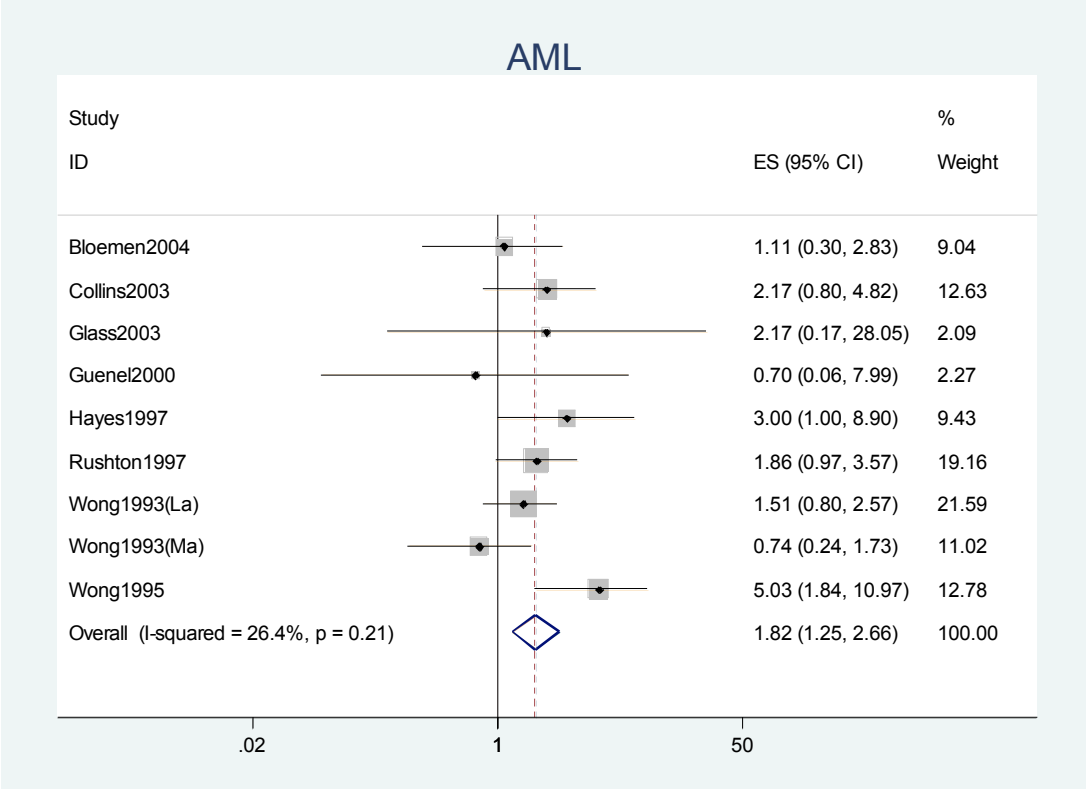
Supplemental Material, Figure 3: Forest plots of studies with *exposure assessment quality* A-B[a] for AML and five lymphoma subtypes in cohort studies of workers exposed to benzene.



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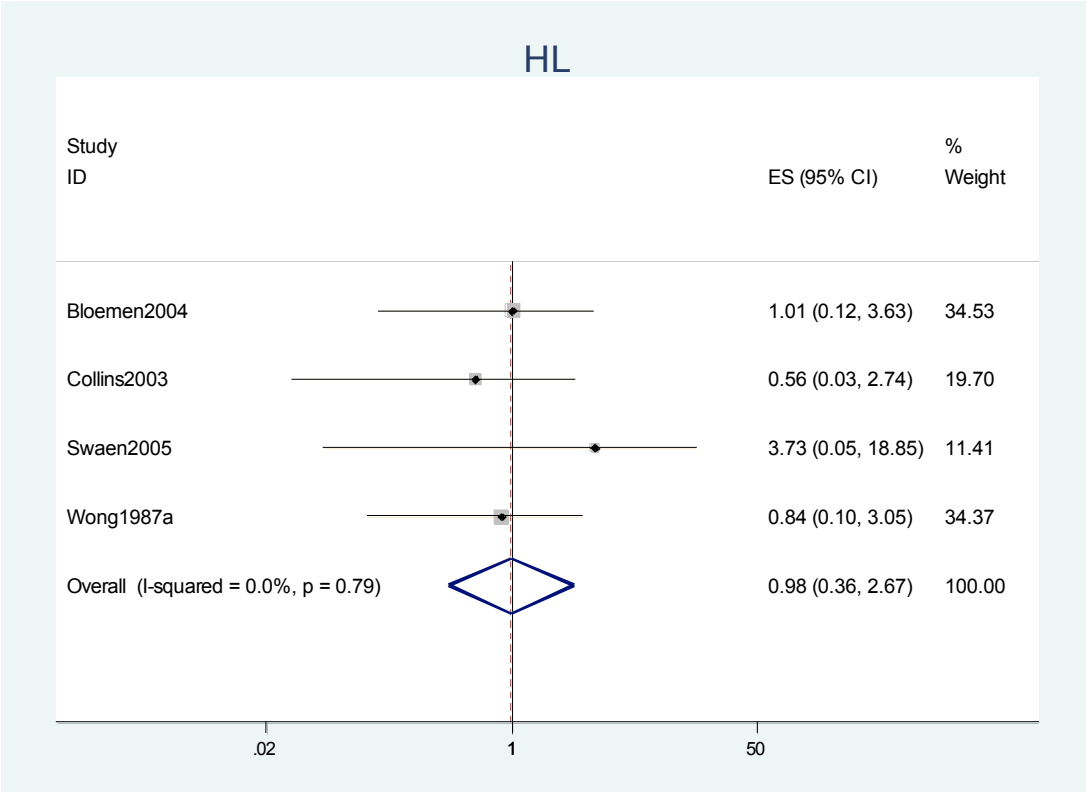
[a] Quantitative exposure estimates for benzene (A), semi-quantitative estimates of benzene exposure or quantitative estimates of exposures containing benzene (B).



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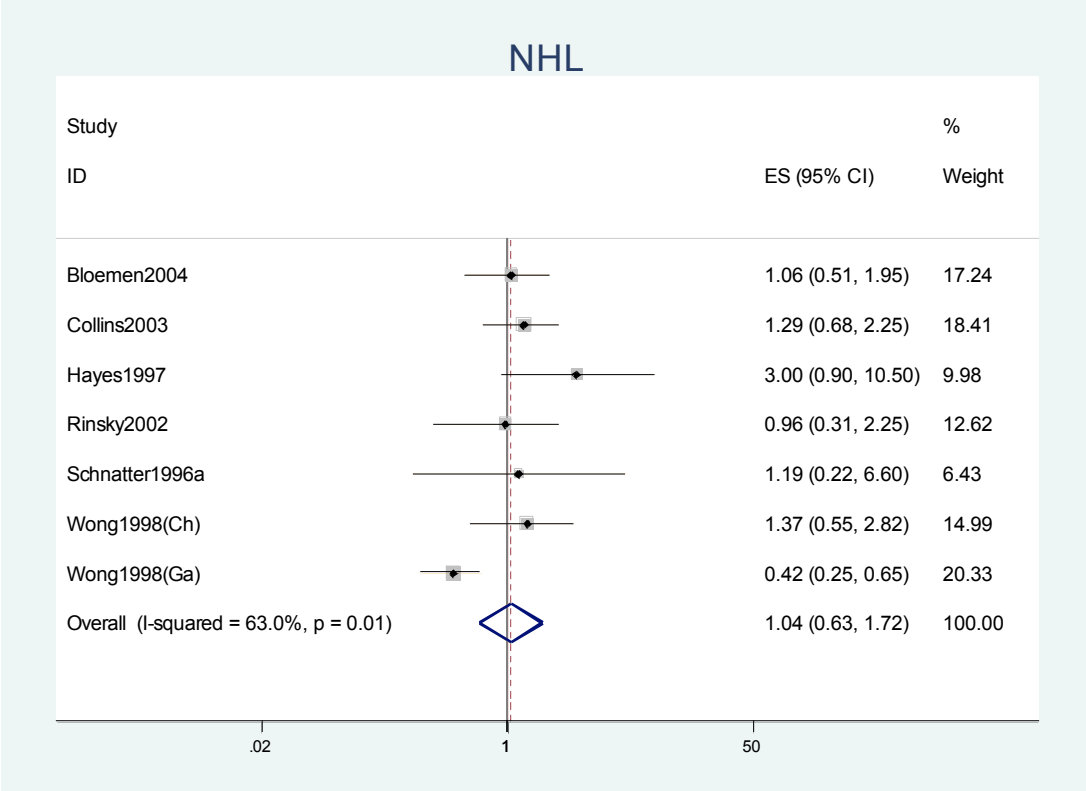

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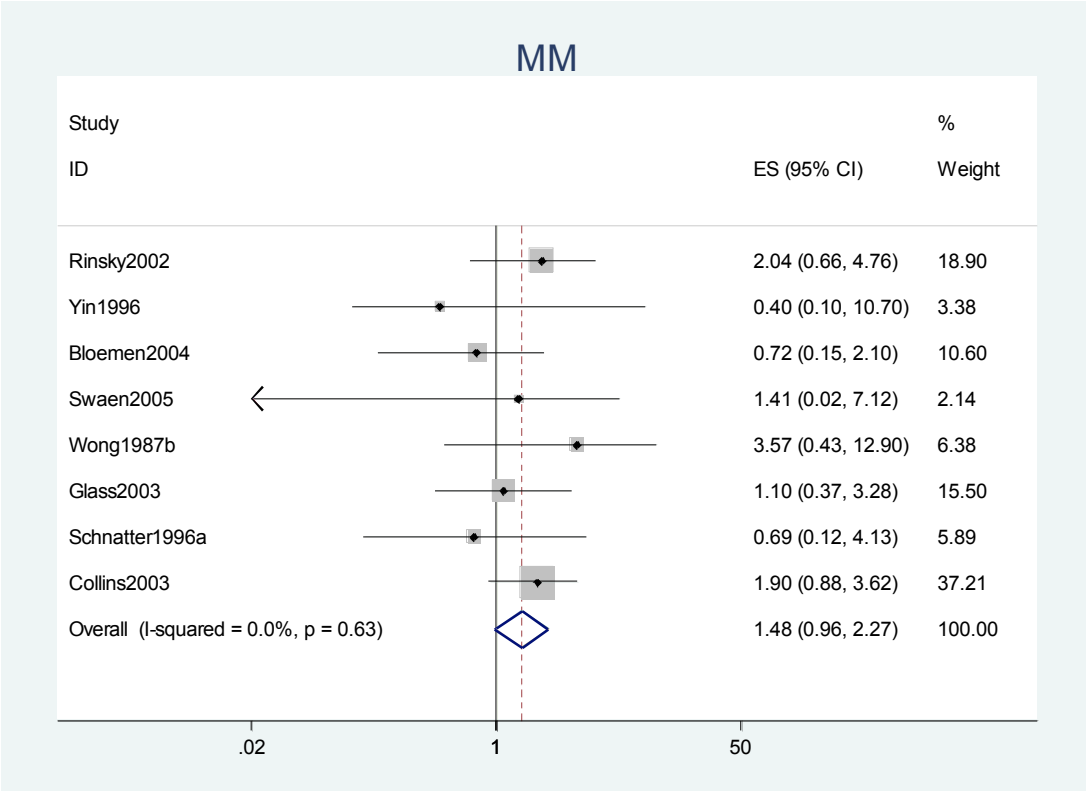

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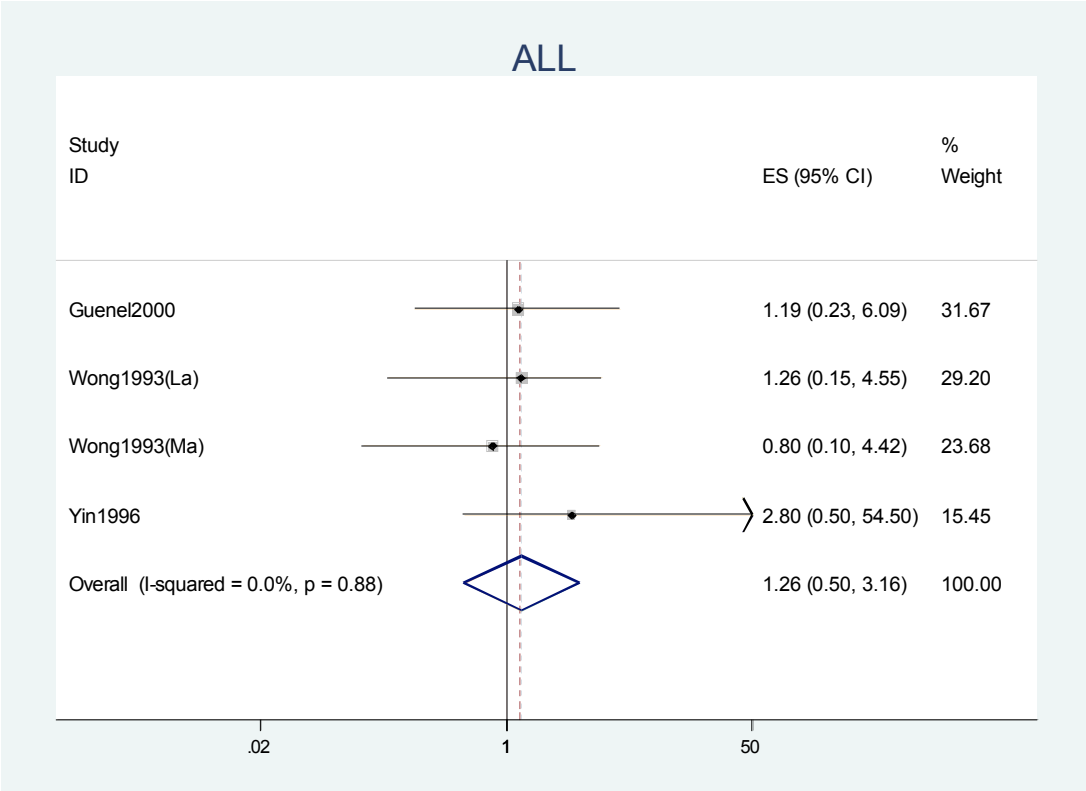

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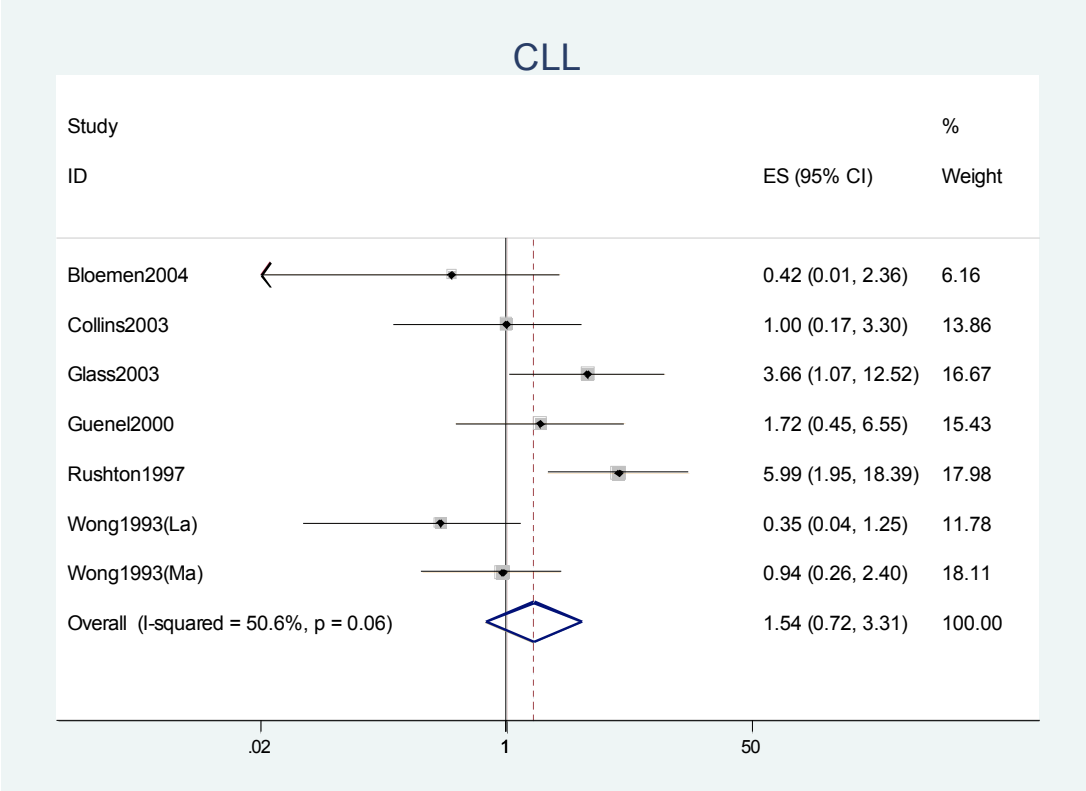

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Supplemental Material, Table 1 Pooled relative risks[a] for AML and five lymphoma subtypes; stratification by start of follow-up and *AML significance level*

Lymphoma subtype	*AML significance level*[b]	N[c]	n[d]	Meta relative risk (all studies)	N[c]	n[d]	Meta relative risk (Start follow-up before 1970)	N[c]	n[d]	Meta relative risk (Start follow-up 1970 and later)
	A-E (*all studies*)	**21**	**217**	**1.68 (1.35-2.10)***	**12**	**119**	**1.43 (1.07-1.92)***	**9**	**98**	**2.08 (1.59-2.72)**
	A-D	21	217	1.68 (1.35-2.10)*	12	119	1.43 (1.07-1.92)*	9	98	2.08 (1.59-2.72)
AML	A-C	16	192	1.88 (1.56-2.27)	8	100	1.72 (1.34-2.23)	8	92	2.11 (1.61-2.77)
	A-B	11	132	2.20 (1.77-2.72)	5	64	2.06 (1.47-2.89)	6	68	2.41 (1.77-3.29)
	A	9	108	2.48 (1.94-3.18)	4	51	2.29 (1.54-3.40)	5	57	2.88 (1.95-3.99)
	A-E (*all studies*)	**27**	**146**	**0.99 (0.83-1.19)**	**19**	**123**	**1.01 (0.83-1.23)**	**8**	**23**	**0.91 (0.59-1.40)**
	A-D	12	69	0.99 (0.77-1.27)	8	58	1.03 (0.78-1.36)	4	11	0.83 (0.47-1.48)
HL	A-C	9	39	0.82 (0.59-1.15)	5	28	0.82 (0.55-1.23)	4	11	0.83 (0.47-1.48)
	A-B	5	7	0.47 (0.22-0.99)	2	6	0.51 (0.20-1.27)	3	1[f]	0.40 (0.11-1.44)
	A	4	7	0.50 (0.23-1.08)	2	6	0.51 (0.20-1.27)	2	1[g]	0.46 (0.10-2.09)
	A-E (*all studies*)	**33**	**647**	**1.00 (0.89-1.13)***	**22**	**452**	**0.93 (0.81-1.06)***	**11**	**195**	**1.21 (0.94-1.55)***
	A-D	15	383	0.97 (0.81-1.16)*	8	208	0.82 (0.66-1.02)*	7	175	1.18 (0.91-1.53)*
NHL[e]	A-C	13	344	0.99 (0.81-1.21)*	6	169	0.81 (0.62-1.07)*	7	175	1.18 (0.91-1.53)*
	A-B	7	130	1.21 (0.85-1.72)*	2	40	0.90 (0.49-1.66)*	5	90	1.38 (0.92-2.06)*
	A	6	101	1.16 (0.77-1.76)*	2	40	0.90 (0.49-1.66)*	4	61	1.40 (0.79-2.51)*
	A-E (*all studies*)	**26**	**284**	**1.12 (0.98-1.27)**	**16**	**204**	**1.07 (0.93-1.24)**	**10**	**80**	**1.26 (0.92-1.71)**
	A-D	14	160	1.15 (0.95-1.40)	7	105	1.09 (0.89-1.33)	7	55	1.27 (0.81-2.00)*
MM	A-C	12	137	1.19 (0.94-1.49)	5	82	1.12 (0.89-1.40)	7	55	1.27 (0.81-2.00)*
	A-B	7	69	1.49 (1.13-1.95)	2	29	1.39 (0.94-2.08)	5	40	1.58 (1.03-2.44)
	A	6	56	1.56 (1.11-2.21)	2	29	1.39 (0.94-2.08)	4	27	1.75 (0.94-3.26)
	A-E (*all studies*)	**17**	**47**	**1.44 (1.03-2.02)**	**10**	**30**	**1.30 (0.88-1.92)**	**7**	**17**	**1.92 (1.00-3.67)**
	A-D	17	47	1.44 (1.03-2.02)	10	30	1.30 (0.88-1.92)	7	17	1.92 (1.00-3.67)
ALL	A-C	11	29	1.41 (0.90-2.19)	5	15	1.09 (0.62-1.92)	6	14	2.10 (1.04-4.25)
	A-B	7	16	1.74 (0.90-3.36)	2	5	1.12 (0.39-3.25)	5	11	2.28 (0.99-5.26)
	A	5	12	1.74 (0.77-3.90)	1	3	1.04 (0.27-4.06)	4	9	2.30 (0.84-6.29)
	A-E (*all studies*)	**18**	**111**	**1.14 (0.78-1.67)***	**11**	**69**	**0.87 (0.50-1.50)***	**7**	**42**	**1.63 (1.09-2.44)**
	A-D	18	111	1.14 (0.78-1.67)*	11	69	0.87 (0.50-1.50)*	7	42	1.63 (1.09-2.44)
CLL	A-C	13	93	1.19 (0.74-1.90)*	7	55	0.84 (0.38-1.84)*	6	38	1.61 (1.00-2.59)
	A-B	8	57	1.37 (0.73-2.56)*	4	38	1.08 (0.29-4.06)*	4	19	1.84 (1.12-3.02)
	A	6	45	1.39 (0.65-2.96)*	3	36	1.47 (0.31-7.00)*	3	9	1.33 (0.64-2.76)

[a] The term relative risk (RR) is used to refer to either the risk ratio, the odds ratio (OR), or the standardized mortality ratio (SMR).
[b] AML RR >1, p<0.1 (A), AML RR >1, p<0.2 (B), AML RR >1, P>0.2 (C), AML RR reported (D), AML RR not reported (E)

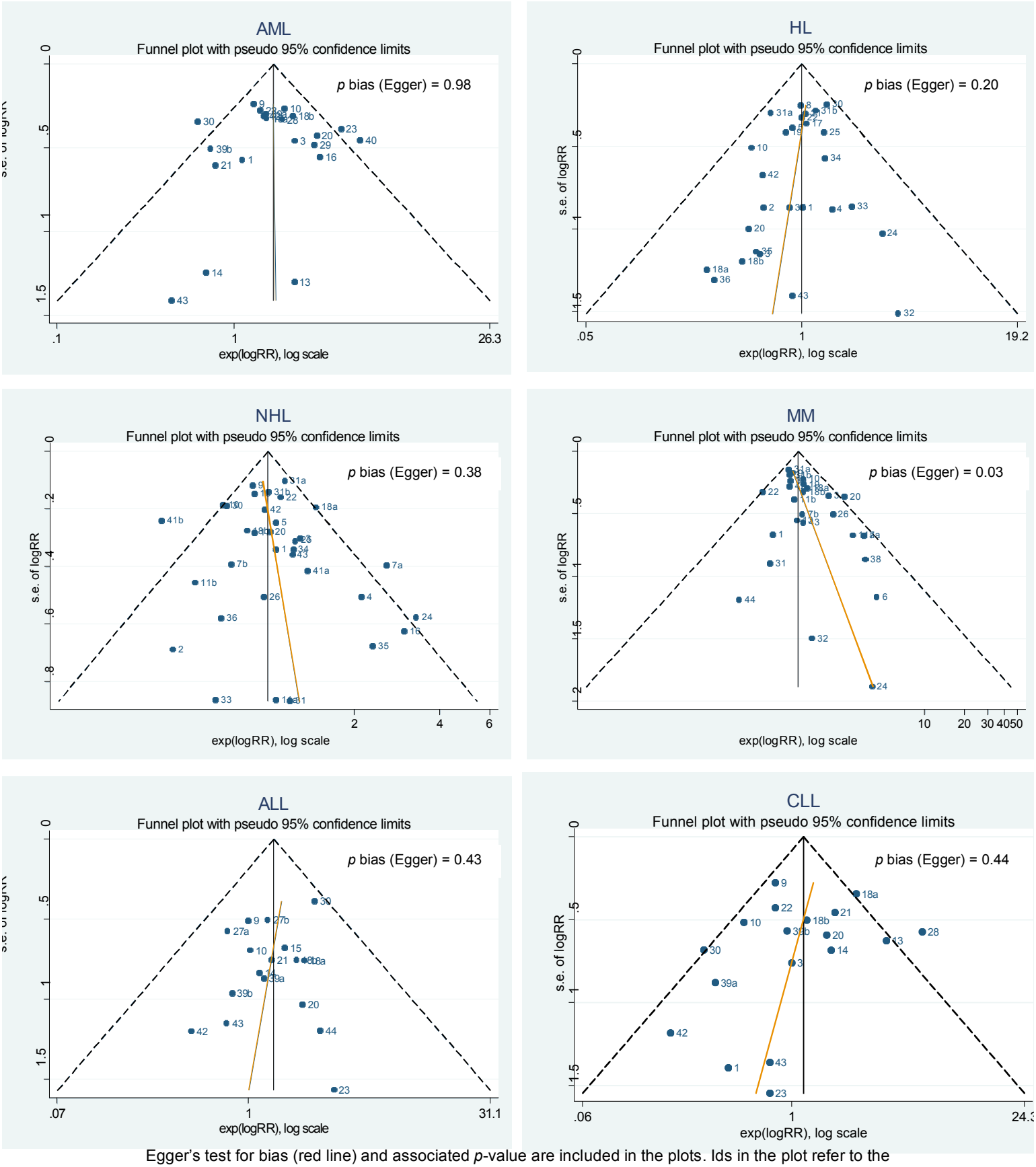
[c] Number of studies
[d] Number of exposed cases
[e] NHL or Lymphosarcoma/Reticulosarcoma (preferred NHL if the study reported both)
[f] Two out of three studies reported null cases (continuity correction was applied in the meta-analysis)
[g] One out of two studies reported null cases (continuity correction was applied in the meta-analysis)
* Significant evidence for between study heterogeneity ($p<0.1$)

Supplemental Material, Table 2 Pooled relative risks[a] for AML and five lymphoma subtypes; stratification by start of follow-up and *exposure assessment quality*

Lymphoma subtype	*Exposure assessment quality*[b]	N[c]	n[d]	Meta relative risk (all studies)	N[c]	n[d]	Meta relative risk (start follow-up before 1970)	N[c]	n[d]	Meta relative risk (start follow-up 1970 and later)
AML	**A-D (*all studies*)**	**21**	**217**	**1.68 (1.35-2.10)***	**12**	**119**	**1.43 (1.07-1.92)***	**9**	**98**	**2.08 (1.59-2.72)**
	A-C	10	108	1.73 (1.26-2.38)	6	57	1.76 (1.11-2.79)*	4	51	1.60 (1.00-2.56)
	A-B	9	95	1.82 (1.25-2.66)	6	57	1.76 (1.11-2.79)*	3	38	2.33 (0.92-5.90)
	A	6	71	2.32 (1.55-3.47)	4	39	2.24 (1.28-3.92)	2	32	2.85 (1.05-7.79)
HL	**A-D (*all studies*)**	**27**	**146**	**0.99 (0.83-1.19)**	**19**	**123**	**1.01 (0.83-1.23)**	**8**	**23**	**0.91 (0.59-1.40)**
	A-C	5	16	0.99 (0.58-1.71)	4	6	0.98 (0.36-2.67)	1	10	1.00 (0.53-1.90)
	A-B	4	6	0.98 (0.36-2.67)	4	6	0.98 (0.36-2.67)	0	0	--
	A	4	6	0.98 (0.36-2.67)	4	6	0.98 (0.36-2.67)	0	0	--
NHL[e]	**A-D (*all studies*)**	**33**	**647**	**1.00 (0.89-1.13)***	**22**	**452**	**0.93 (0.81-1.06)***	**11**	**195**	**1.21 (0.94-1.55)***
	A-C	8	106	1.03 (0.70-1.51)*	6	53	0.92 (0.57-1.49)*	2	53	1.51 (0.61-3.78)
	A-B	7	69	1.04 (0.63-1.72)*	6	53	0.92 (0.57-1.49)*	1	16	3.00 (0.88-10.25)
	A	6	50	1.27 (0.90-1.79)	5	34	1.19 (0.83-1.69)	1	16	3.00 (0.88-10.25)
MM	**A-D (*all studies*)**	**26**	**284**	**1.12 (0.98-1.27)**	**16**	**204**	**1.07 (0.93-1.24)**	**10**	**80**	**1.26 (0.92-1.71)**
	A-C	9	37	1.15 (0.74-1.79)	6	21	1.65 (1.02-2.66)	3	16	0.68 (0.40-1.17)
	A-B	8	28	1.48 (0.96-2.27)	6	21	1.65 (1.02-2.66)	2	7	0.92 (0.34-2.47)
	A	8	28	1.48 (0.96-2.27)	6	21	1.65 (1.02-2.66)	2	7	0.92 (0.34-2.47)
ALL	**A-D (*all studies*)**	**17**	**47**	**1.44 (1.03-2.02)**	**10**	**30**	**1.30 (0.88-1.92)**	**7**	**17**	**1.92 (1.00-3.67)**
	A-C	4	11	1.26 (0.5-3.16)	2	3	1.03 (0.29-3.65)	2	8	1.58 (0.41-6.04)
	A-B	4	11	1.26 (0.5-3.16)	2	3	1.03 (0.29-3.65)	2	8	1.58 (0.41-6.04)
	A	1	5	2.80 (0.27-29.23)	0	0	--	1	5	2.80 (0.27-29.23)
CLL	**A-D (*all studies*)**	**18**	**111**	**1.14 (0.78-1.67)***	**11**	**69**	**0.87 (0.50-1.50)***	**7**	**42**	**1.63 (1.09-2.44)**
	A-C	8	61	1.38 (0.71-2.69)*	5	38	1.16 (0.39-3.41)*	3	23	1.56 (0.62-3.97)
	A-B	7	53	1.54 (0.72-3.31)*	5	38	1.16 (0.39-3.41)*	2	15	2.59 (1.05-6.41)
	A	4	43	2.44 (0.88-6.75)	3	32	1.80 (0.38-8.63)*	1	11	3.66 (1.07-12.52)

[a] The term relative risk (RR) is used to refer to either the risk ratio, the odds ratio (OR), or the standardized mortality ratio (SMR).
[b] Quantitative exposure estimates for benzene (A), semi-quantitative estimates of benzene exposure or quantitative estimates of exposures containing benzene (B), some industrial hygiene sampling results (C), qualitative indication that benzene exposure had occurred (D).
[c] Number of studies
[d] Number of exposed cases
[e] NHL or Lymphosarcoma/Reticulosarcoma (preferred NHL if the study reported both)
* Significant evidence for between study heterogeneity (p<0.1)

Supplemental material, Figure 4: Funnel plots for AML and five lymphoma subtypes with pseudo 95% confidence limits.



Egger's test for bias (red line) and associated *p*-value are included in the plots. Ids in the plot refer to the references in the legend.

Supplemental material, Legend funnel plots Figure 4

ID	Reference	Subcohort
1	(Bloemen et al. 2004)	
2	(Collingwood et al. 1996)	
3	(Collins et al. 2003)	
4	(Consonni et al. 1999)	
5	(Dagg et al. 1992)	
6	(Decoufle et al. 1983)	
7a	(Delzell et al. 1992)	Oil and gas division
7b	(Delzell et al. 1992)	Refining division
8	(Divine et al. 1999a)	
9	(Divine et al. 1999b)	
10	(Divine and Hartman 2000)	
11a	(Fu et al. 1996)	Italian cohort
11b	(Fu et al. 1996)	UK cohort
12	(Glass et al. 2003)	
13	(Atkinson et al. 2001)	
14	(Guenel et al. 2002)	
15	(Gun et al. 2006)	
16	(Hayes et al. 1997)	
17	(Honda et al. 1995)	
18a	(Huebner et al. 2004)	Louisiana cohort
18b	(Huebner et al. 2004)	Texas cohort
19	(Kaplan 1986)	
20	(Kirkeleit et al. 2008)	
21	(Lewis et al. 2003)	
22	(Lynge et al. 1997)	
23	(McCraw et al. 1985)	
24	(Nilsson et al. 1998)	
25	(Pukkala 1998)	
26	(Rinsky et al. 2002)	
27a	(Rushton 1993)	Refinery workers cohort
27b	(Rushton 1993)	Distribution workers cohort
28	(Rushton and Romaniuk 1997)	
29	(Sathiakumar et al. 1995)	Oil and gas division
30	(Satin et al. 1996)	
31	(Schnatter et al. 1996)	
31a	(Sorahan 2007)	Refinery workers cohort
31b	(Sorahan 2007)	Distribution workers cohort
32	(Swaen et al. 2005)	
33	(Tsai et al. 1993)	
34	(Tsai et al. 1996)	
35	(Tsai et al. 2003)	
36	(Waxweiler et al. 1983)	
37	(Wong 1987a)	
38	(Wong 1987b)	
39a	(Wong et al. 1993)	Land-based workers cohort
39b	(Wong et al. 1993)	Marine workers cohort

40	(Wong 1995)	
41a	(Wong 1998)	US chemical workers cohort (see Wong 1987a and Wong 1987b)
41b	(Wong 1998)	US gasoline distribution employees cohort (see Wong et al. 1993)
42	(Wong et al. 2001a)	
43	(Wong et al. 2001b)	
44	(Yin et al. 1996)	

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Corrected 12 November 2010

In the manuscript originally published online, data shown for the ‘AML Significance level’ in Table 1 differed from the correct values used in the analysis due to a sorting error. In addition, one risk estimate used in the meta-analysis for NHL was classified incorrectly as 'AML Significance level' C instead of as 'AML Significance level' E. Correction of the 'AML Significance level' for this risk estimate resulted in minor changes in some of the meta relative risks reported in Table 3 and in Supplemental Material, Table 1. These errors have been corrected.