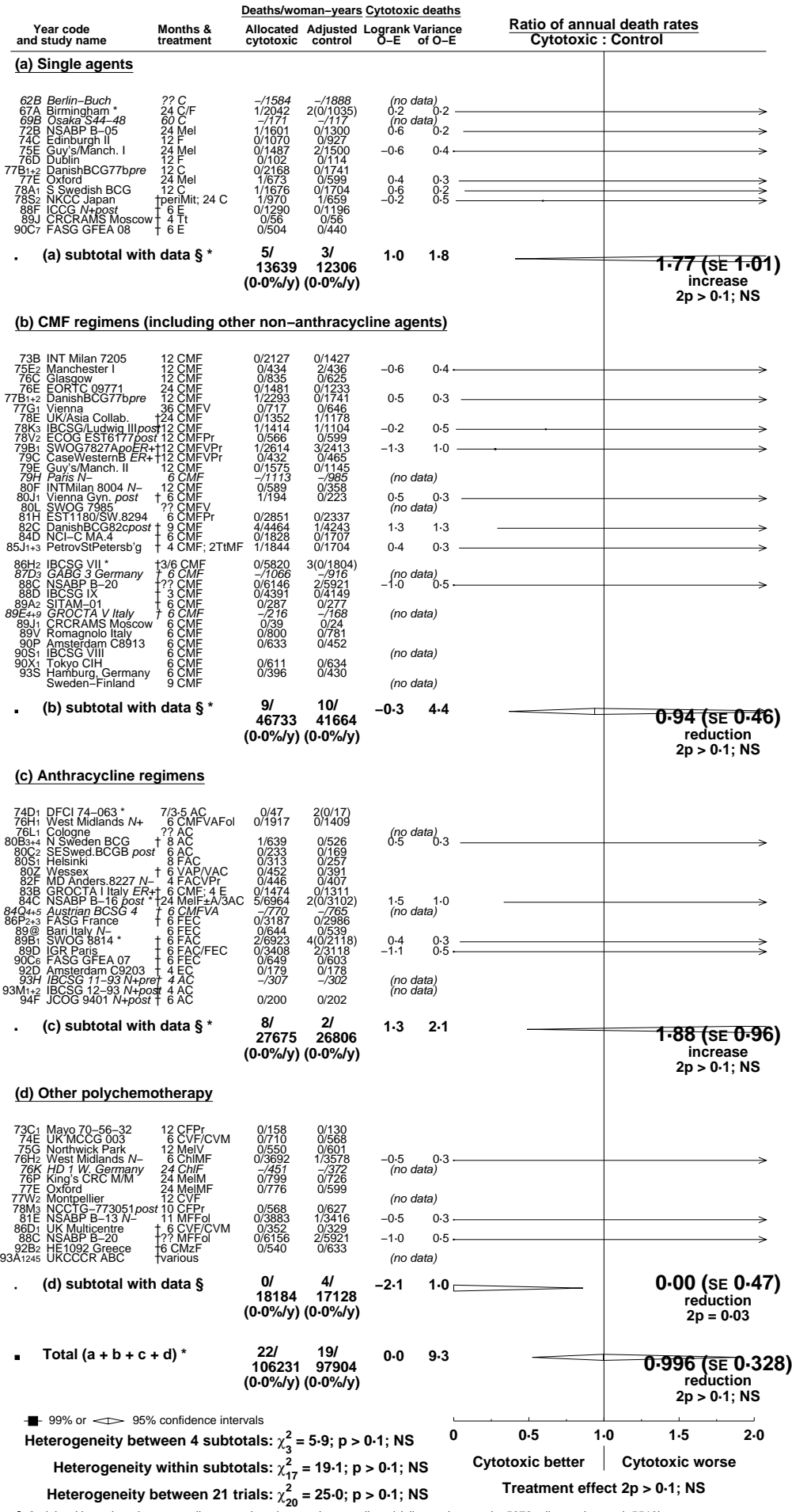


■ 99% or ◊ 95% confidence intervals
Heterogeneity between 4 subtotals: $\chi^2_3 = 6.6$; $p = 0.09$
Heterogeneity within subtotals: $\chi^2_{69} = 82.7$; $p > 0.1$; NS
Heterogeneity between 73 trials: $\chi^2_{72} = 89.3$; $p = 0.08$
 * For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.
 † Chemotherapy plus tamoxifen versus same tamoxifen alone
 09:41:30 7 May 2003
 Not for publication or citation



■ 99% or ◁ 95% confidence intervals

Heterogeneity between 4 subtotals: $\chi^2_3 = 5.9$; $p > 0.1$; NS

Heterogeneity within subtotals: $\chi^2_{17} = 19.1$; $p > 0.1$; NS

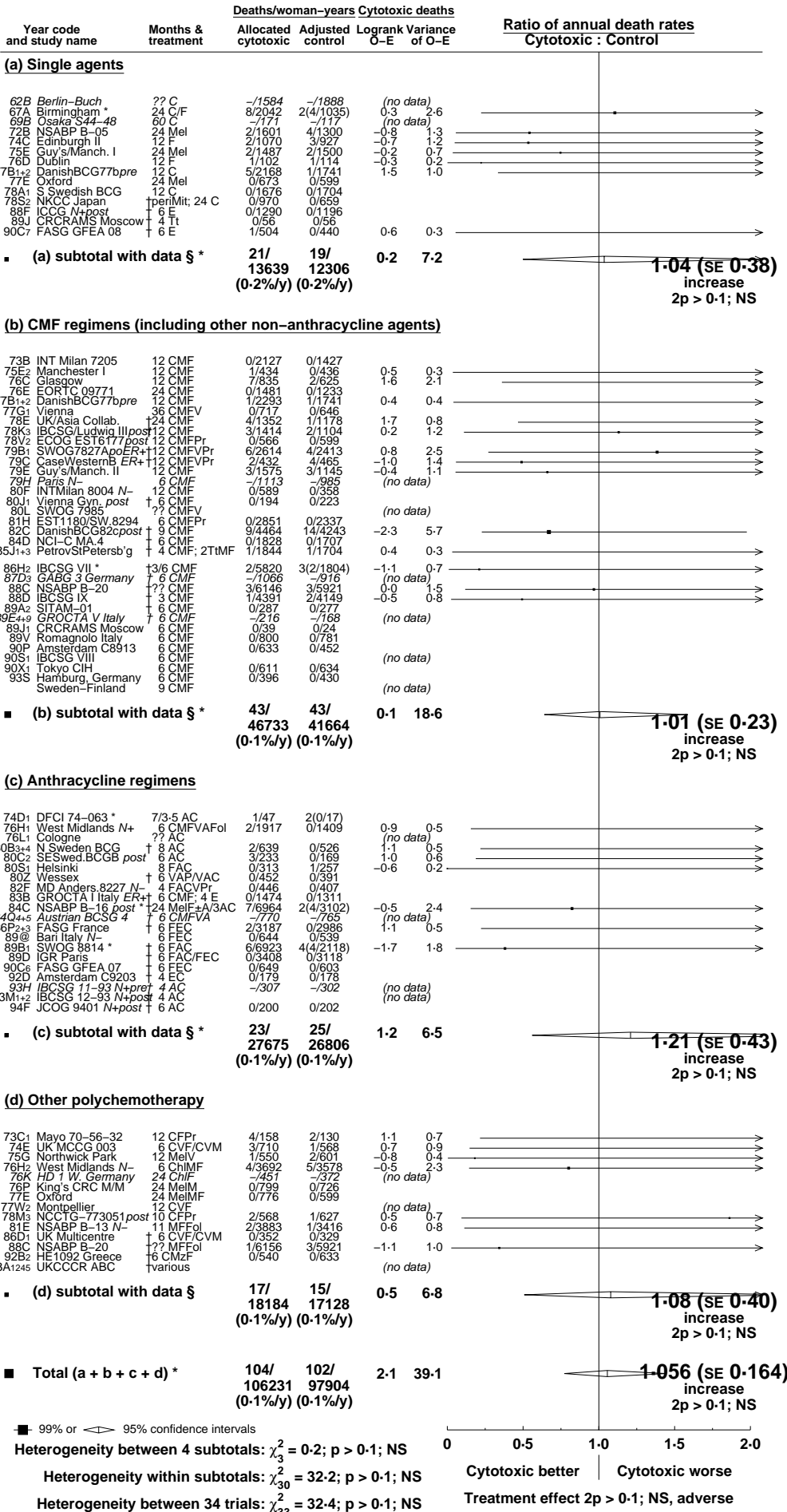
Heterogeneity between 21 trials: $\chi^2_{20} = 25.0$; $p > 0.1$; NS

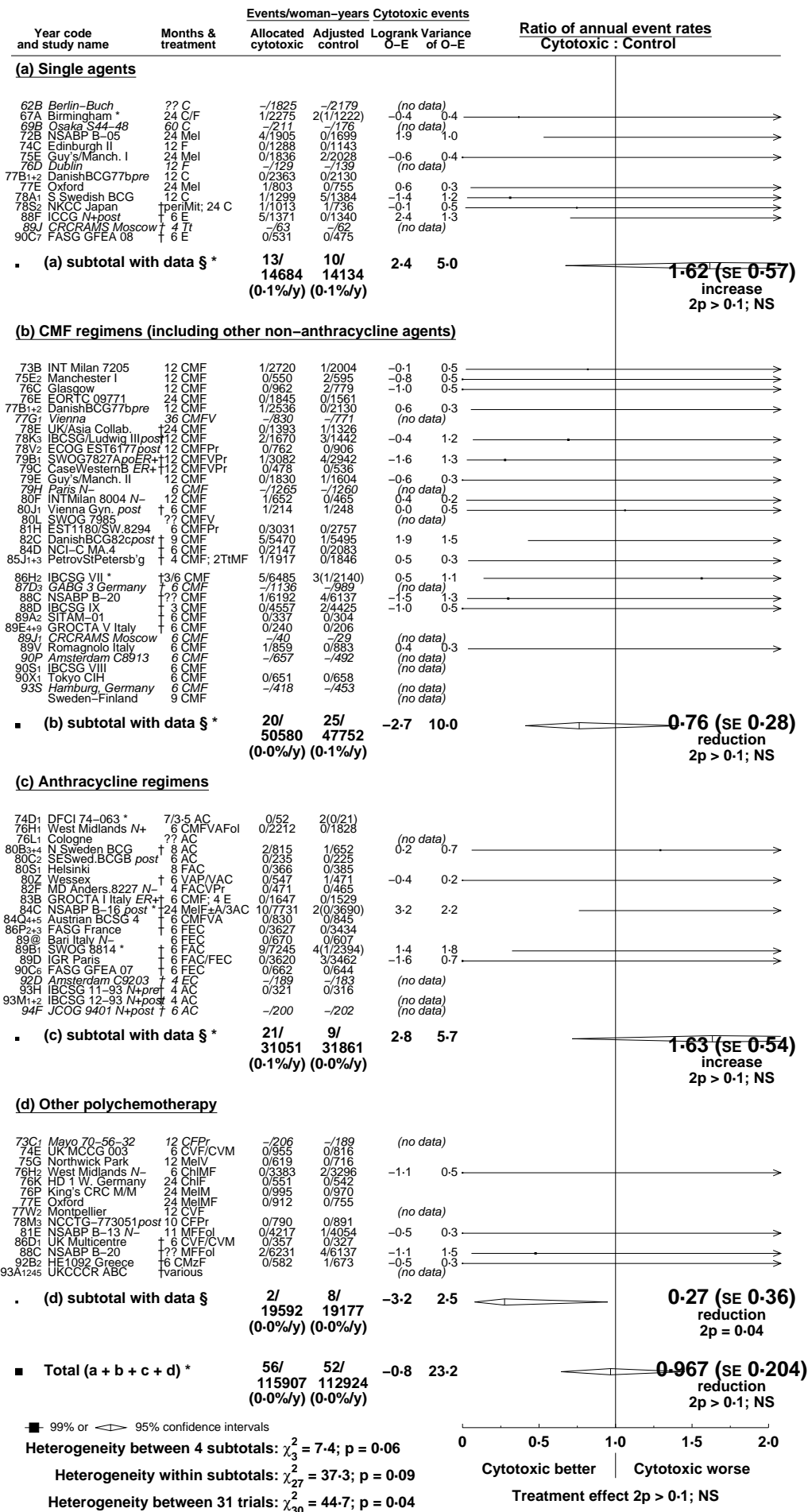
§ 8 trials with no data do not contribute to subtotals or to the overall total (allocated cytotoxic: 5678; allocated control: 5513)

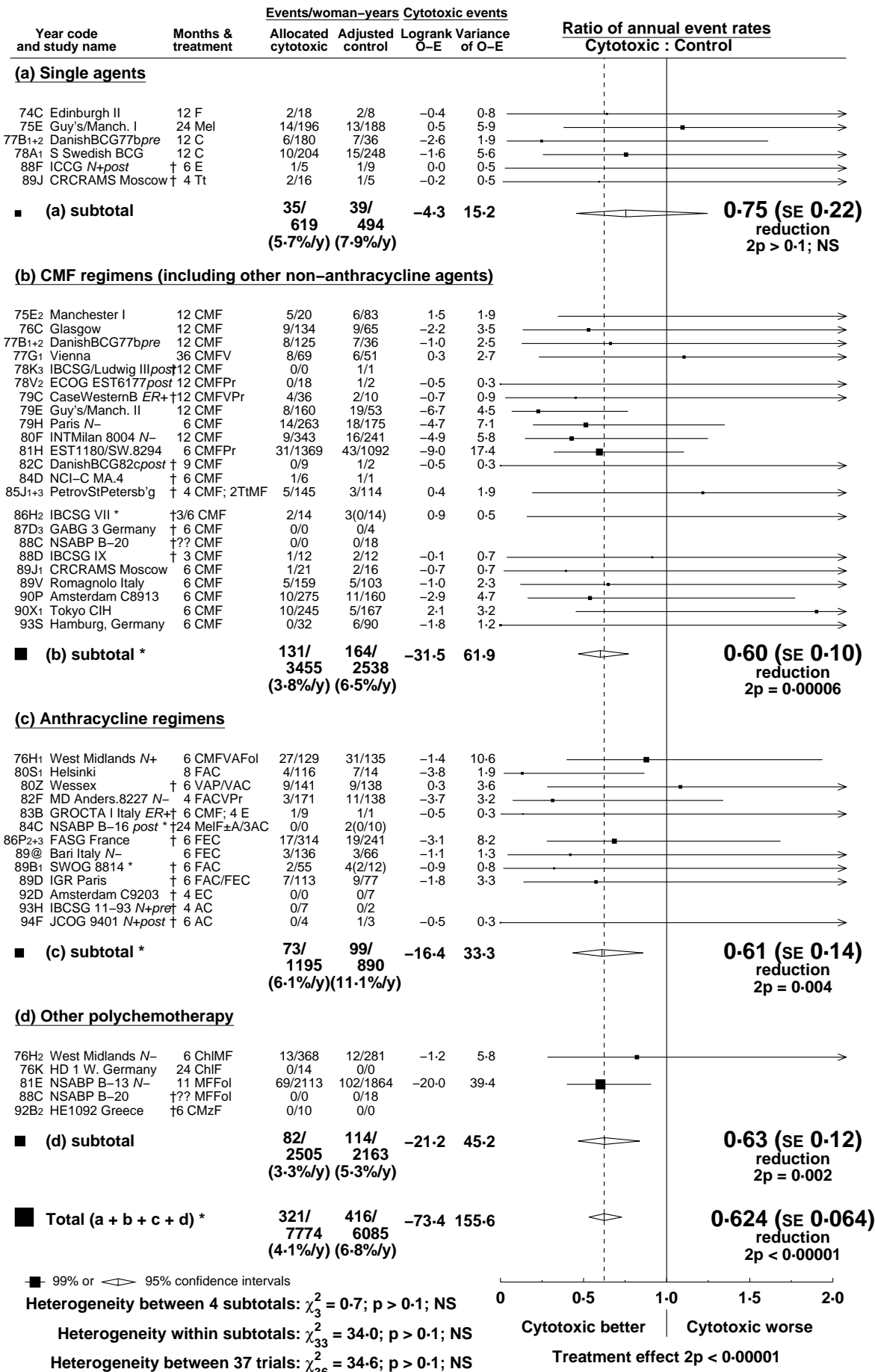
* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

† Chemotherapy plus tamoxifen versus same tamoxifen alone

0 0.5 1.0 1.5 2.0
Cytotoxic better | Cytotoxic worse
Treatment effect 2p > 0.1; NS

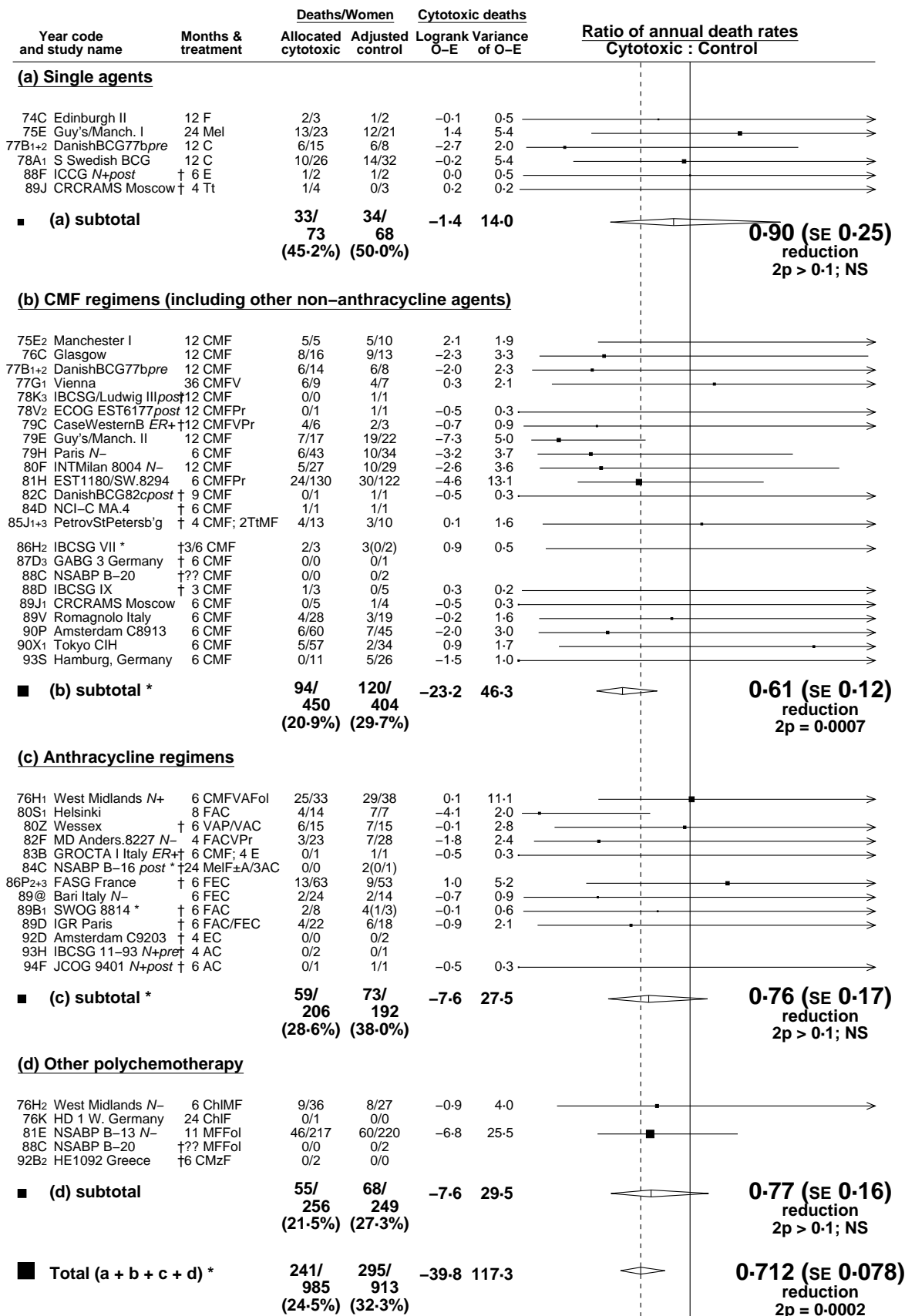






* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.

† Chemotherapy plus tamoxifen versus same tamoxifen alone

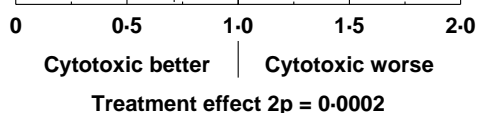


■ 99% or ◊ 95% confidence intervals

Heterogeneity between 4 subtotals: $\chi^2_3 = 2.3$; $p > 0.1$; NS

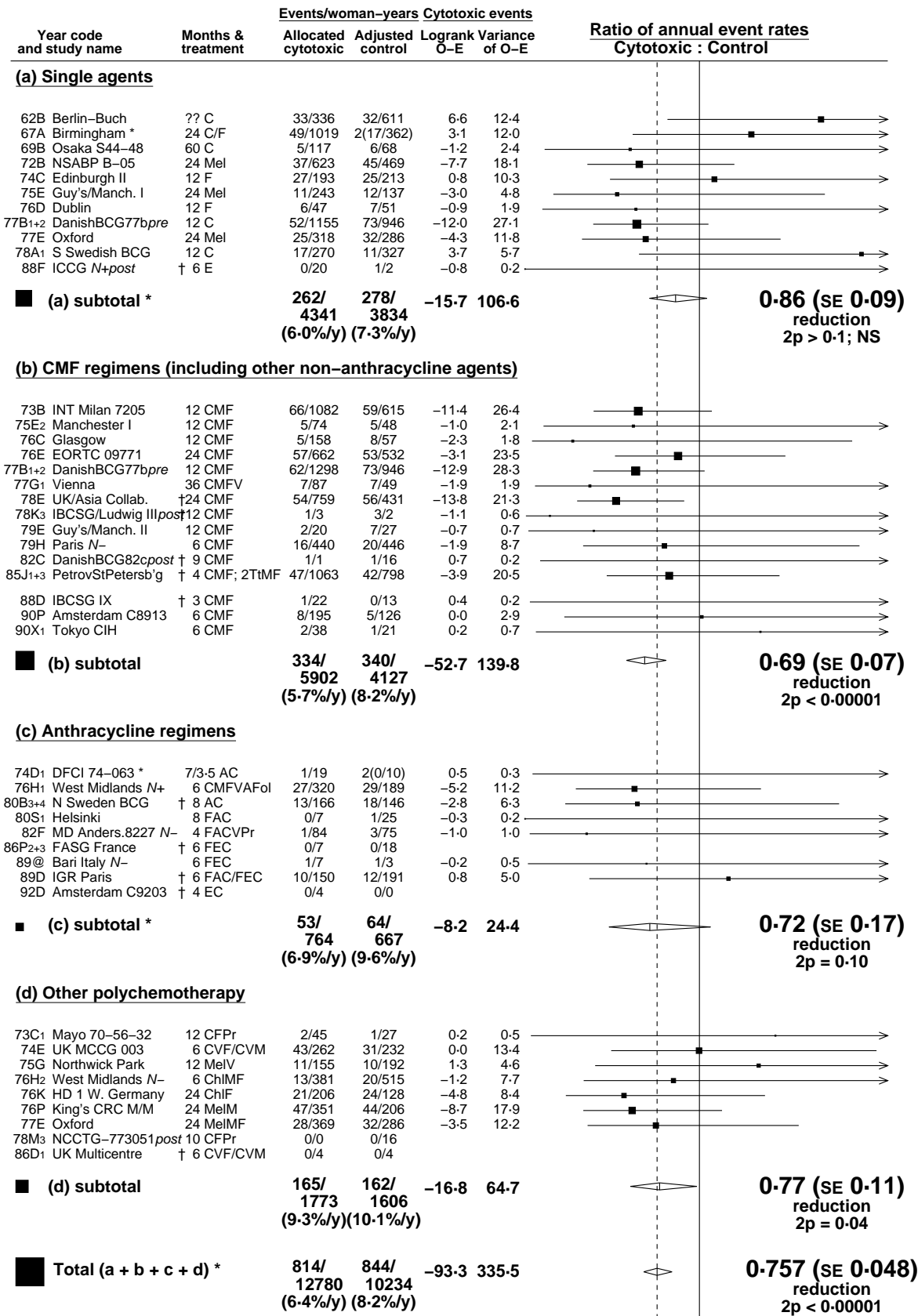
Heterogeneity within subtotals: $\chi^2_{33} = 35.7$; $p > 0.1$; NS

Heterogeneity between 37 trials: $\chi^2_{36} = 38.0$; $p > 0.1$; NS



* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

† Chemotherapy plus tamoxifen versus same tamoxifen alone



■ 99% or ◊ 95% confidence intervals

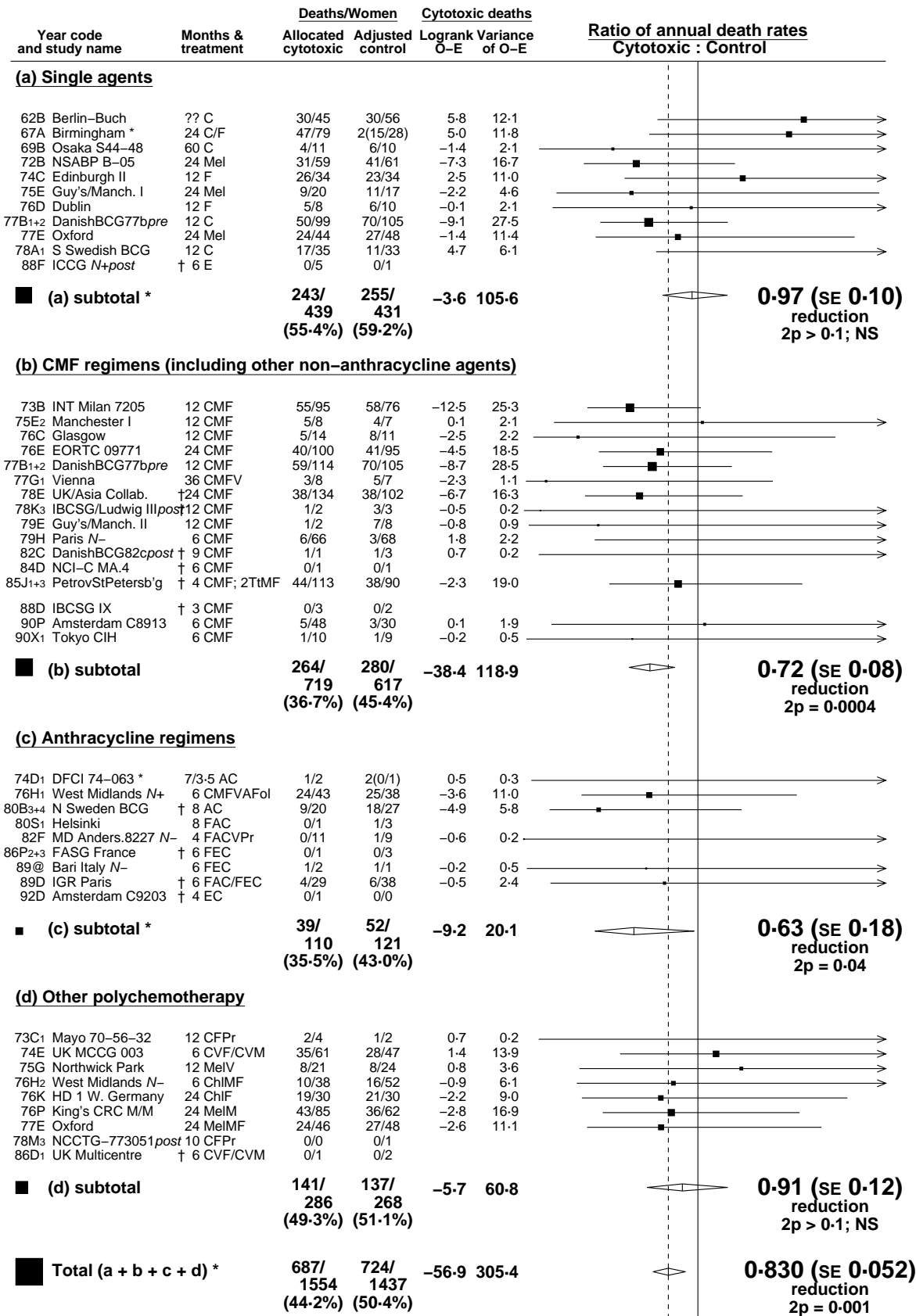
Heterogeneity between 4 subtotals: $\chi^2_3 = 3.3$; $p > 0.1$; NS

Heterogeneity within subtotals: $\chi^2_{36} = 41.8$; $p > 0.1$; NS

Heterogeneity between 40 trials: $\chi^2_{39} = 45.1$; $p > 0.1$; NS

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.

† Chemotherapy plus tamoxifen versus same tamoxifen alone



■ 99% or ◊ 95% confidence intervals

Heterogeneity between 4 subtotals: $\chi^2_3 = 6.7$; $p = 0.08$

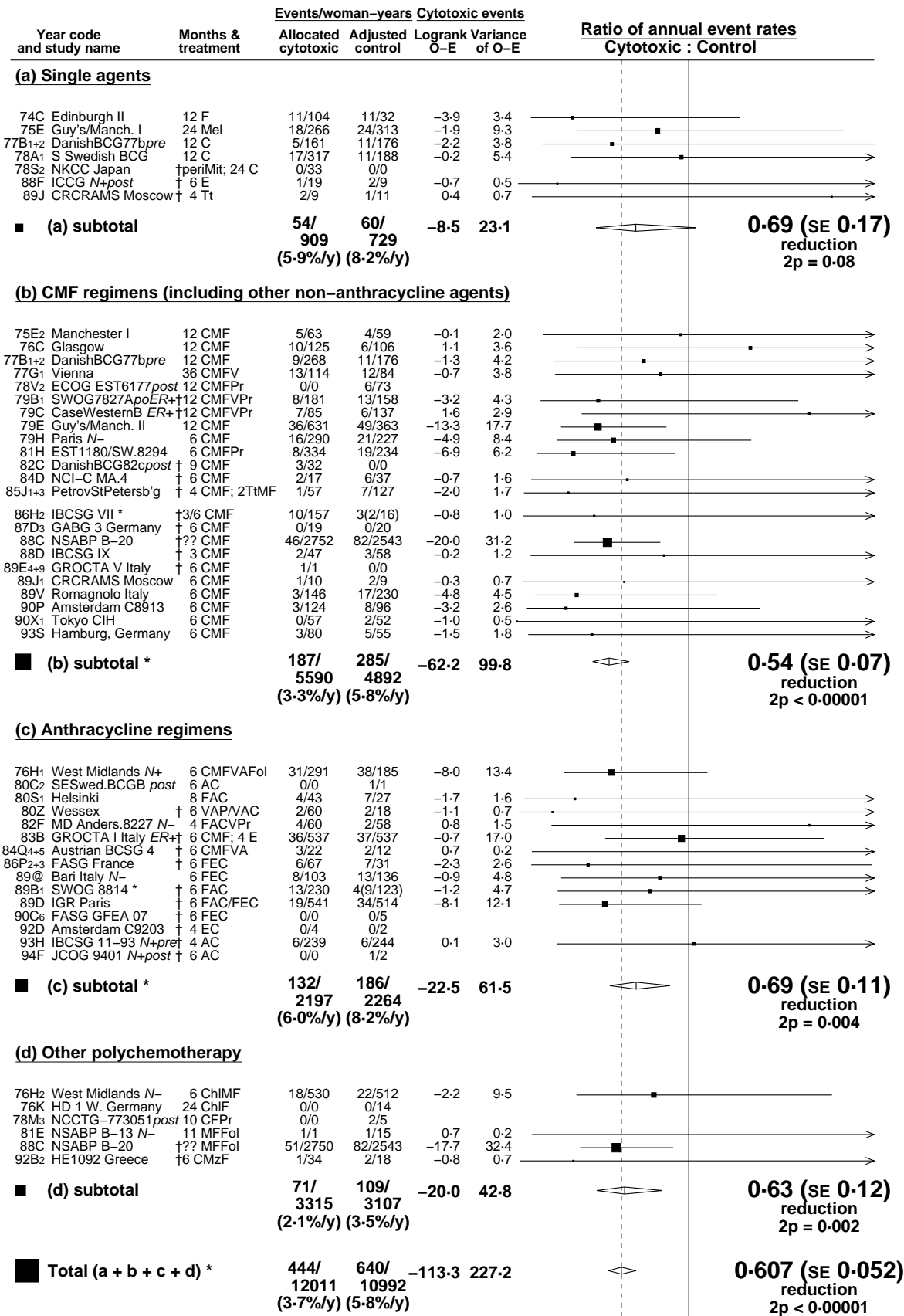
Heterogeneity within subtotals: $\chi^2_{33} = 38.1$; $p > 0.1$; NS

Heterogeneity between 37 trials: $\chi^2_{36} = 44.8$; $p > 0.1$; NS

0 0.5 1.0 1.5 2.0
Cytotoxic better | Cytotoxic worse
Treatment effect 2p = 0.001

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

† Chemotherapy plus tamoxifen versus same tamoxifen alone



■ 99% or ◊ 95% confidence intervals

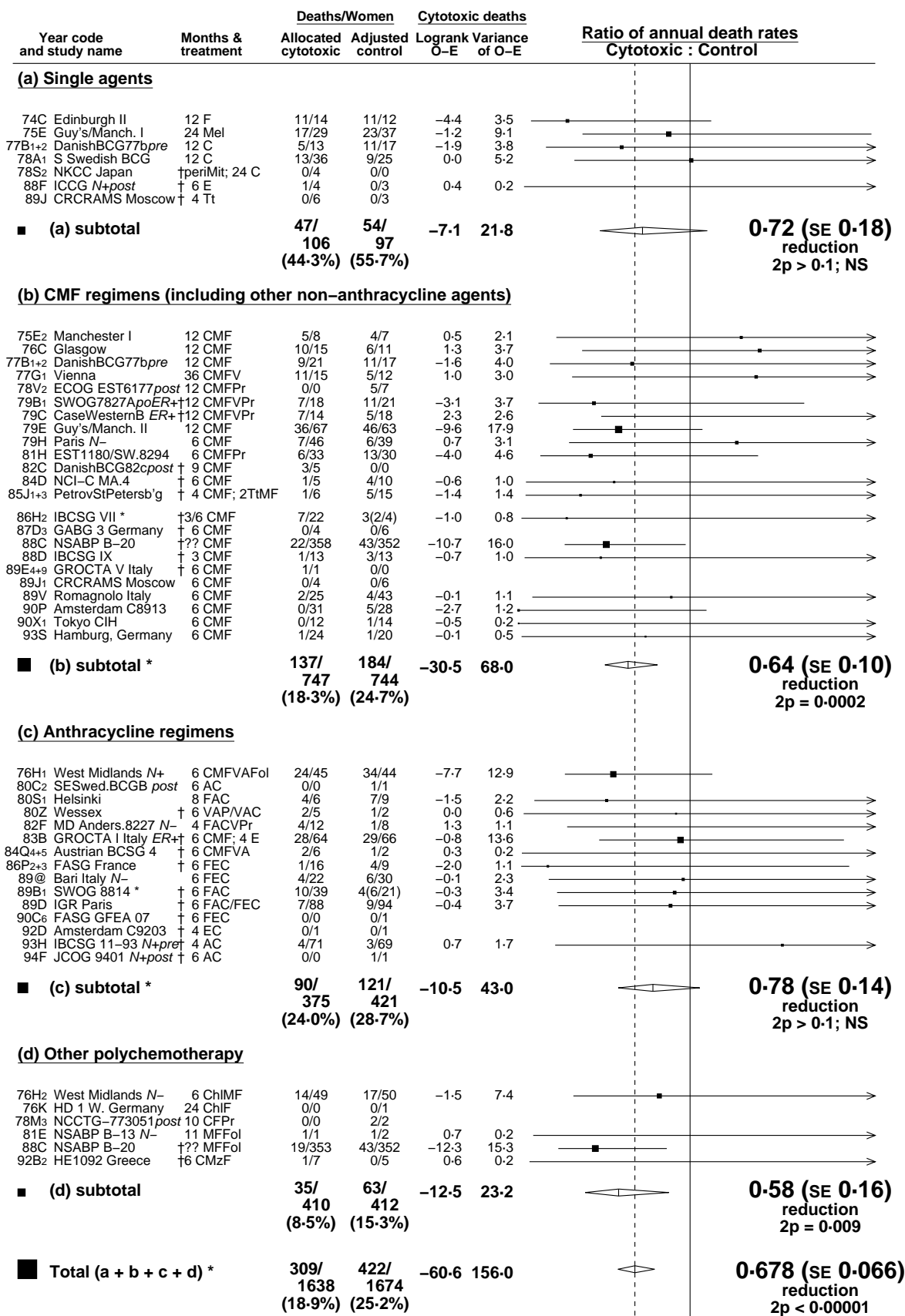
Heterogeneity between 4 subtotals: $\chi^2_3 = 3.1$; $p > 0.1$; NS

Heterogeneity within subtotals: $\chi^2_{36} = 33.0$; $p > 0.1$; NS

Heterogeneity between 40 trials: $\chi^2_{39} = 36.1$; $p > 0.1$; NS

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.

† Chemotherapy plus tamoxifen versus same tamoxifen alone



■ 99% or ◊ 95% confidence intervals

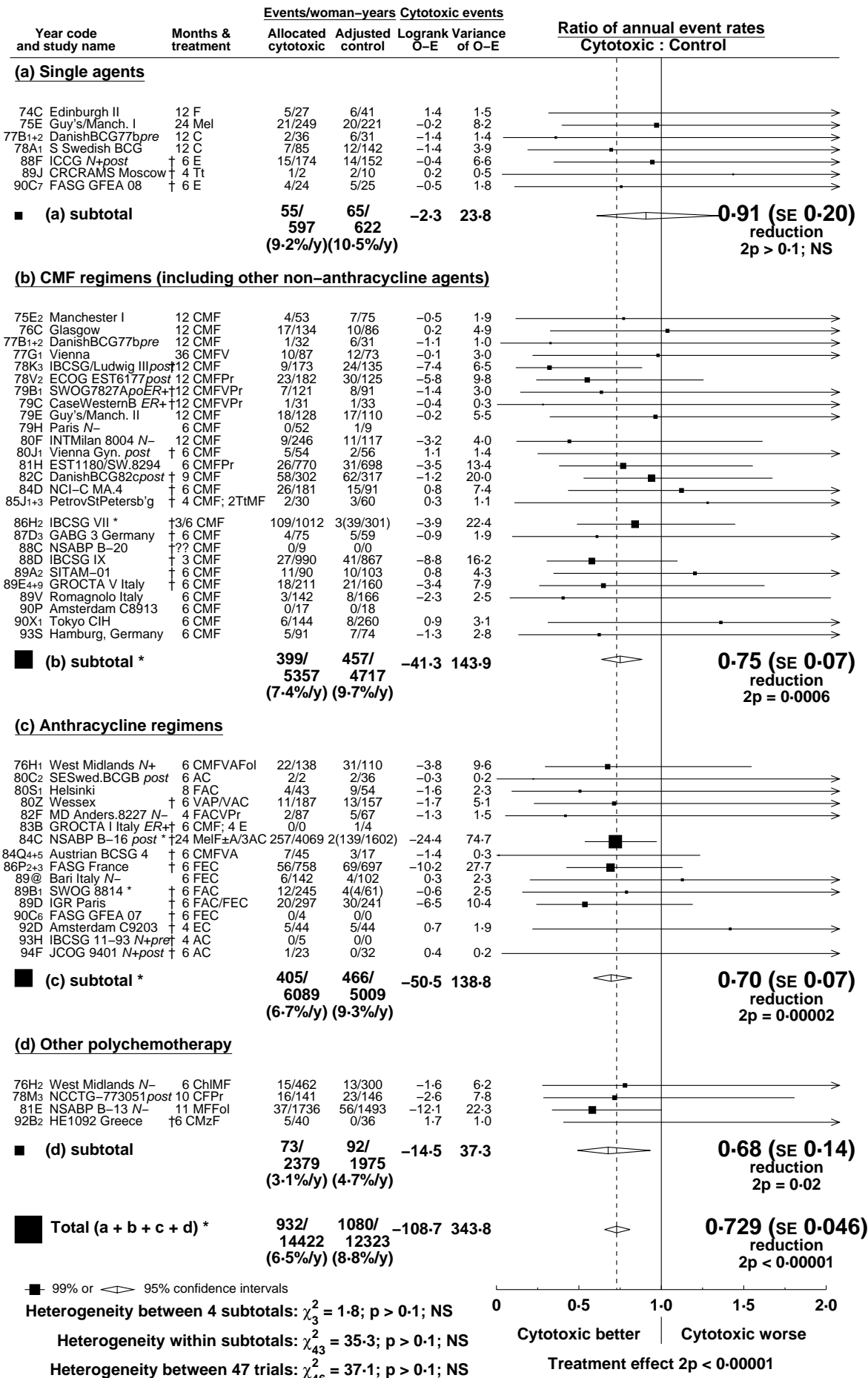
Heterogeneity between 4 subtotals: $\chi^2_3 = 1.8$; $p > 0.1$; NS

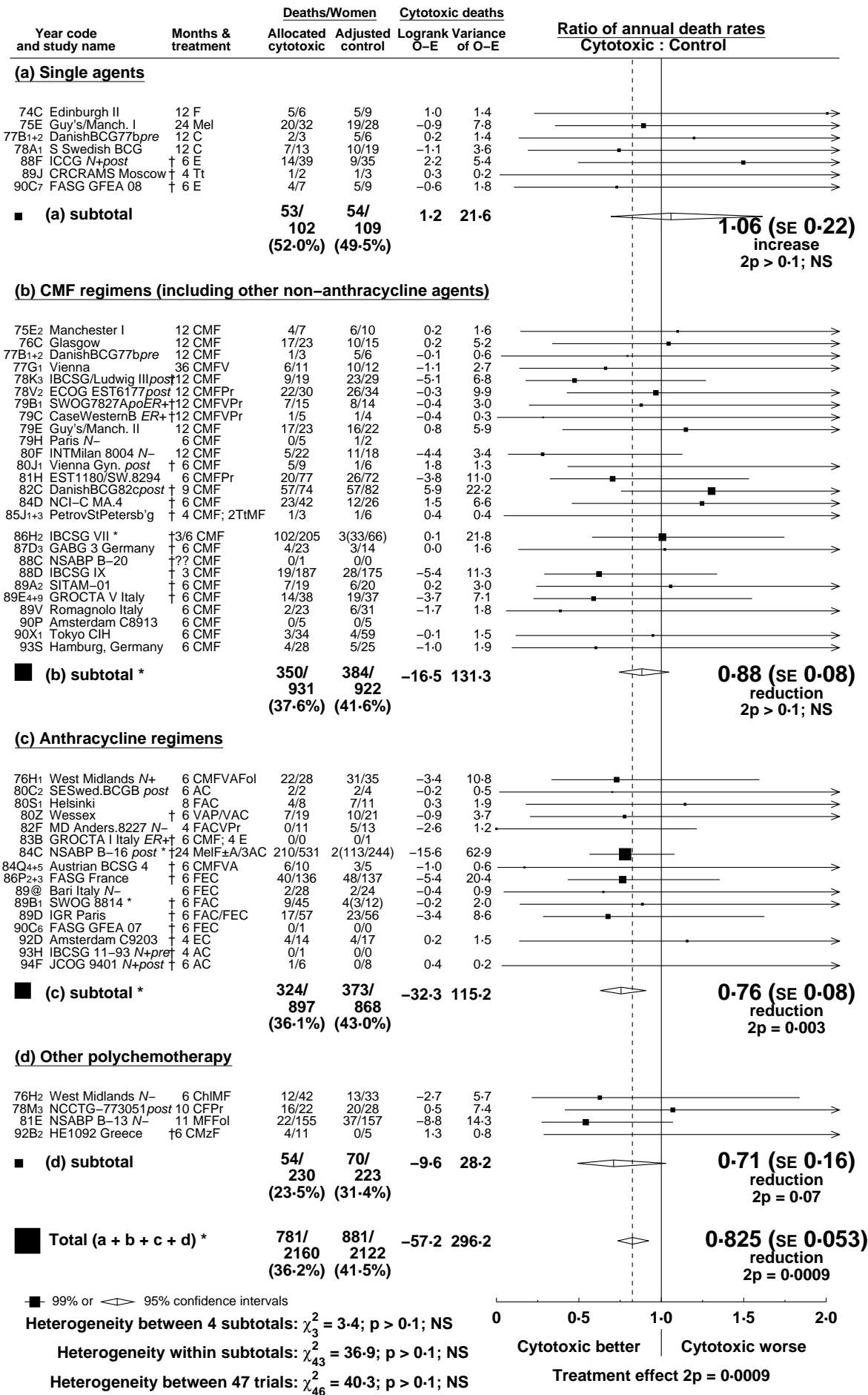
Heterogeneity within subtotals: $\chi^2_{34} = 40.1$; $p > 0.1$; NS

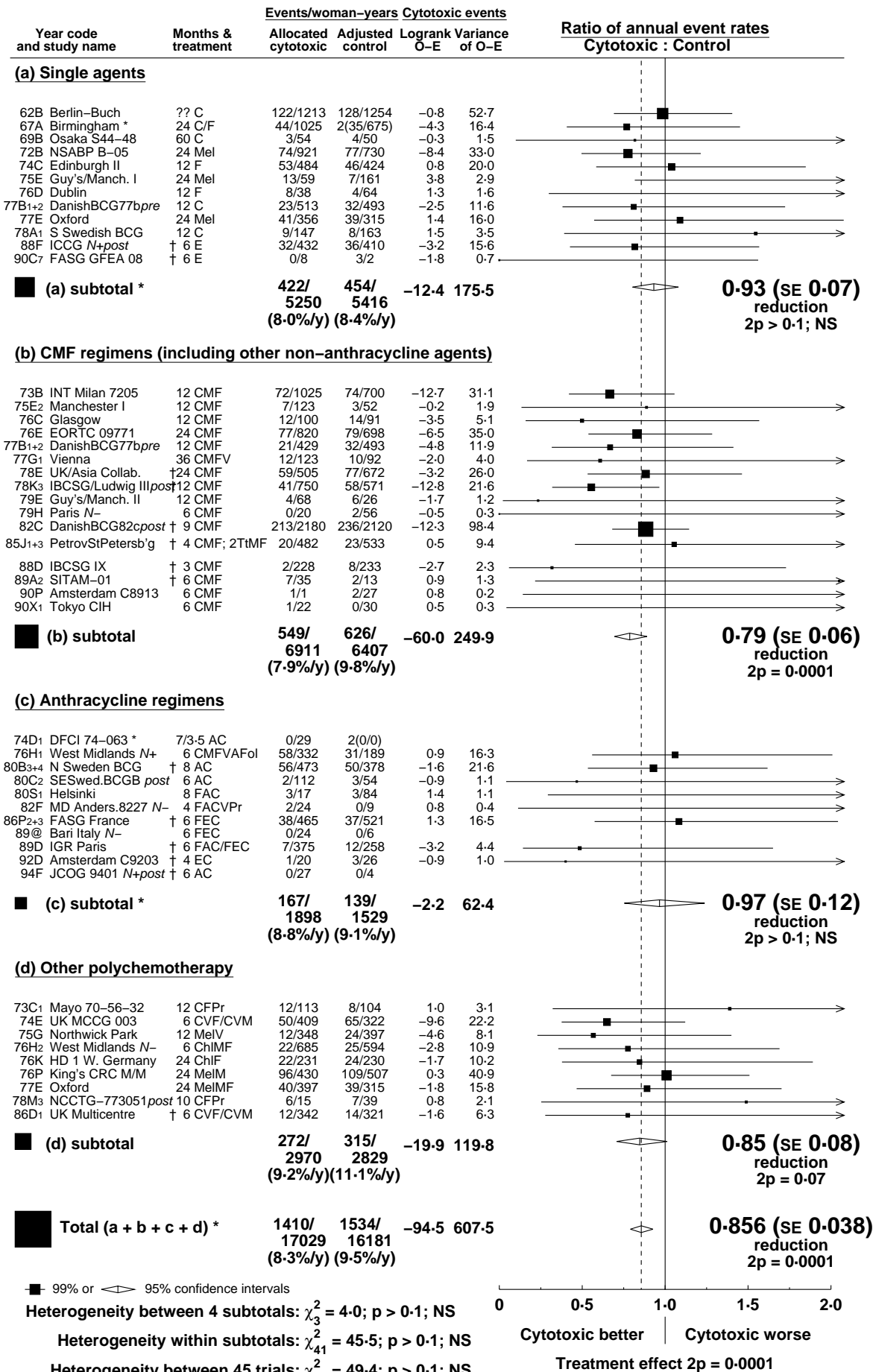
Heterogeneity between 38 trials: $\chi^2_{37} = 41.9$; $p > 0.1$; NS

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

† Chemotherapy plus tamoxifen versus same tamoxifen alone

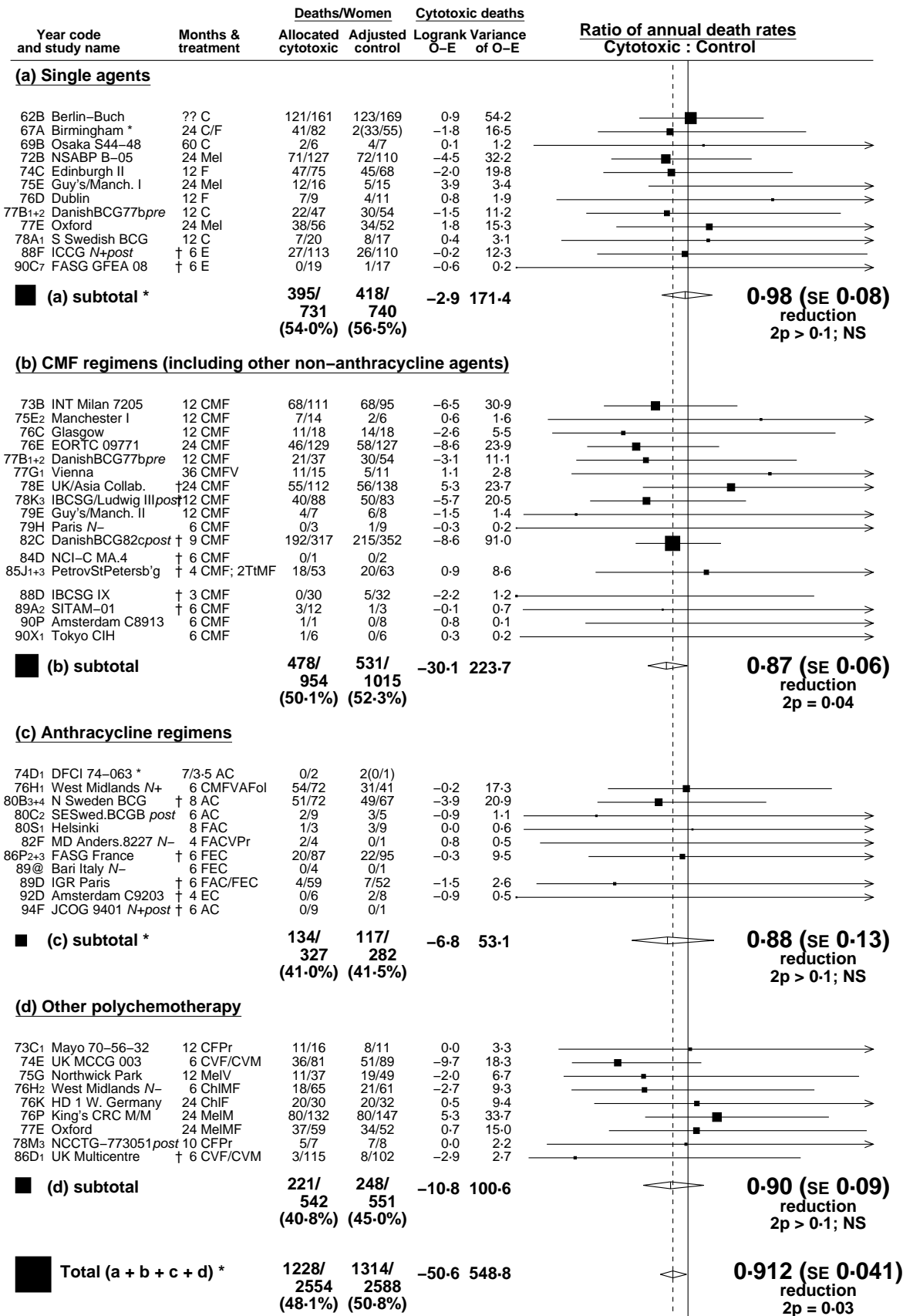






* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.

† Chemotherapy plus tamoxifen versus same tamoxifen alone



■ 99% or ◊ 95% confidence intervals

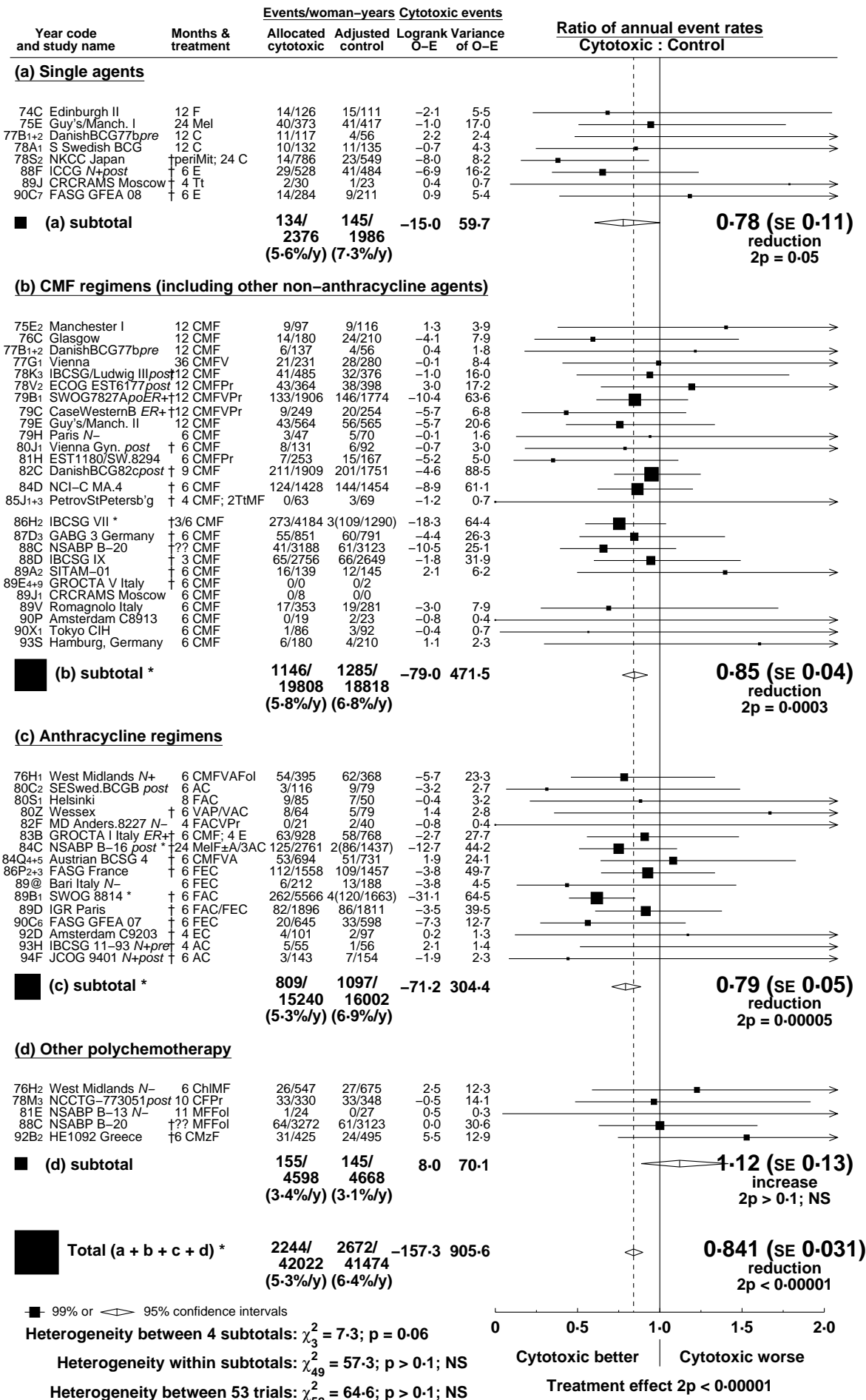
Heterogeneity between 4 subtotals: $\chi^2_3 = 1.5; p > 0.1; NS$

Heterogeneity within subtotals: $\chi^2_{41} = 39.6; p > 0.1; NS$

Heterogeneity between 45 trials: $\chi^2_{44} = 41.1; p > 0.1; NS$

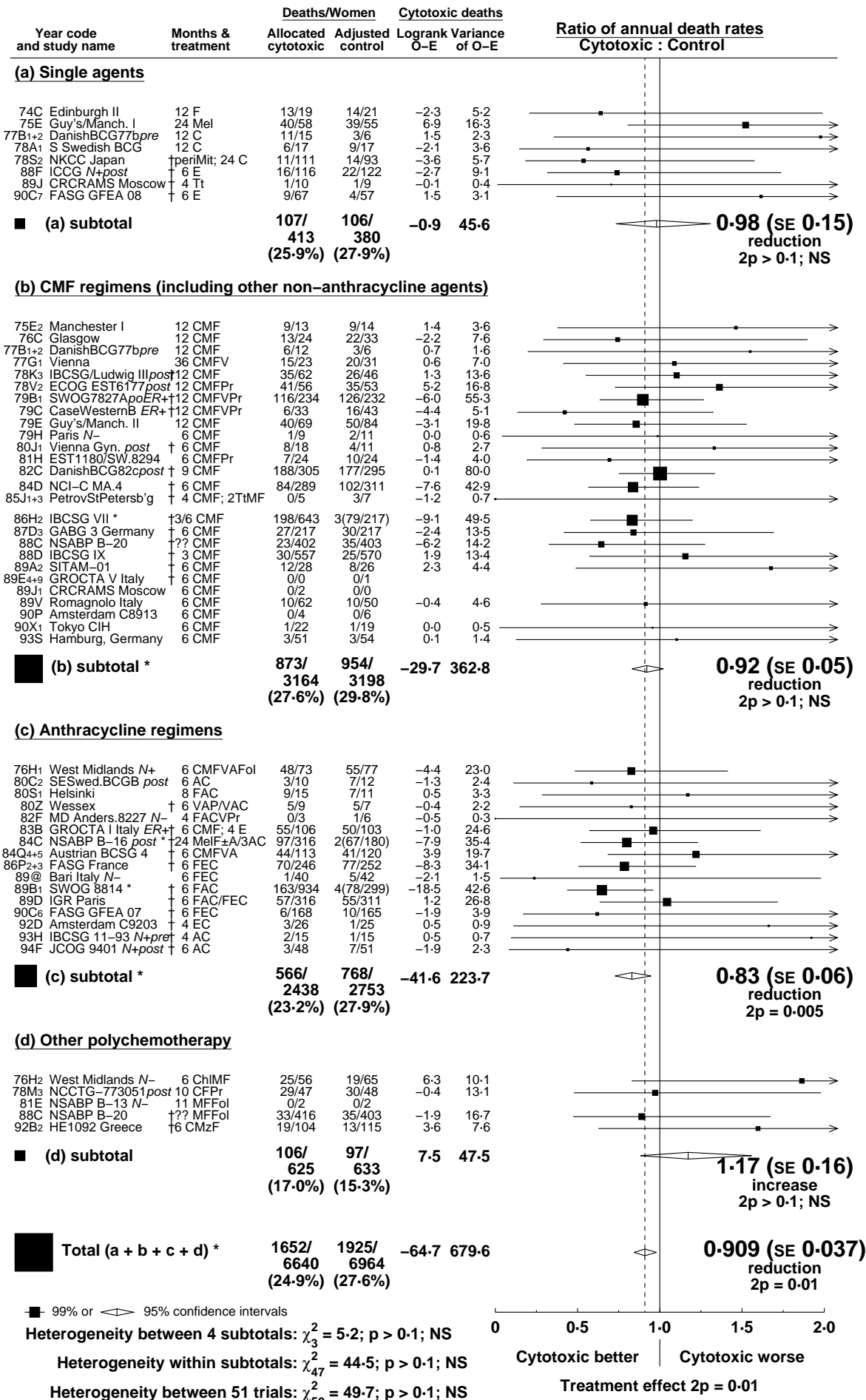
* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

† Chemotherapy plus tamoxifen versus same tamoxifen alone



* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.

† Chemotherapy plus tamoxifen versus same tamoxifen alone



■ 99% or ◊ 95% confidence intervals

Heterogeneity between 4 subtotals: $\chi^2_3 = 5.2$; $p > 0.1$; NS

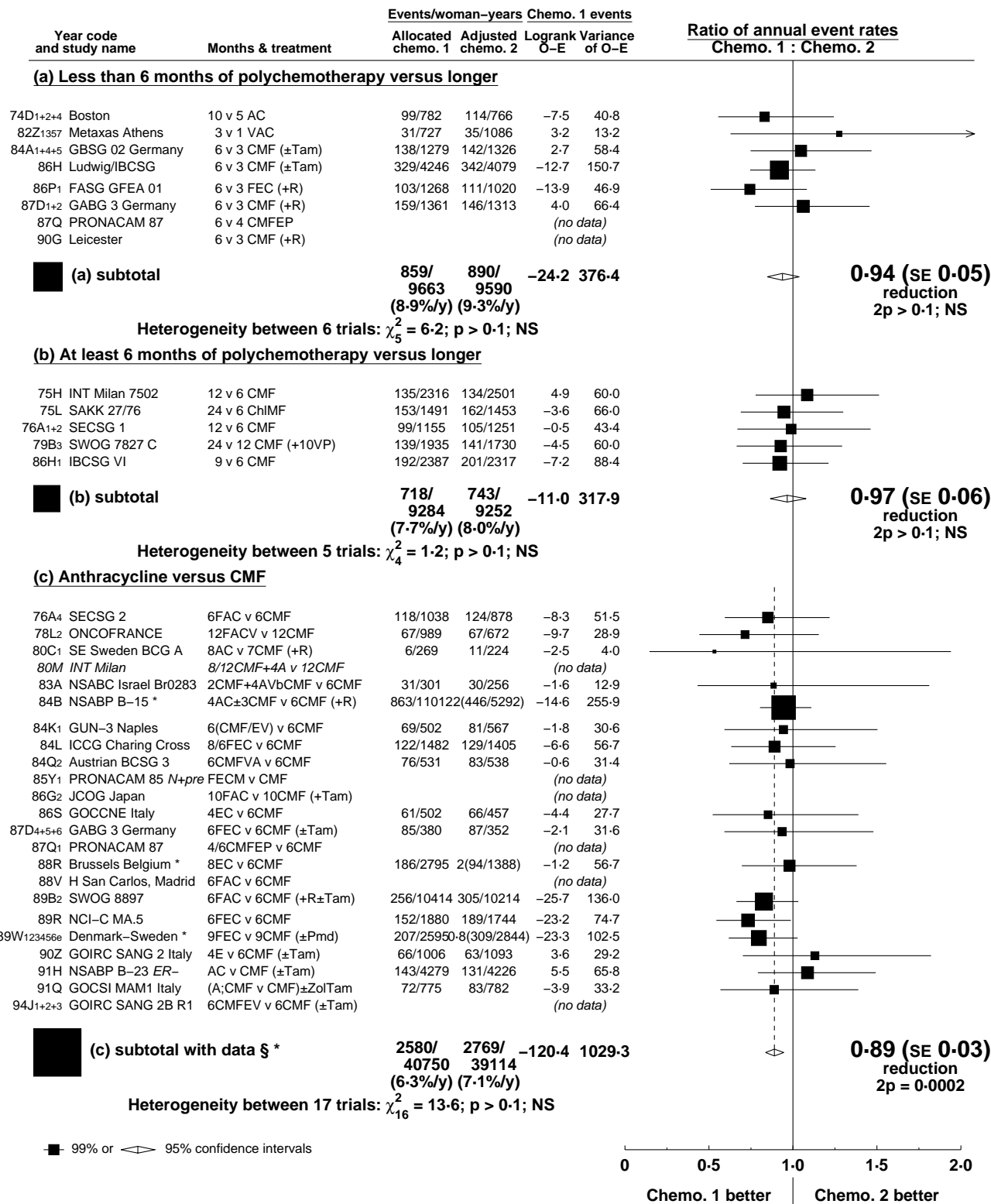
Heterogeneity within subtotals: $\chi^2_{47} = 44.5$; $p > 0.1$; NS

Heterogeneity between 51 trials: $\chi^2_{50} = 49.7$; $p > 0.1$; NS

Treatment effect $2p = 0.01$

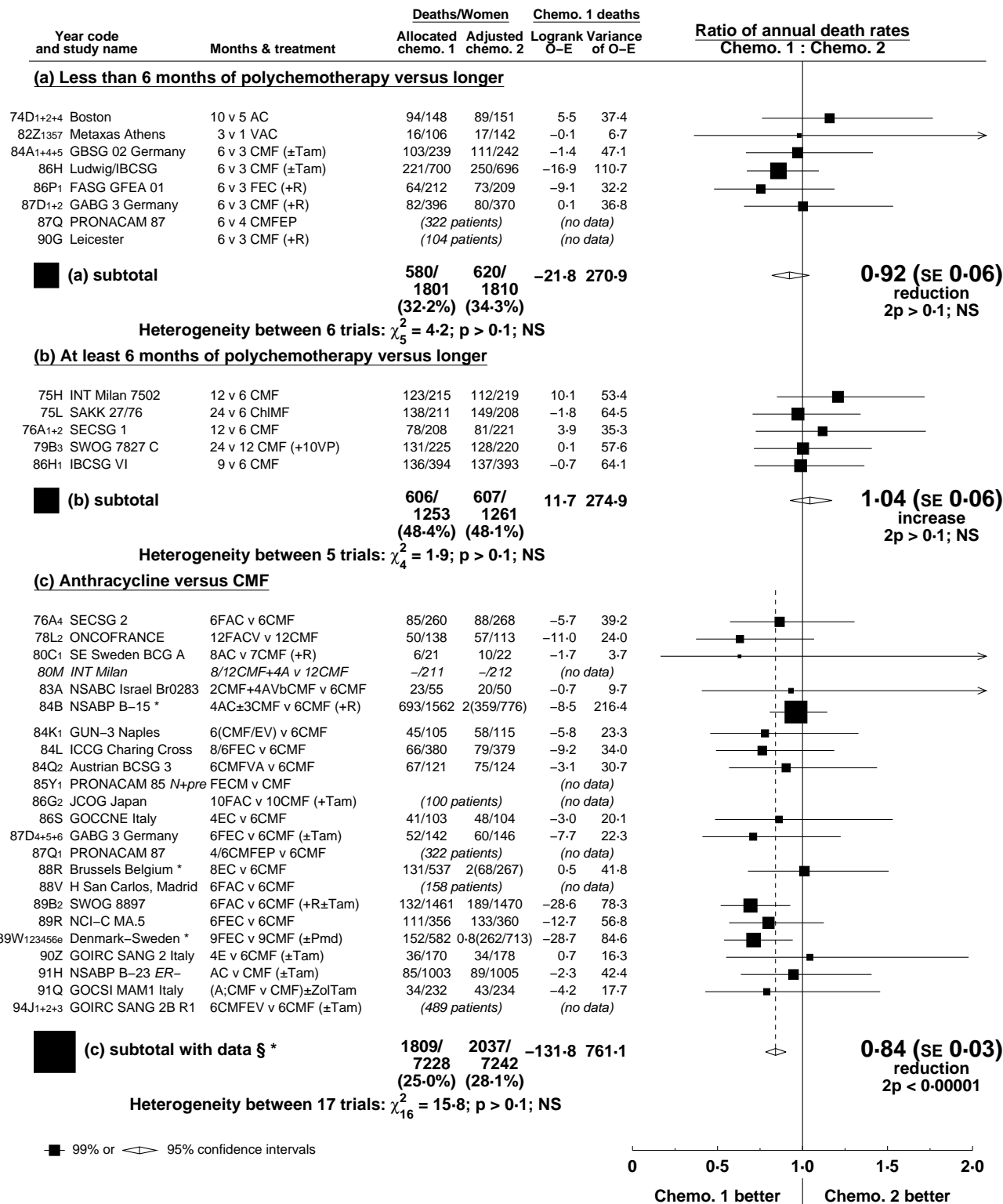
* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

† Chemotherapy plus tamoxifen versus same tamoxifen alone



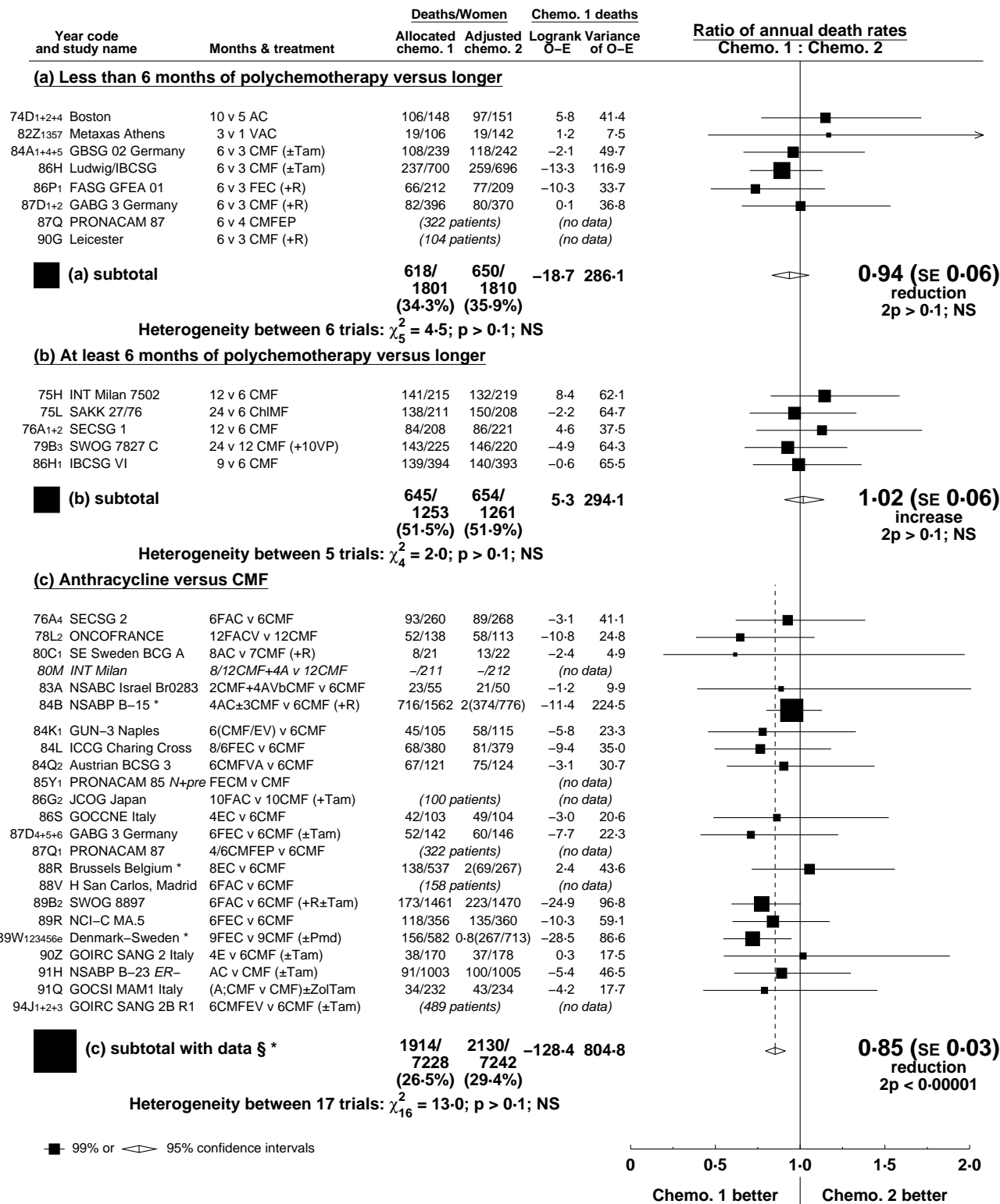
§ 1 trial with no data does not contribute to subtotals or to the overall total.

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s).



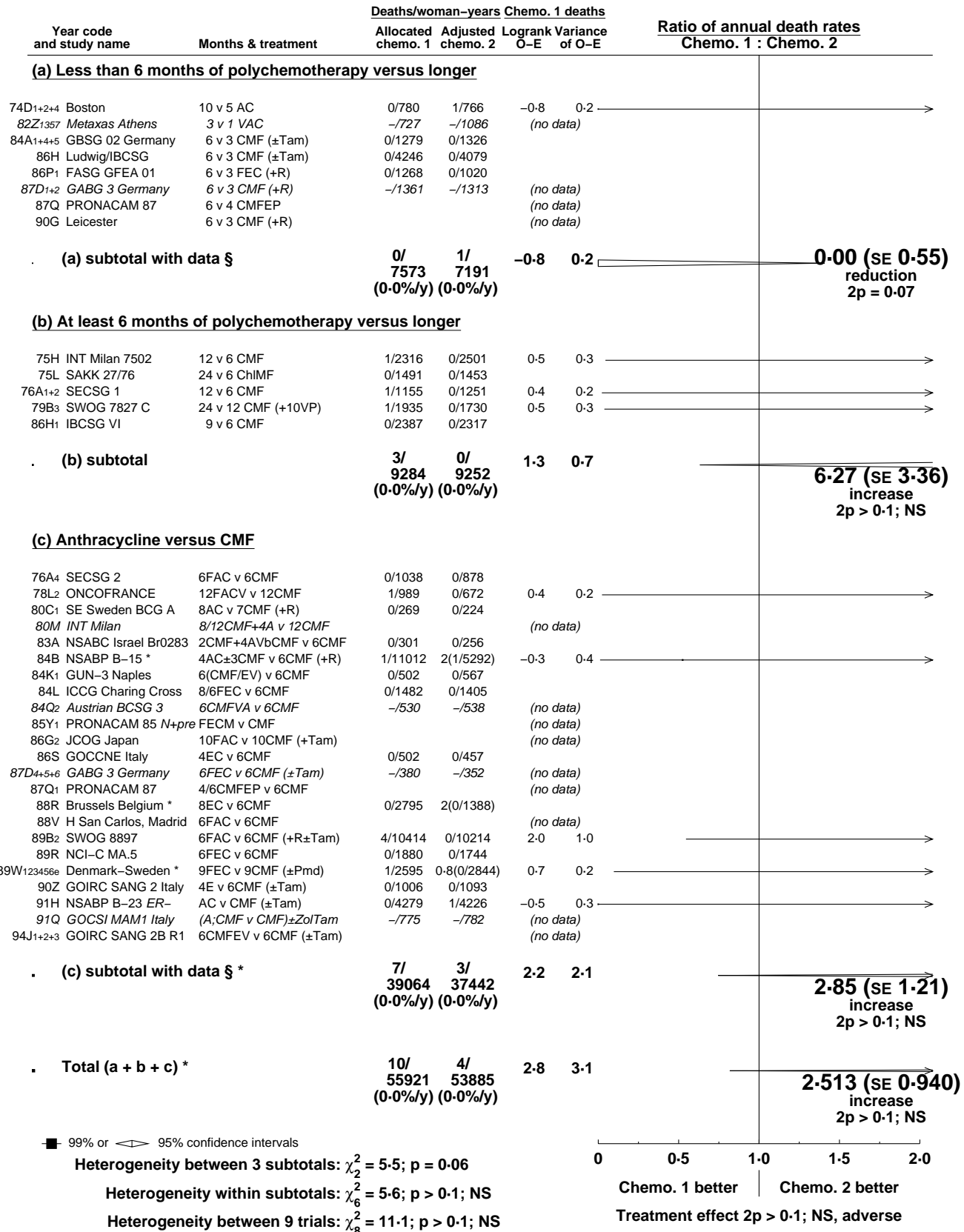
§ 1 trial with no data does not contribute to subtotals or to the overall total (allocated chemo. 1: 211; allocated chemo. 2: 212)

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s).



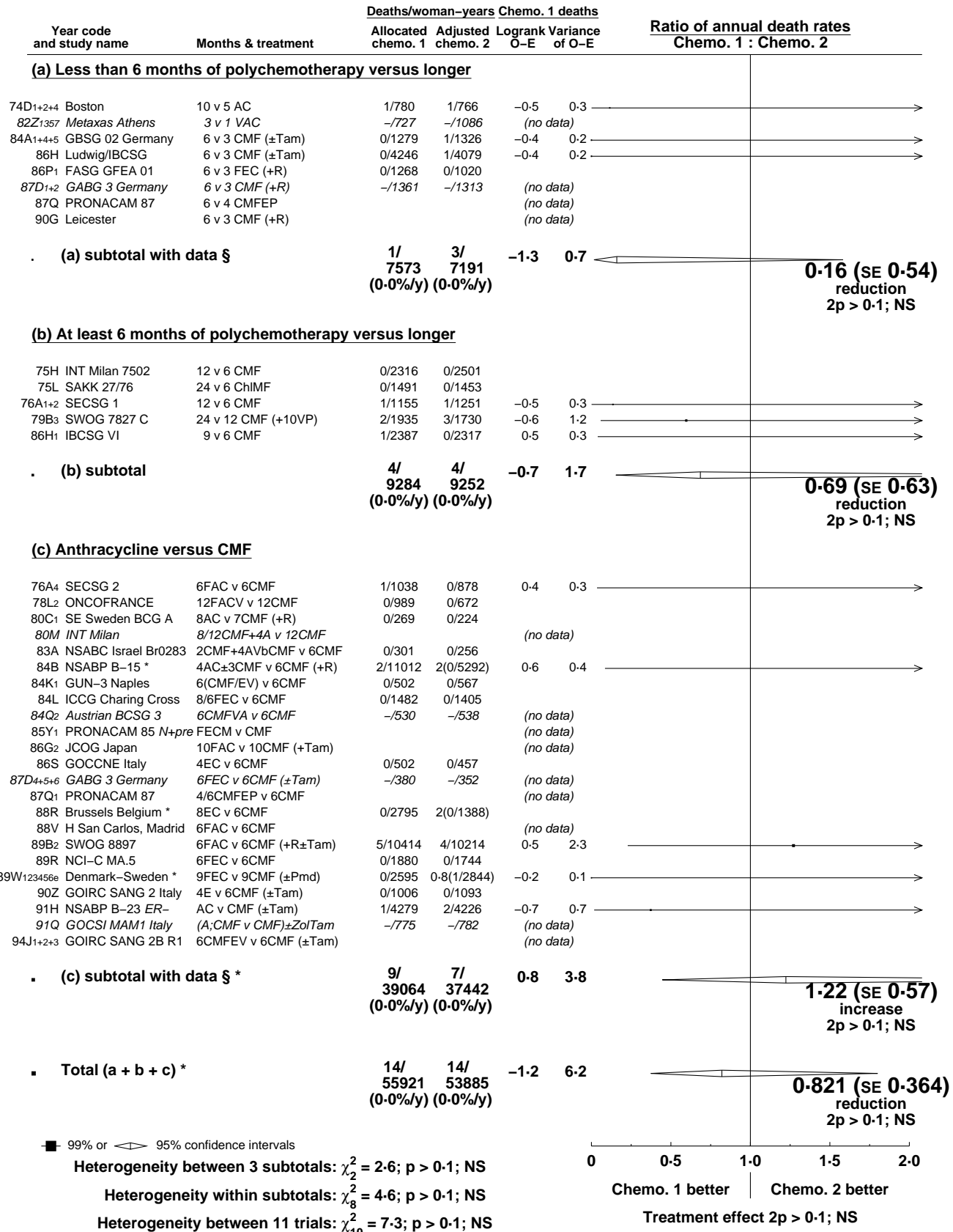
§ 1 trial with no data does not contribute to subtotals or to the overall total (allocated chemo. 1: 211; allocated chemo. 2: 212)

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s).



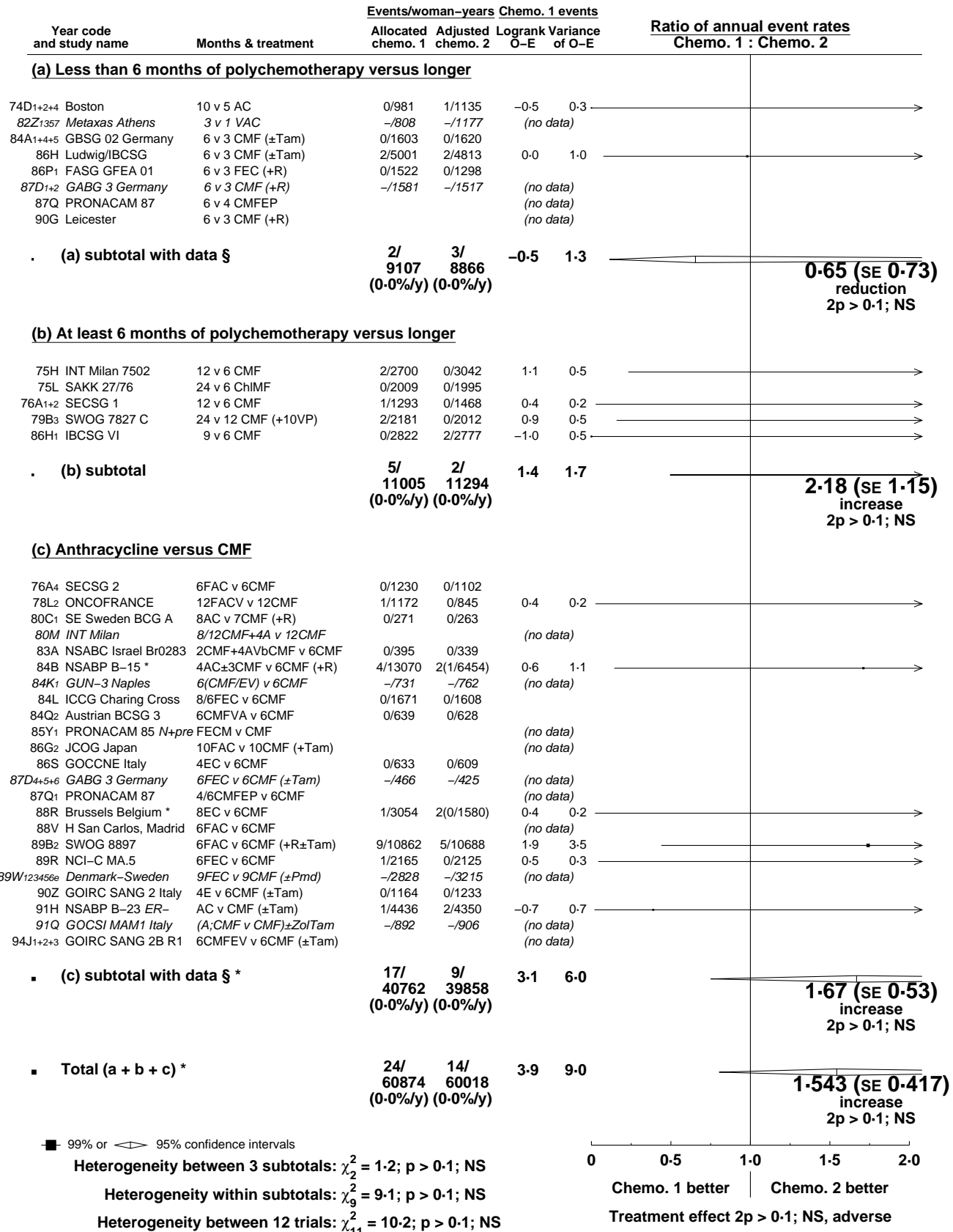
§ 6 trials with no data do not contribute to subtotals or to the overall total (allocated chemo. 1: 3773; allocated chemo. 2: 4071)

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.



§ 6 trials with no data do not contribute to subtotals or to the overall total (allocated chemo. 1: 3773; allocated chemo. 2: 4071)

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.



§ 7 trials with no data do not contribute to subtotals or to the overall total (allocated chemo. 1: 7306; allocated chemo. 2: 8002)

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.

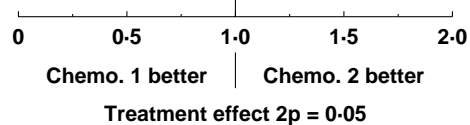
Year code and study name	Months & treatment	Events/woman-years Chemo. 1 events				Ratio of annual event rates Chemo. 1 : Chemo. 2	
		Allocated chemo. 1	Adjusted chemo. 2	Logrank O-E	Variance of O-E		
(a) Less than 6 months of polychemotherapy versus longer							
74D1+2+4 Boston	10 v 5 AC	13/83	18/147	0.6	5.8		
82Z1357 Metaxas Athens	3 v 1 VAC	6/85	6/116	1.6	2.5		
84A1+4+5 GBSG 02 Germany	6 v 3 CMF (±Tam)	17/112	21/168	1.0	7.3		
86H Ludwig/BCSG	6 v 3 CMF (±Tam)	51/582	58/530	-5.6	23.9		
86P1 FASG GFEA 01	6 v 3 FEC (+R)	26/272	25/221	-1.3	11.1		
87D1+2 GABG 3 Germany	6 v 3 CMF (+R)	54/394	35/298	3.5	19.2		
■ (a) subtotal		167/ 1528	163/ 1480	-0.1	69.8		1.00 (SE 0.12) reduction 2p > 0.1; NS
(b) At least 6 months of polychemotherapy versus longer							
75H INT Milan 7502	12 v 6 CMF	9/152	10/170	0.4	4.2		
76A1+2 SECSG 1	12 v 6 CMF	7/60	11/84	-1.1	4.0		
79B3 SWOG 7827 C	24 v 12 CMF (+10VP)	55/983	61/844	-6.1	25.7		
86H1 IBCSG VI	9 v 6 CMF	58/647	43/586	2.7	22.4		
■ (b) subtotal		129/ 1842	125/ 1684	-4.0	56.2		0.93 (SE 0.13) reduction 2p > 0.1; NS
(c) Anthracycline versus CMF							
76A4 SECSG 2	6FAC v 6CMF	19/156	27/129	-4.2	9.1		
80C1 SE Sweden BCG A	8AC v 7CMF (+R)	3/40	3/76	0.8	1.3		
83A NSABC Israel Br0283	2CMF+4AVbCMF v 6CMF	9/42	2/46	2.9	2.2		
84B NSABP B-15 *	4AC±3CMF v 6CMF (+R)	620/8035	2(333/4146)	-7.4	192.3		
84K1 GUN-3 Naples	6(CMF/EV) v 6CMF	7/58	13/53	-2.8	4.0		
84L ICCG Charing Cross	8/6FEC v 6CMF	29/267	34/248	-3.8	13.6		
84Q2 Austrian BCSG 3	6CMFVA v 6CMF	32/283	31/239	-1.5	13.1		
86S GOCCNE Italy	4EC v 6CMF	12/108	15/79	-2.5	5.4		
87D4+5+6 GABG 3 Germany	6FEC v 6CMF (±Tam)	13/74	13/25	-3.6	4.1		
88R Brussels Belgium *	8EC v 6CMF	36/444	2(18/137)	-4.7	8.8		
89B2 SWOG 8897	6FAC v 6CMF (+R±Tam)	73/3055	82/3070	-3.4	37.5		
89R NCI-C MA.5	6FEC v 6CMF	34/426	47/388	-7.1	16.8		
89W123456e Denmark-Sweden *	9FEC v 9CMF (±Pmd)	83/1047	0.9(116/1032)	-13.0	41.2		
90Z GOIRC SANG 2 Italy	4E v 6CMF (±Tam)	15/196	10/146	-1.1	4.7		
91H NSABP B-23 ER-	AC v CMF (±Tam)	87/2368	70/2356	8.7	37.9		
91Q GOCSI MAM1 Italy	(A;CMF v CMF)±ZolTam	19/105	22/160	2.4	8.2		
■ (c) subtotal *		1091/ 16704	1182/ 16559	-40.3	400.2		0.90 (SE 0.05) reduction 2p = 0.04
■ Total (a + b + c) *		1387/ 20074	1470/ 19723	-44.5	526.3		0.919 (SE 0.042) reduction 2p = 0.05

■ 99% or ◊ 95% confidence intervals

Heterogeneity between 3 subtotals: $\chi^2_2 = 0.6$; $p > 0.1$; NS

Heterogeneity within subtotals: $\chi^2_{23} = 27.9$; $p > 0.1$; NS

Heterogeneity between 26 trials: $\chi^2_{25} = 28.5$; $p > 0.1$; NS



* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.

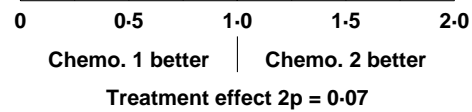
Year code and study name	Months & treatment	Deaths/Women		Chemo. 1 deaths		Logrank O-E	Variance of O-E	Ratio of annual death rates Chemo. 1 : Chemo. 2
		Allocated chemo. 1	Adjusted chemo. 2	O-E	Variance of O-E			
(a) Less than 6 months of polychemotherapy versus longer								
74D1+2+4 Boston	10 v 5 AC	17/20	10/17	3.7	5.3			
82Z1357 Metaxas Athens	3 v 1 VAC	0/6	2/21	-0.3	0.2			
84A1+4+5 GBSG 02 Germany	6 v 3 CMF (±Tam)	24/61	23/56	0.3	10.7			
86H Ludwig/BCSG	6 v 3 CMF (±Tam)	66/217	84/225	-8.4	35.5			
86P1 FASG GFEA 01	6 v 3 FEC (+R)	29/108	38/105	-6.5	15.8			
87D1+2 GABG 3 Germany	6 v 3 CMF (+R)	24/164	29/145	-2.7	12.4			
■ (a) subtotal		160/ 576 (27.8%)	186/ 569 (32.7%)	-13.8	80.0			0.84 (SE 0.10) reduction 2p > 0.1; NS
(b) At least 6 months of polychemotherapy versus longer								
75H INT Milan 7502	12 v 6 CMF	43/64	40/73	6.9	19.0			
76A1+2 SECSG 1	12 v 6 CMF	8/27	9/31	0.5	3.9			
79B3 SWOG 7827 C	24 v 12 CMF (+10VP)	2/4	0/2	0.7	0.5			
86H1 IBCSG VI	9 v 6 CMF	69/208	73/213	-1.6	33.7			
■ (b) subtotal		122/ 303 (40.3%)	122/ 319 (38.2%)	6.6	57.1			1.12 (SE 0.14) increase 2p > 0.1; NS
(c) Anthracycline versus CMF								
76A4 SECSG 2	6FAC v 6CMF	29/89	26/83	-1.0	12.5			
80C1 SE Sweden BCG A	8AC v 7CMF (+R)	2/6	4/7	-0.6	1.4			
83A NSABC Israel Br0283	2CMF+4AVbCMF v 6CMF	3/9	4/9	-1.1	1.7			
84B NSABP B-15 *	4AC±3CMF v 6CMF (+R)	34/87	2(16/33)	-2.4	9.3			
84K1 GUN-3 Naples	6(CMF/EV) v 6CMF	1/3	2/5	-0.5	0.7			
84L ICCG Charing Cross	8/FEC v 6CMF	27/133	24/139	2.5	12.1			
84Q2 Austrian BCSG 3	6CMFVA v 6CMF	0/0	1/1					
86S GOCCNE Italy	4EC v 6CMF	13/40	17/46	-1.9	7.0			
87D4+5+6 GABG 3 Germany	6FEC v 6CMF (±Tam)	12/34	11/30	0.3	5.3			
88R Brussels Belgium *	8EC v 6CMF	36/143	2(16/80)	3.5	11.6			
89B2 SWOG 8897	6FAC v 6CMF (+R±Tam)	26/364	47/393	-9.6	18.0			
89R NCI-C MA.5	6FEC v 6CMF	53/174	59/168	-5.7	26.4			
89W123456e Denmark-Sweden *	9FEC v 9CMF (±Pmd)	14/112	0.9(19/102)	-4.5	7.2			
90Z GOIRC SANG 2 Italy	4E v 6CMF (±Tam)	4/37	6/46	-0.5	2.4			
91H NSABP B-23 ER-	AC v CMF (±Tam)	1/1	0/2	0.7	0.2			
91Q GOCSI MAM1 Italy	(A;CMF v CMF)±ZolTam	10/64	14/73	-1.2	5.6			
■ (c) subtotal *		265/ 1296 (20.4%)	296/ 1319 (22.4%)	-22.2	121.4			0.83 (SE 0.08) reduction 2p = 0.04
■ Total (a + b + c) *		547/ 2175 (25.1%)	604/ 2207 (27.4%)	-29.4	258.5			0.893 (SE 0.059) reduction 2p = 0.07

■ 99% or ◊ 95% confidence intervals

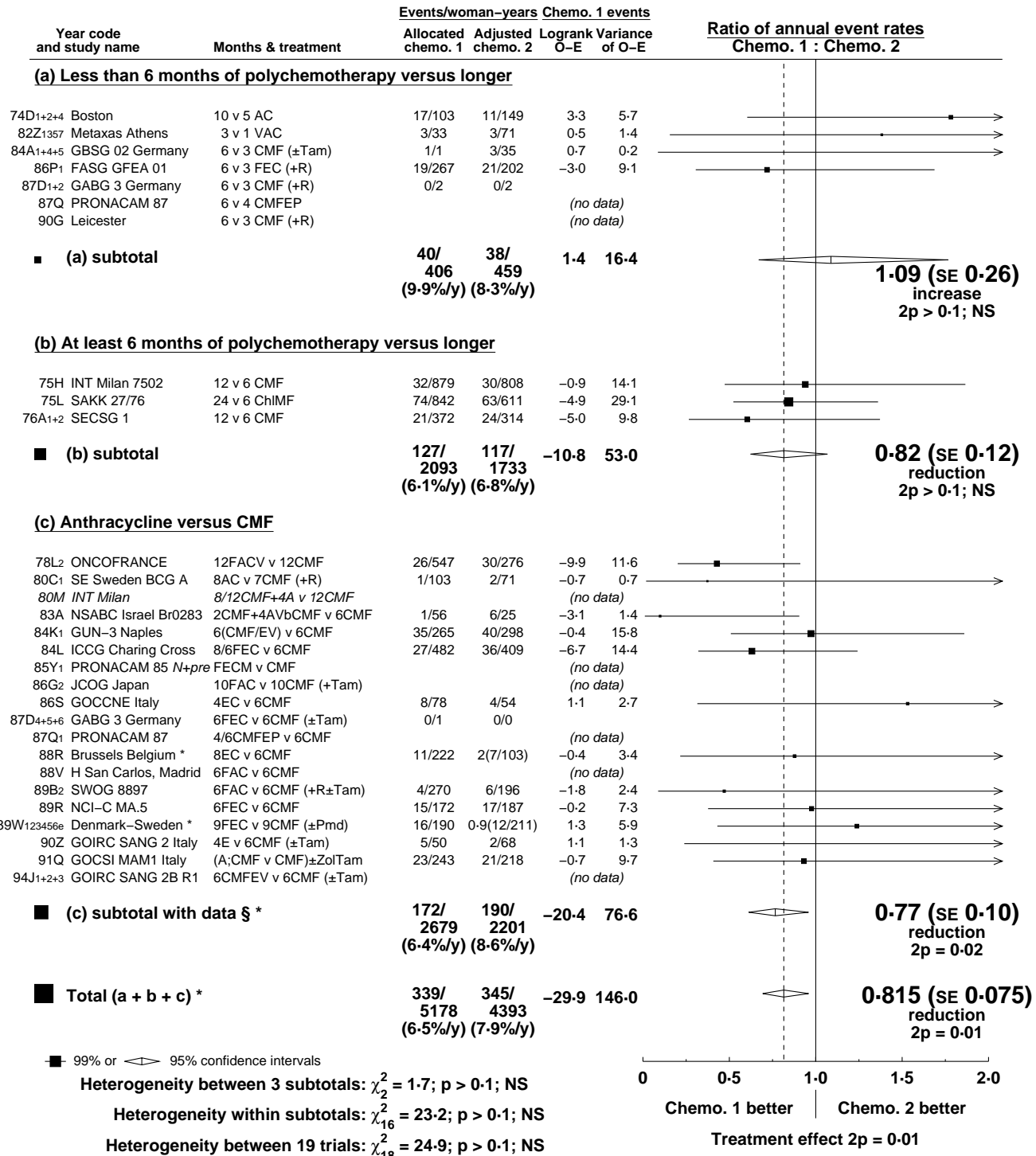
Heterogeneity between 3 subtotals: $\chi^2_2 = 3.9$; $p > 0.1$; NS

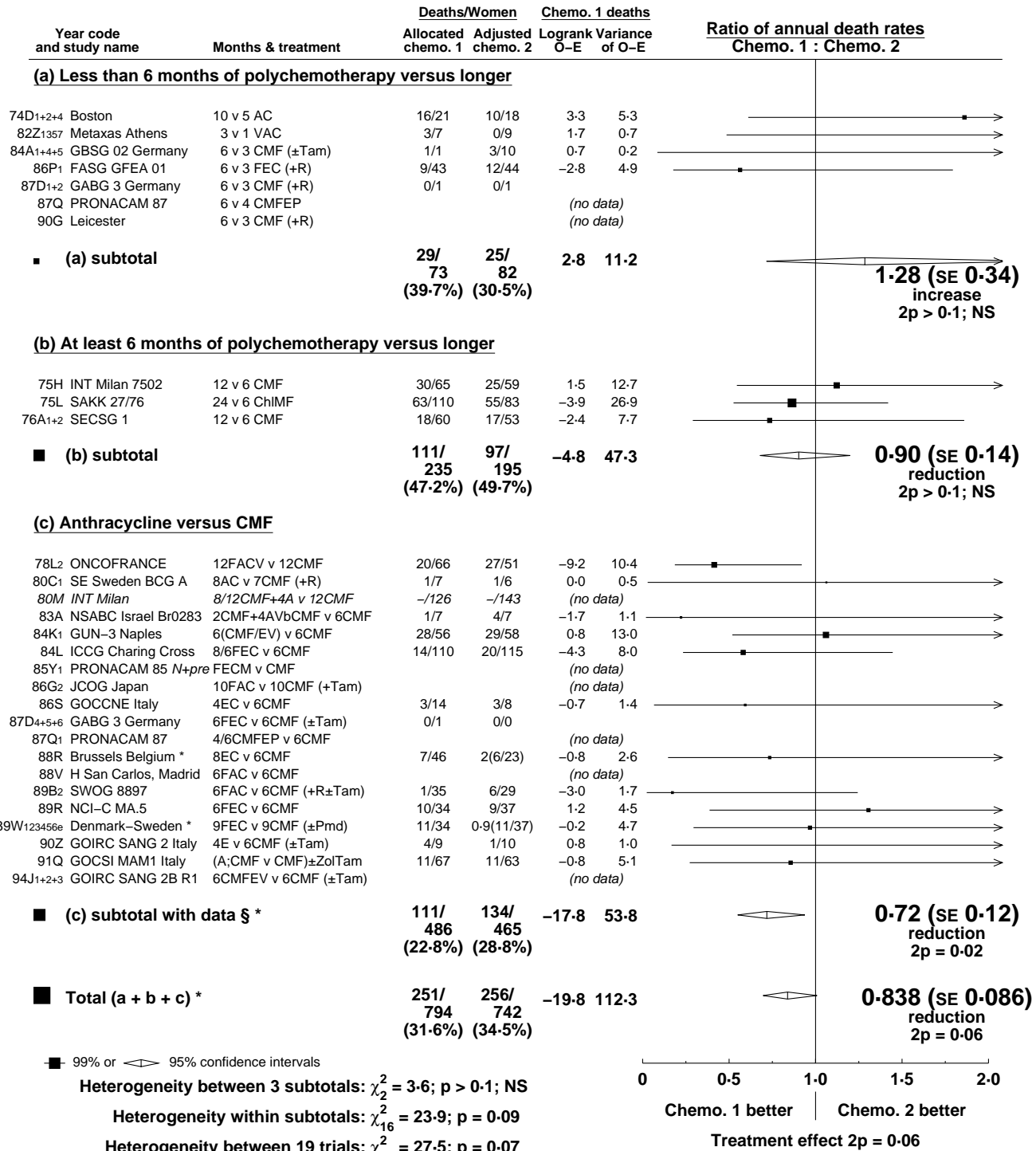
Heterogeneity within subtotals: $\chi^2_{22} = 20.5$; $p > 0.1$; NS

Heterogeneity between 25 trials: $\chi^2_{24} = 24.4$; $p > 0.1$; NS



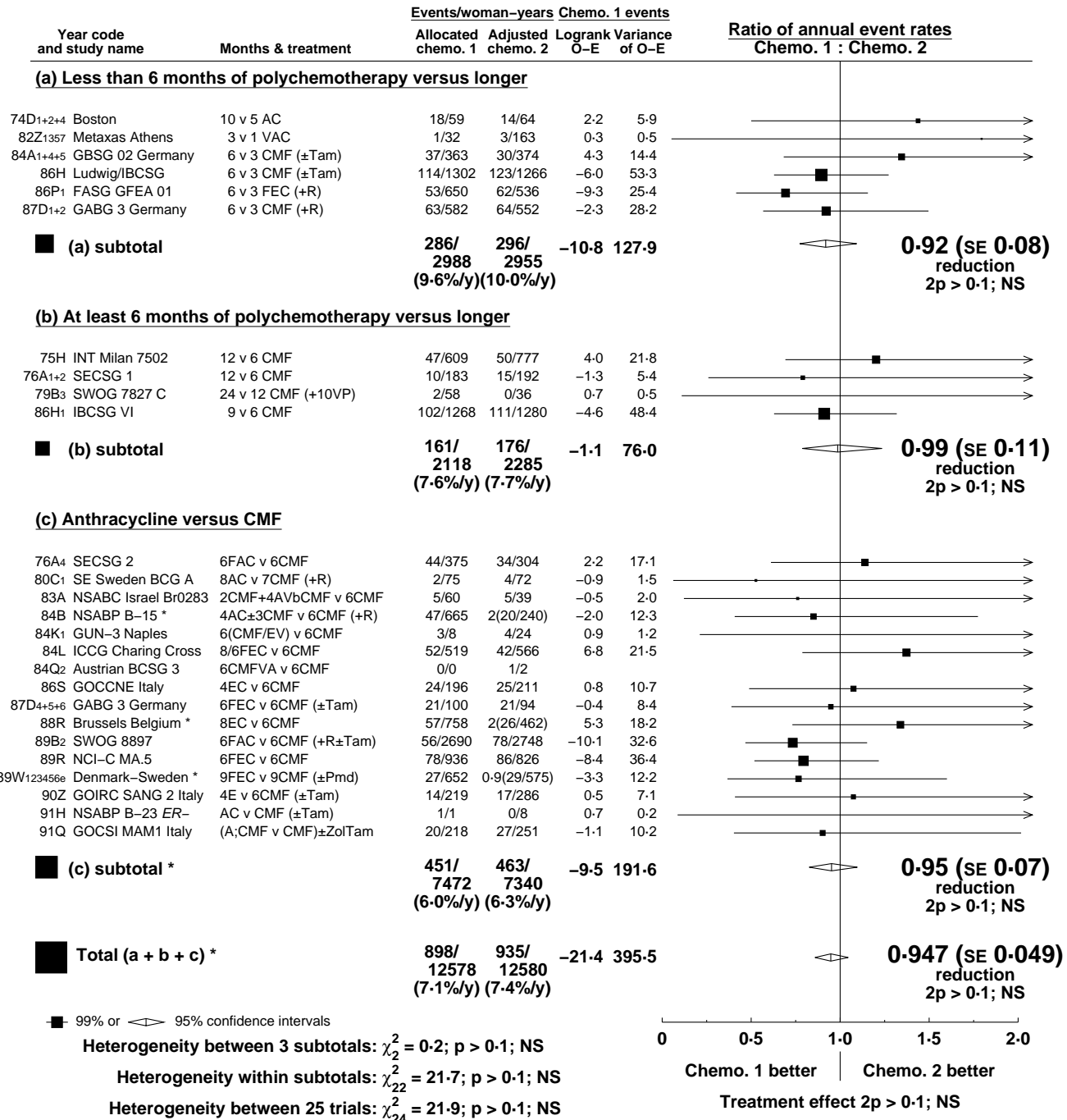
* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.



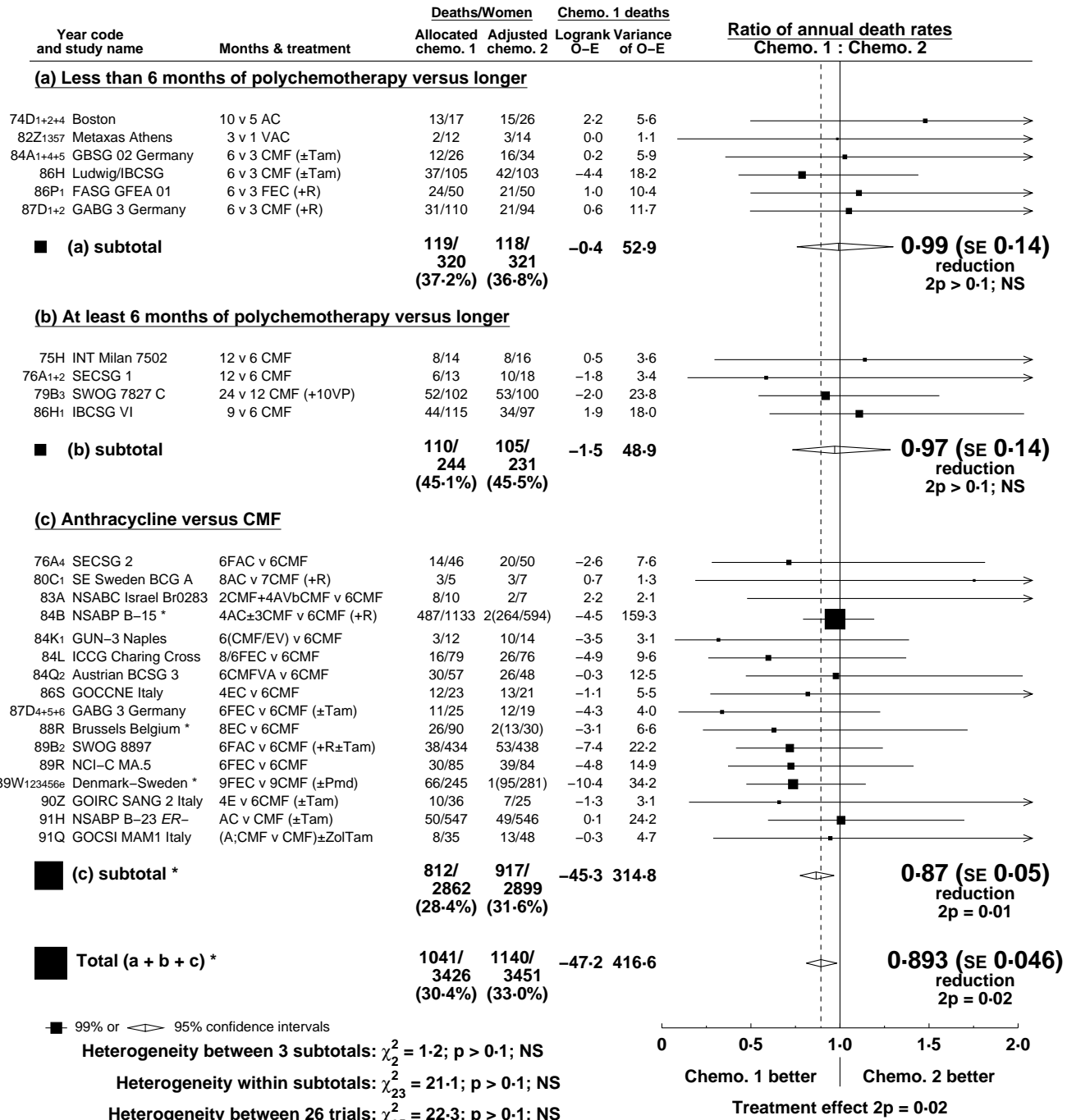


§ 1 trial with no data does not contribute to subtotals or to the overall total (allocated chemo. 1: 126; allocated chemo. 2: 143)

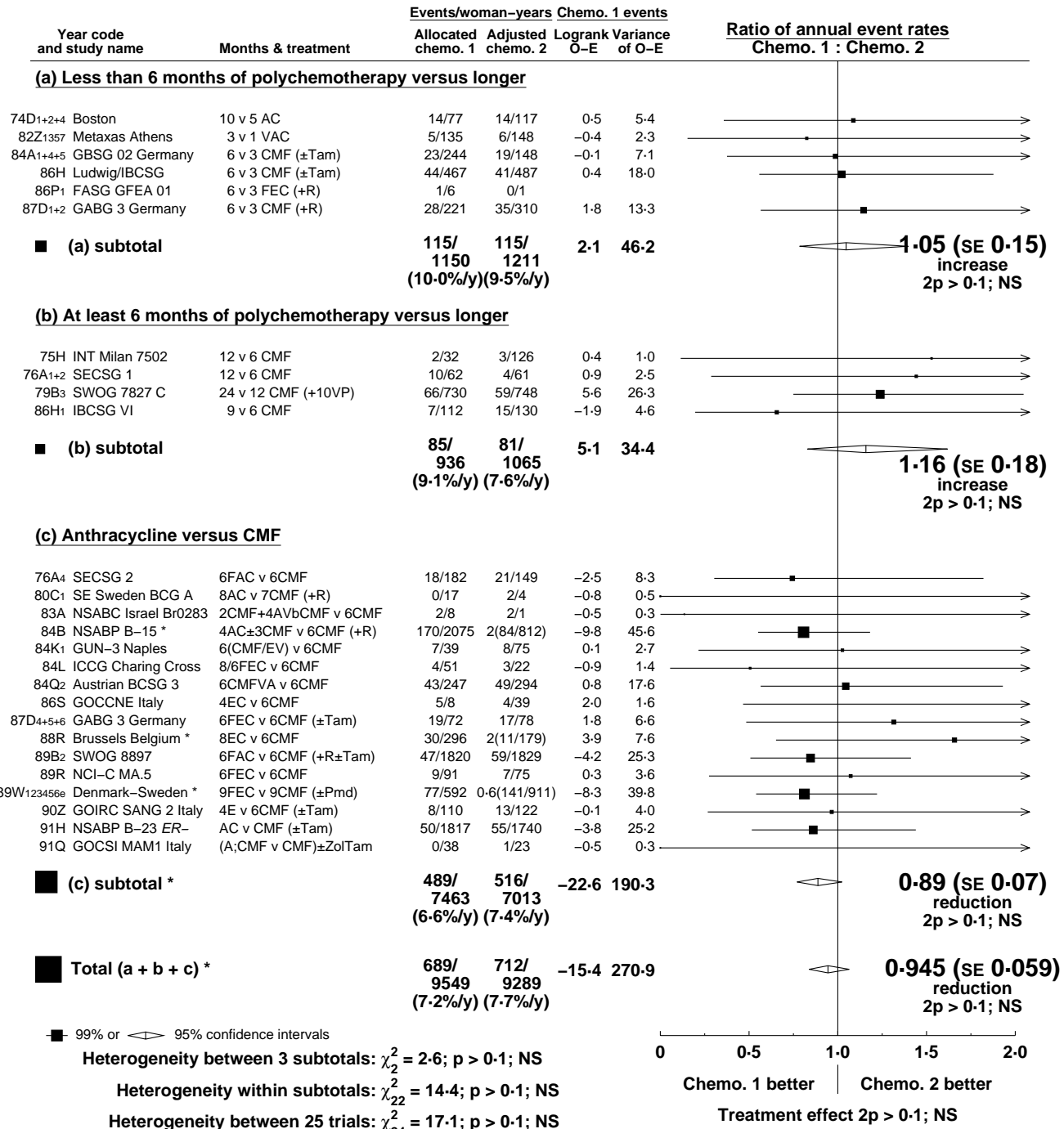
* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.



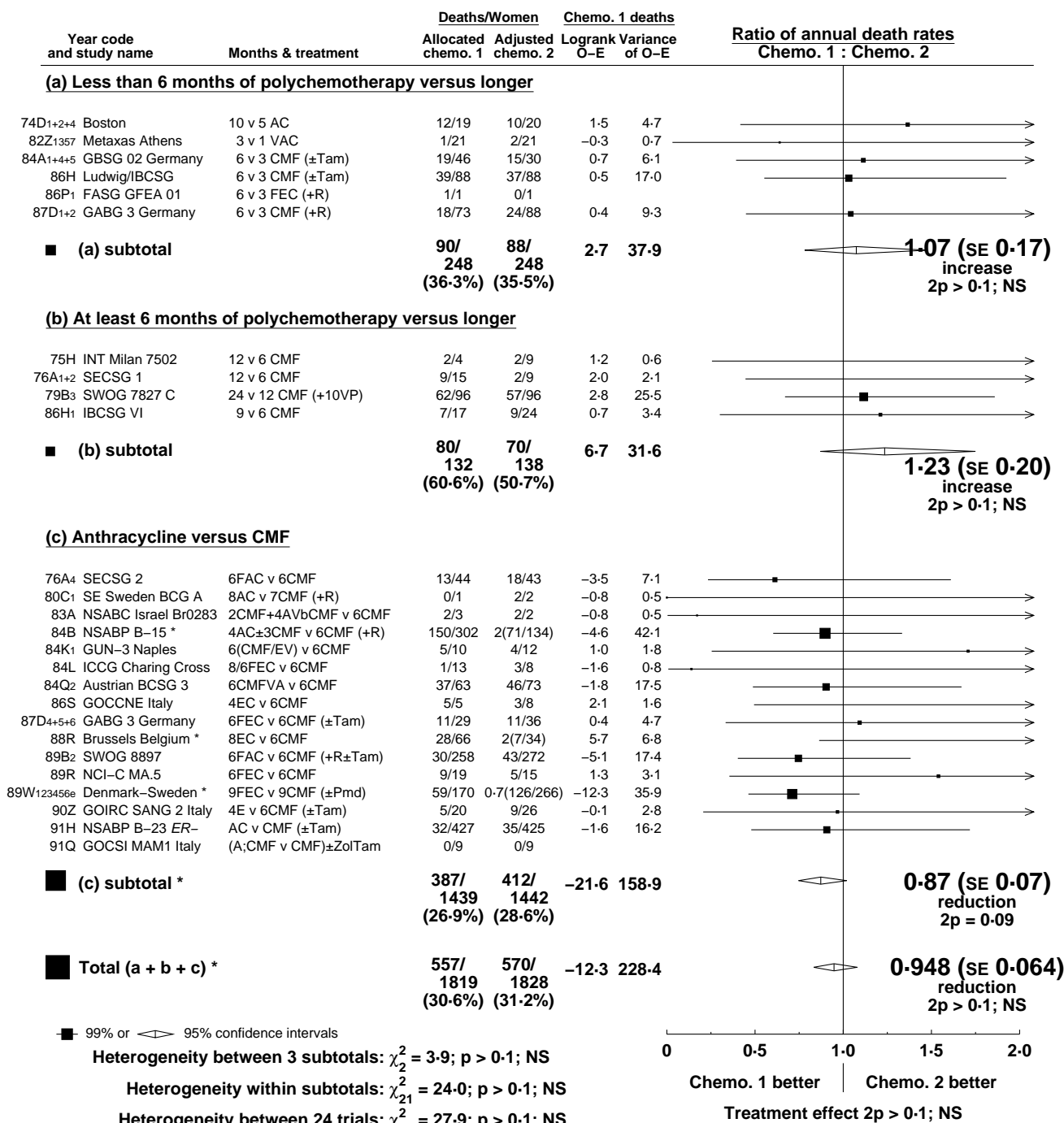
* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.



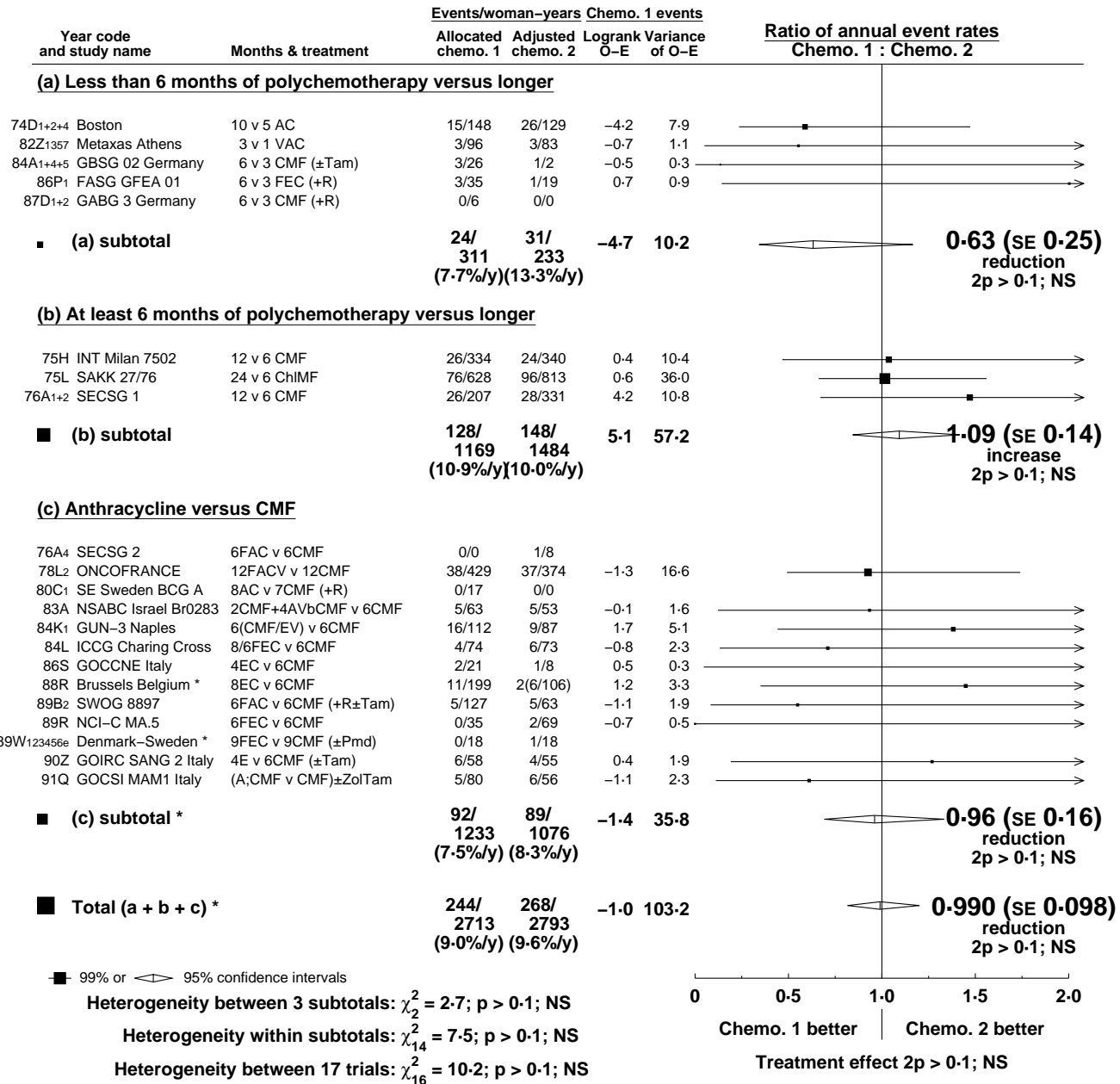
* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.



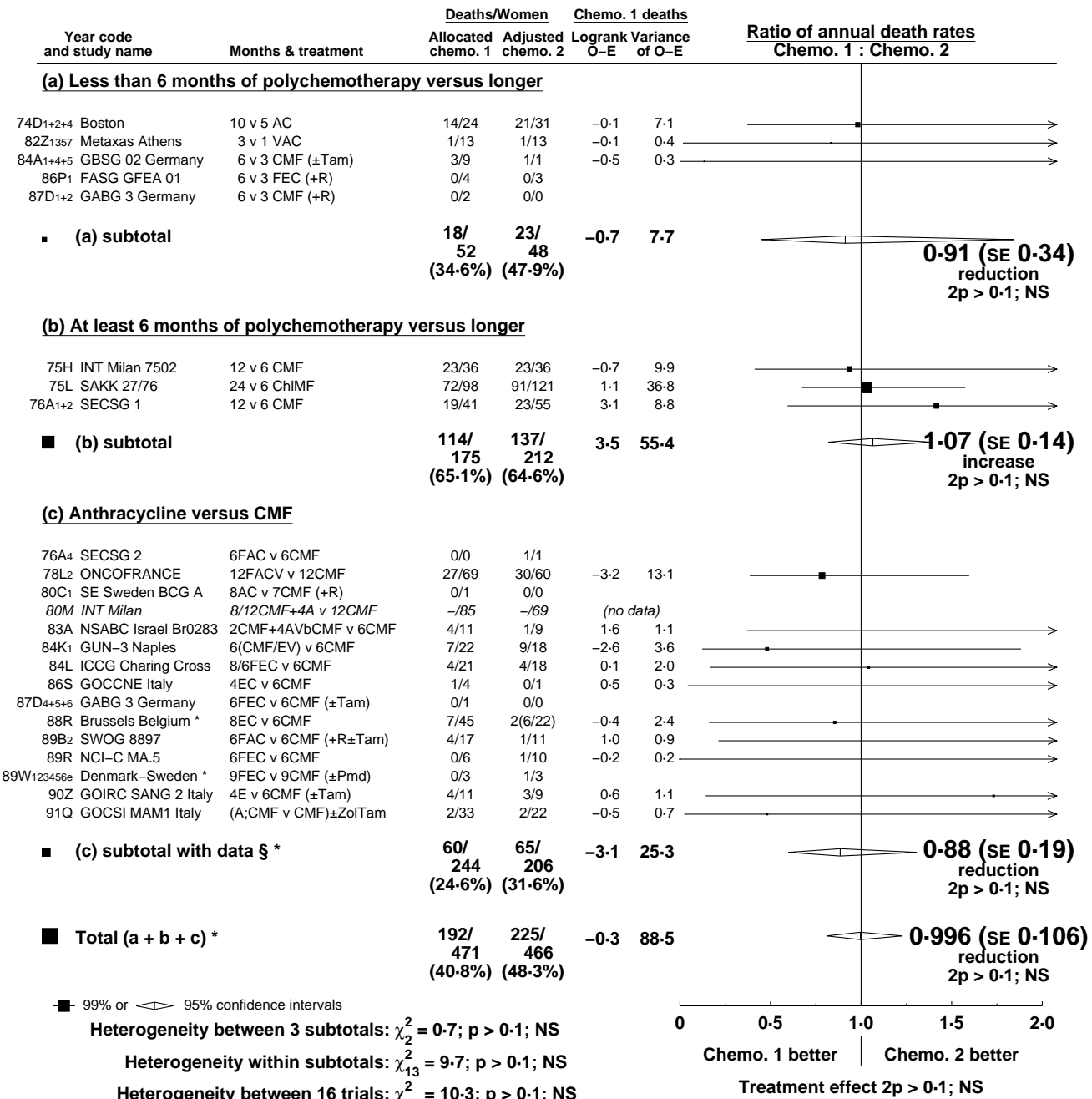
* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.



* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.



* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.



§ 1 trial with no data does not contribute to subtotals or to the overall total (allocated chemo. 1: 85; allocated chemo. 2: 69)

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

Year code and study name	Months & treatment	Events/woman-years Chemo. 1 events				Ratio of annual event rates Chemo. 1 : Chemo. 2	
		Allocated chemo. 1	Adjusted chemo. 2	Logrank O-E	Variance of O-E		
(a) Less than 6 months of polychemotherapy versus longer							
74D1+2+4 Boston	10 v 5 AC	20/306	28/134	-9.8	9.5		
82Z1357 Metaxas Athens	3 v 1 VAC	9/241	10/411	-2.0	3.4		
84A1+4+5 GBSG 02 Germany	6 v 3 CMF (±Tam)	54/481	63/552	-0.7	24.0		
86H Ludwig/BCSG	6 v 3 CMF (±Tam)	109/1732	107/1642	-2.4	50.2		
86P1 FASG GFEA 01	6 v 3 FEC (+R)	1/36	2/39	-0.6	0.7		
87D1+2 GABG 3 Germany	6 v 3 CMF (+R)	12/154	11/148	0.2	5.3		
■ (a) subtotal		205/2950 (6.9%/y)	221/2926 (7.6%/y)	-11.2	93.0		0.89 (SE 0.10) reduction 2p > 0.1; NS
(b) At least 6 months of polychemotherapy versus longer							
75H INT Milan 7502	12 v 6 CMF	18/267	17/277	1.0	7.6		
76A1+2 SECSG 1	12 v 6 CMF	21/201	16/172	0.7	7.4		
79B3 SWOG 7827 C	24 v 12 CMF (+10VP)	5/45	4/26	0.2	2.0		
86H1 IBCSG VI	9 v 6 CMF	25/358	32/321	-4.4	12.9		
■ (b) subtotal		69/871 (7.9%/y)	69/796 (8.7%/y)	-2.6	30.0		0.92 (SE 0.17) reduction 2p > 0.1; NS
(c) Anthracycline versus CMF							
76A4 SECSG 2	6FAC v 6CMF	31/260	35/256	-1.3	14.2		
80C1 SE Sweden BCG A	8AC v 7CMF (+R)	0/16	0/0				
83A NSABC Israel Br0283	2CMF+4AVbCMF v 6CMF	9/70	10/90	-0.3	4.1		
84B NSABP B-15 *	4AC±3CMF v 6CMF (+R)	26/237	2(9/94)	0.6	6.0		
84K1 GUN-3 Naples	6(CMF/EV) v 6CMF	1/14	3/16	-1.1	0.7		
84L ICGG Charing Cross	8/FEC v 6CMF	6/85	8/84	-1.1	3.2		
84Q2 Austrian BCSG 3	6CMFVA v 6CMF	0/0	1/1				
86S GOCCNE Italy	4EC v 6CMF	10/88	17/66	-4.6	5.5		
87D4+5+6 GABG 3 Germany	6FEC v 6CMF (±Tam)	31/123	33/148	1.0	12.2		
88R Brussels Belgium *	8EC v 6CMF	40/859	2(24/393)	-2.9	13.1		
89B2 SWOG 8897	6FAC v 6CMF (+R±Tam)	60/2102	59/1986	-1.3	28.5		
89R NCI-C MA.5	6FEC v 6CMF	16/219	30/198	-7.6	10.1		
89W123456e Denmark-Sweden *	9FEC v 9CMF (±Pmd)	4/92	0.8(10/96)	-1.1	1.5		
90Z GOIRC SANG 2 Italy	4E v 6CMF (±Tam)	18/362	17/411	0.3	7.3		
91H NSABP B-23 ER-	AC v CMF (±Tam)	0/7	0/16				
91Q GOCSI MAM1 Italy	(A;CMF v CMF)±ZolTam	5/90	6/71	-0.5	2.4		
■ (c) subtotal *		257/4624 (5.6%/y)	291/4391 (6.6%/y)	-19.8	108.7		0.83 (SE 0.09) reduction 2p = 0.06
■ Total (a + b + c) *		531/8445 (6.3%/y)	581/8113 (7.2%/y)	-33.6	231.7		0.865 (SE 0.061) reduction 2p = 0.03

■ 99% or ◊ 95% confidence intervals

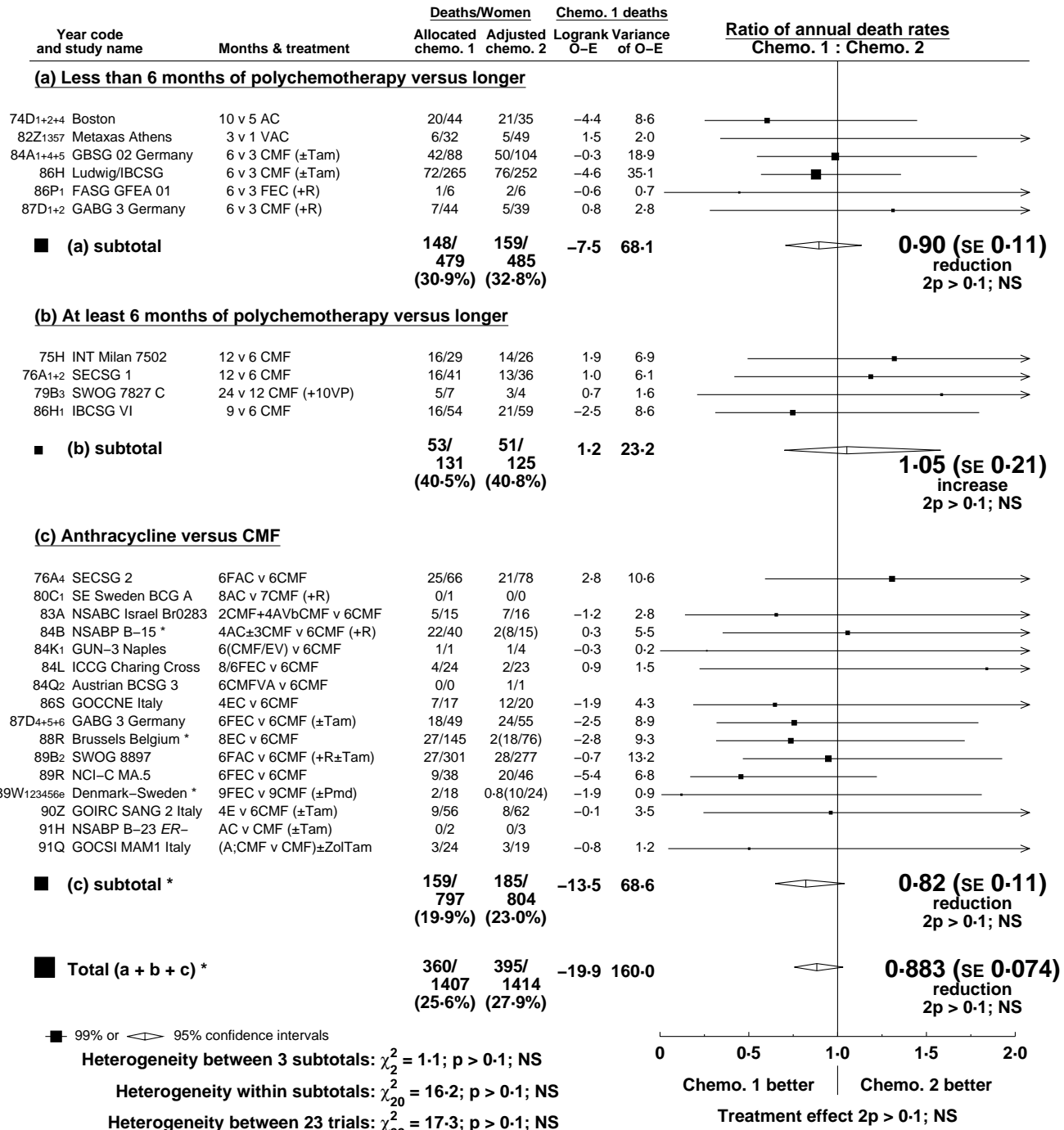
Heterogeneity between 3 subtotals: $\chi^2_2 = 0.3$; $p > 0.1$; NS

Heterogeneity within subtotals: $\chi^2_{20} = 22.1$; $p > 0.1$; NS

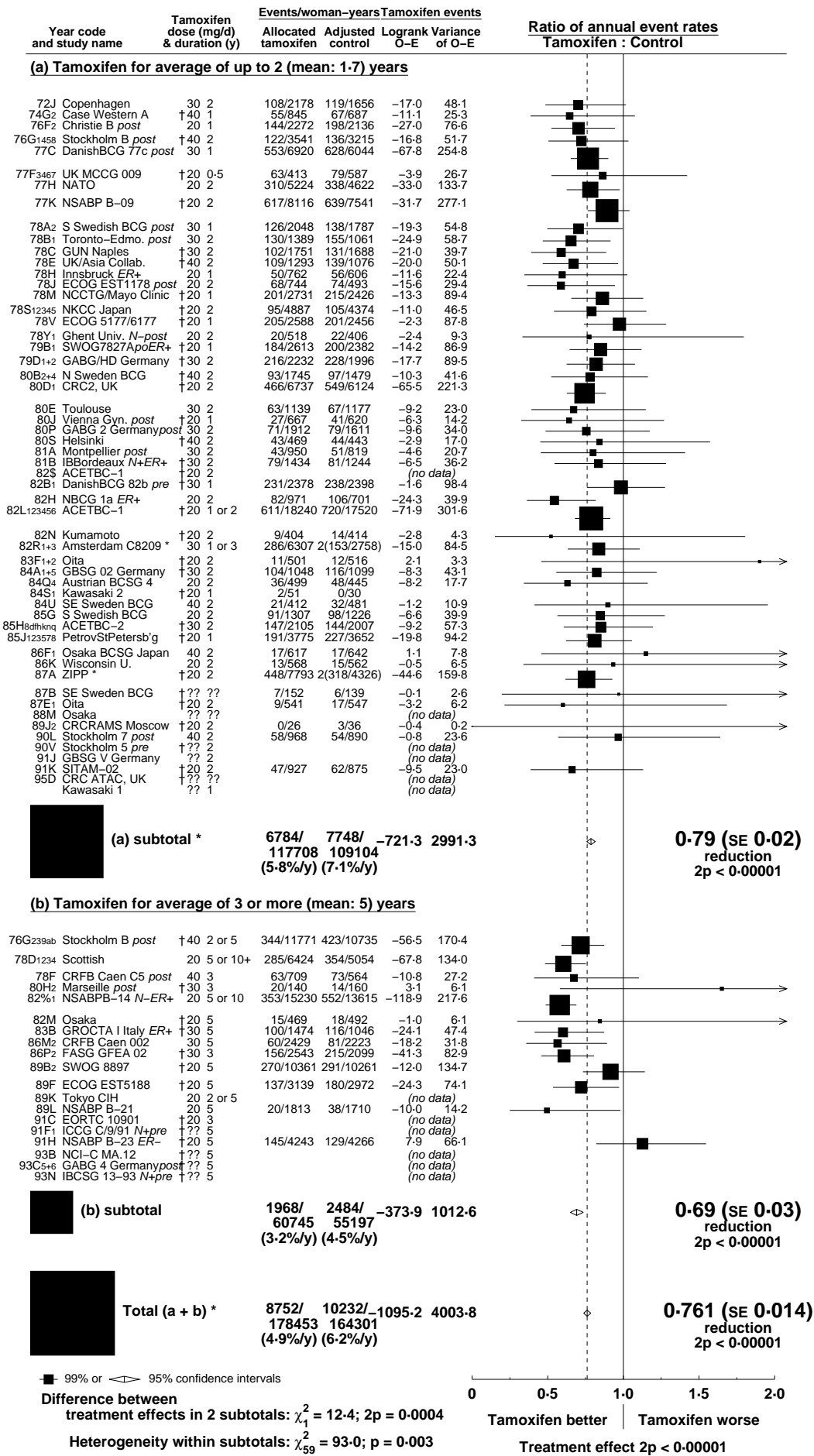
Heterogeneity between 23 trials: $\chi^2_{22} = 22.4$; $p > 0.1$; NS

0 0.5 1.0 1.5 2.0
Chemo. 1 better | Chemo. 2 better
Treatment effect 2p = 0.03

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.



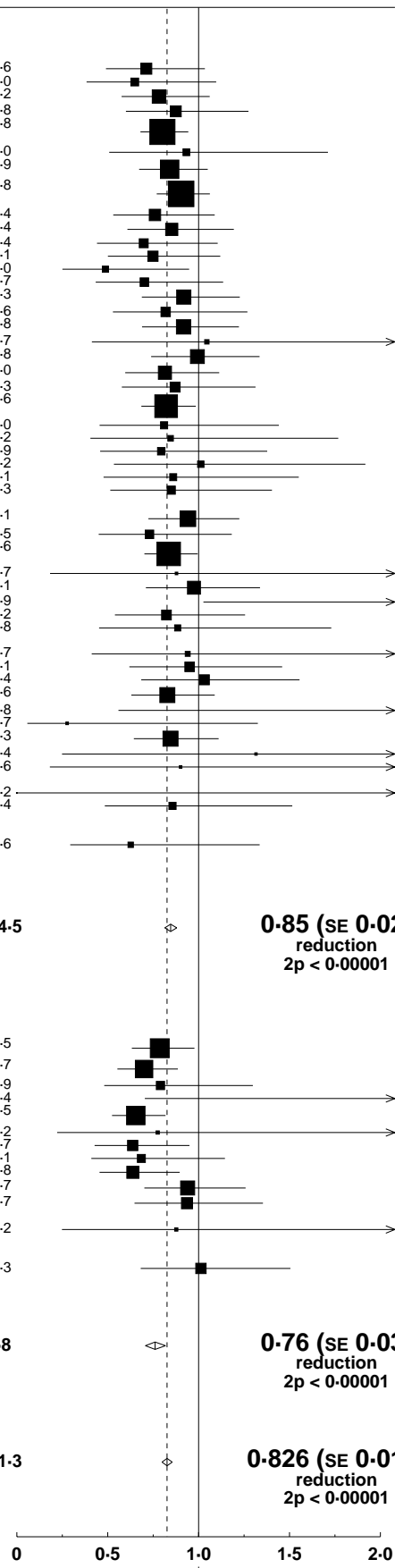
* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.



* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.
† Tamoxifen plus chemotherapy versus same chemotherapy alone

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Not for publication or citation

Year code and study name	Tamoxifen dose (mg/d) & duration (y)	Deaths/Women		Tamoxifen deaths		Ratio of annual death rates Tamoxifen : Control
		Allocated tamoxifen	Adjusted control	Logrank O-E	Variance of O-E	
(a) Tamoxifen for average of up to 2 (mean: 1.7) years						
72J Copenhagen	30 2	102/168	113/154	-16.2	47.6	
74G2 Case Western A	†40 1	45/97	62/101	-10.4	24.0	
76F2 Christie B post	20 1	131/282	179/306	-17.5	71.2	
76G1458 Stockholm B post	†40 2	112/273	122/269	-6.3	46.8	
77C DanishBCG 77c post	30 1	541/927	620/915	-55.1	247.8	
77F3467 UK MCCG 009	†20 0.5	39/123	56/140	-1.3	18.0	
77H NATO	20 2	291/563	318/568	-23.3	133.9	
77K NSABP B-09	†20 2	541/950	580/941	-25.8	255.8	
78A2 S Swedish BCG post	30 1	116/239	126/236	-14.1	51.4	
78B1 Toronto-Edmo. post	30 2	119/199	139/201	-9.3	58.4	
78C GUN Naples	†30 2	79/206	95/227	-11.3	31.4	
78E UK/Asia Collab.	†40 2	82/240	107/248	-11.9	41.1	
78H Innsbruck ER+	20 1	29/130	43/107	-10.8	15.0	
78J ECOG EST1178 post	20 2	66/91	71/90	-10.2	28.7	
78M NCCTG/Mayo Clinic	†20 1	174/311	185/319	-6.8	79.3	
78S12345 NKCC Japan	†20 2	71/648	79/587	-6.9	34.6	
78V ECOG 5177/6177	†20 1	175/303	184/307	-7.0	80.8	
78Y1 Ghent Univ. N-post	20 2	18/73	15/65	0.3	7.7	
79B1 SWOG7827ApoER+	†20 1	164/325	167/325	-0.5	75.8	
79D1+2 GABG/HD Germany	†30 2	150/308	170/306	-14.0	68.0	
80B2+4 N Sweden BCG	†40 2	87/183	91/185	-5.4	39.3	
80D1 CRC2, UK	†20 2	404/947	472/965	-39.7	201.6	
80E Toulouse	30 2	59/125	52/126	-4.2	20.0	
80J Vienna Gyn. post	†20 1	24/79	33/86	-2.0	12.2	
80P GABG 2 Germany post	30 2	46/285	49/293	-5.0	21.9	
80S Helsinki	†40 2	39/81	41/78	0.2	16.2	
81A Montpellier post	30 2	41/101	46/102	-2.9	19.1	
81B IBBordeaux N+ER+	†30 2	55/166	58/160	-4.3	26.3	
82S ACETBC-1	†20 2	(228 patients)	(no data)	(no data)	(no data)	
82B1 DanishBCG 82b pre	†30 1	207/344	225/350	-5.8	96.1	
82H NBCG 1a ER+	20 2	60/190	68/179	-9.0	28.5	
82L123456 ACETBC-1	†20 1 or 2	437/2654	507/2655	-39.1	217.6	
82N Kumamoto	†20 2	7/89	6/95	-0.3	2.7	
82R+3 Amsterdam C8209 *	30 1 or 3	220/850	2(11/411)	-1.7	66.1	
83F+2 Oita	†20 2	10/62	5/63	3.6	1.9	
84A+5 GBSG 02 Germany	†30 2	78/187	96/194	-7.2	37.2	
84Q4 Austrian BCSG 4	20 2	31/73	36/78	-1.8	14.8	
84S1 Kawasaki 2	†20 1	1/12	0/8	(no data)	(no data)	
84U SE Sweden BCG	40 2	18/51	26/63	-0.6	9.7	
85G S Swedish BCG	20 2	79/213	82/215	-1.8	36.1	
85H8athkinq ACETBC-2	†30 2	106/461	87/444	1.2	39.4	
85J123578 PetrovStPetersb'g	†20 1	180/434	213/449	-16.7	88.6	
86F1 Osaka BCSG Japan	40 2	8/122	4/129	2.7	2.8	
86K Wisconsin U.	20 2	2/70	10/70	-3.5	2.7	
87A ZIPP *	†20 2	239/1765	2(167/945)	-15.0	89.3	
87B SE Sweden BCG	?? ??	6/21	5/19	0.7	2.4	
87E1 Oita	†20 2	5/136	6/138	-0.3	2.6	
88M Osaka	?? ??	(no data)	(no data)	(no data)	(no data)	
89J2 CRCRAMS Moscow	†20 2	0/10	2/11	-0.4	0.2	
90L Stockholm 7 post	40 2	47/186	49/180	-3.2	20.4	
90V Stockholm 5 pre	†?? 2	(≥700 patients)	(no data)	(no data)	(no data)	
91V GBSG V Germany	†?? 2	(361 patients)	(no data)	(no data)	(no data)	
91K SITAM-02	†20 2	23/202	30/195	-5.4	11.6	
95D CRC ATAC, UK	†?? ??	(no data)	(no data)	(no data)	(no data)	
Kawasaki 1	?? 1	(100 patients)	(no data)	(no data)	(no data)	



(a) subtotal * 5564/ 6286/ -425.4 2544.5
16555 16654
(33.6%) (37.7%)

0.85 (SE 0.02)
reduction
2p < 0.00001

(b) Tamoxifen for average of 3 or more (mean: 5) years

76G239ab Stockholm B post	†40 2 or 5	291/1101	346/1095	-33.8	140.5	
78D1234 Scottish	20 5 or 10+	252/667	307/656	-42.7	119.7	
78F CRFB Caen C5 post	40 3	58/89	67/90	-6.3	26.9	
80Hz Marseille post	†30 3	15/37	8/34	3.9	4.4	
82%1 NSABPB-14 N-ER+	20 5 or 10	214/1439	338/1453	-56.6	133.5	
82M Osaka	†20 5	11/53	12/55	-1.1	4.2	
83B GROCTA I Italy ER+	†30 5	83/171	99/168	-18.8	41.7	
86M2 CRFB Caen 002	30 5	50/250	60/244	-9.5	25.1	
86P2 FASG GFEA 02	†30 3	103/390	145/386	-25.9	57.8	
89B2 SWOG 8897	†20 5	154/1458	167/1473	-4.8	77.7	
89F ECOG EST5188	†20 5	98/516	106/511	-3.2	48.7	
89K Tokyo CIH	20 2 or 5	(220 patients)	(no data)	(no data)	(no data)	
89L NSABP B-21	20 5	8/337	9/336	-0.5	4.2	
91C EORTC 10901	†20 3	(1845 patients)	(no data)	(no data)	(no data)	
91F1 ICCG C/9/91 N+pre	?? 5	(no data)	(no data)	(no data)	(no data)	
91H NSABP B-23 ER-	†20 5	88/1004	86/1004	0.5	42.3	
93B NCI-C MA.12	?? 5	(672 patients)	(no data)	(no data)	(no data)	
93C+6 GABG 4 Germany post	?? 5	(≥764 patients)	(no data)	(no data)	(no data)	
93N IBCSG 13-93 N+pre	?? 5	(1294 patients)	(no data)	(no data)	(no data)	

(b) subtotal 1425/ 1750/ -199.1 726.8
7512 7505
(19.0%) (23.3%)

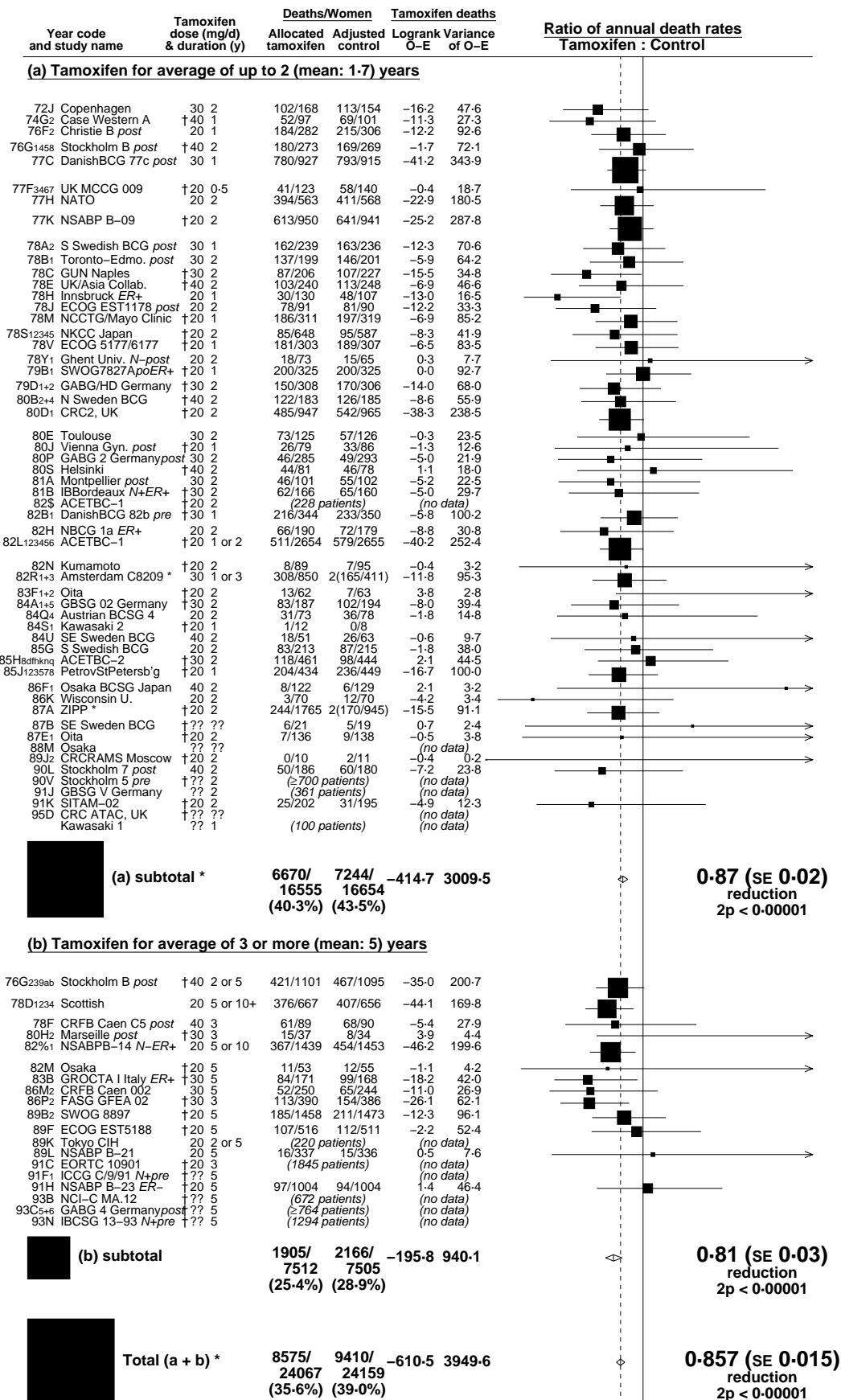
0.76 (SE 0.03)
reduction
2p < 0.00001

Total (a + b) * 6989/ 8036/ -624.4 3271.3
24067 24159
(29.0%) (33.3%)

0.826 (SE 0.016)
reduction
2p < 0.00001

■ 99% or ◊ 95% confidence intervals
Difference between treatment effects in 2 subtotals: $\chi^2_1 = 6.4$; 2p = 0.01
Heterogeneity within subtotals: $\chi^2_{59} = 62.6$; p > 0.1; NS
Heterogeneity between 61 trials: $\chi^2_{60} = 69.1$; p > 0.1; NS

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.
† Tamoxifen plus chemotherapy versus same chemotherapy alone



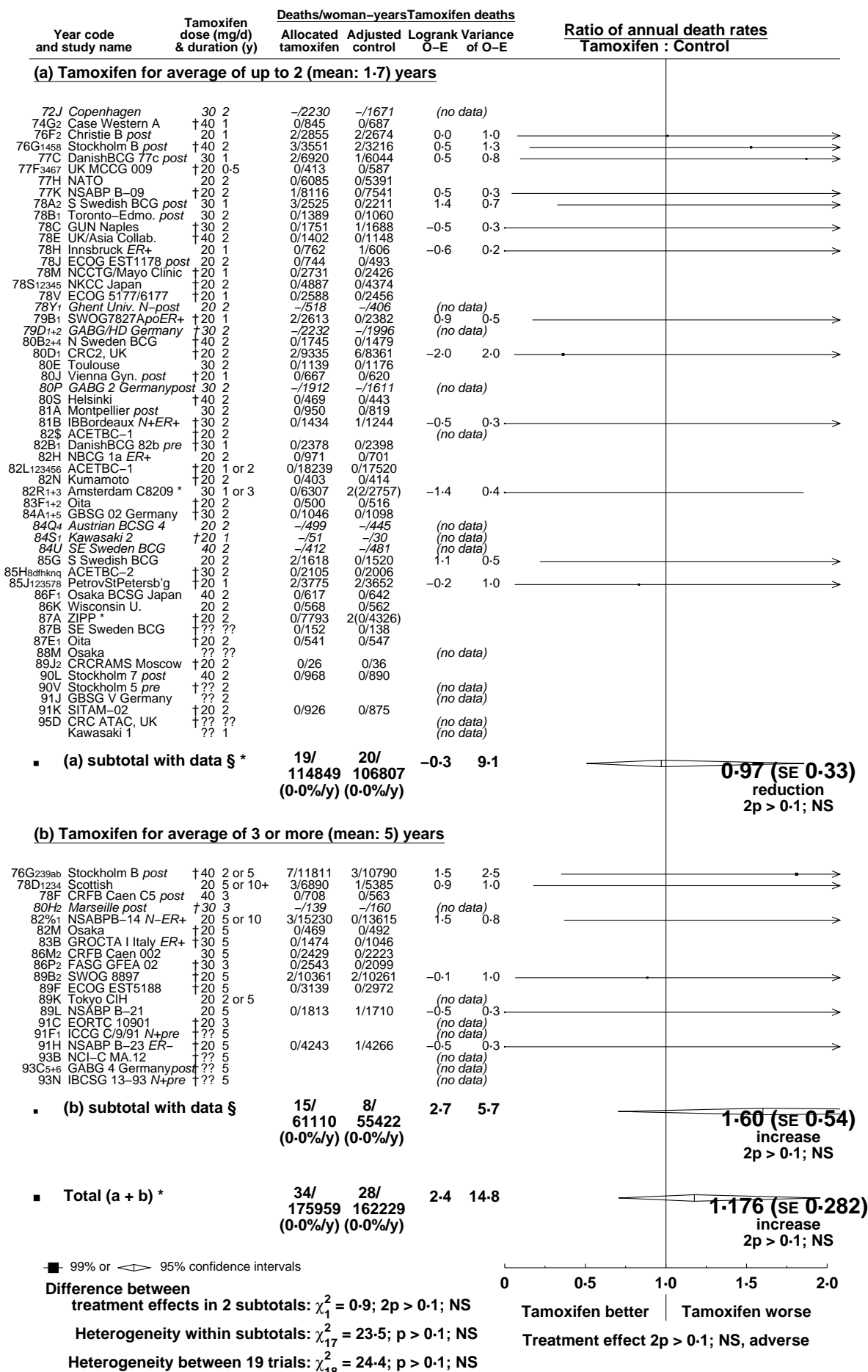
■ 99% or ◊ 95% confidence intervals

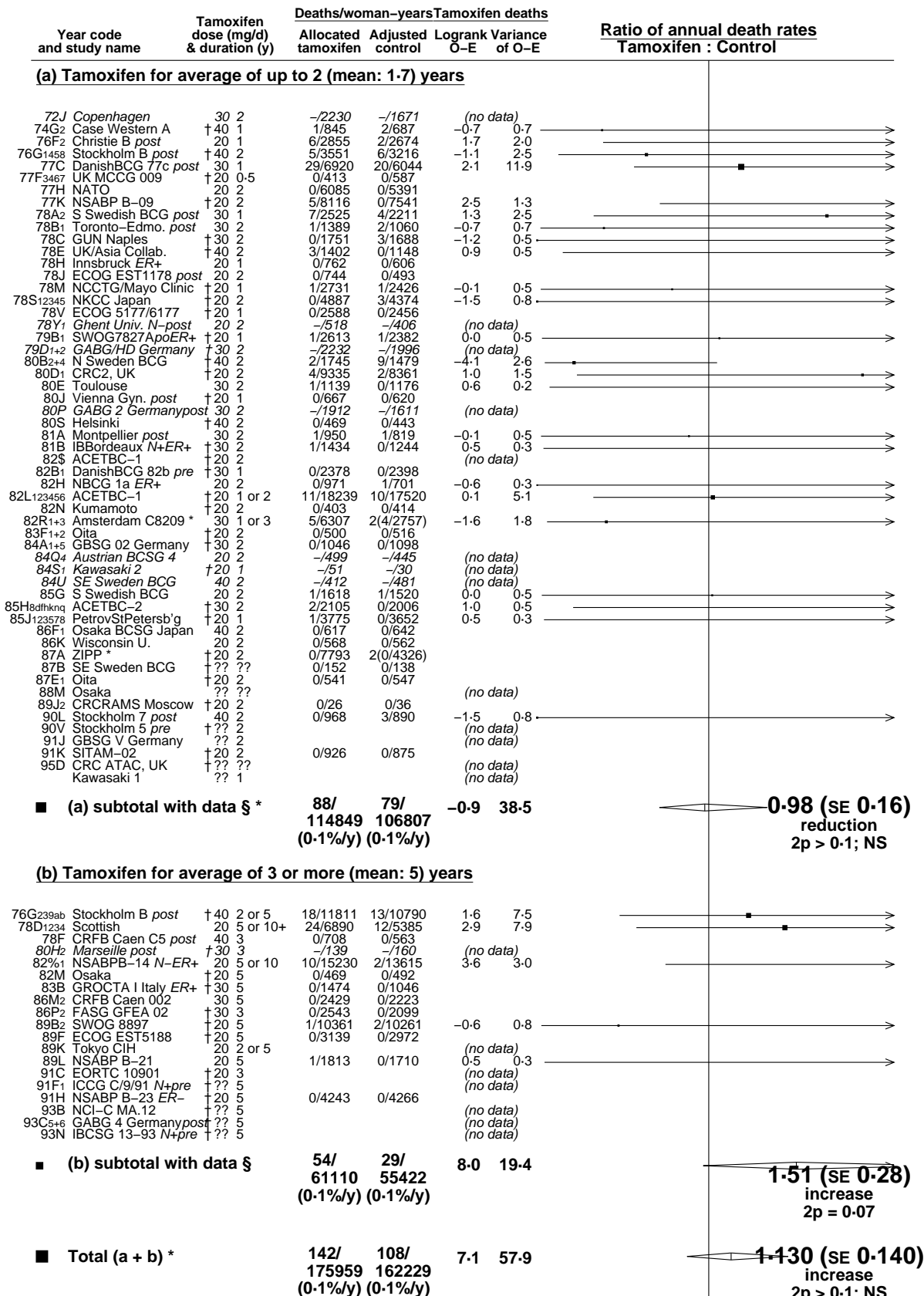
Difference between treatment effects in 2 subtotals: $\chi^2_1 = 3.6$; $2p = 0.06$

Heterogeneity within subtotals: $\chi^2_{59} = 58.5$; $p > 0.1$; NS

Heterogeneity between 61 trials: $\chi^2_{60} = 62.0$; $p > 0.1$; NS

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.
 † Tamoxifen plus chemotherapy versus same chemotherapy alone





■ 99% or ◊ 95% confidence intervals

Difference between treatment effects in 2 subtotals: $\chi^2_1 = 2.4$; 2p > 0.1; NS

Heterogeneity within subtotals: $\chi^2_{27} = 38.8$; p = 0.07

Heterogeneity between 29 trials: $\chi^2_{28} = 41.2$; p = 0.05

§ 8 trials with no data do not contribute to subtotals or to the overall total (allocated tamoxifen: 7993; allocated control: 6800)

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

† Tamoxifen plus chemotherapy versus same chemotherapy alone

Year code and study name	Tamoxifen dose (mg/d) & duration (y)	Deaths/woman-years		Tamoxifen deaths		Ratio of annual death rates Tamoxifen : Control
		Allocated tamoxifen	Adjusted control	Logrank O-E	Variance of O-E	

(a) Tamoxifen for average of up to 2 (mean: 1.7) years

72J Copenhagen	30 2	-/2230	-/1671	(no data)		
74G2 Case Western A	†40 1	2/845	3/687	-0.5	1.2	
76F2 Christie B post	20 1	27/2855	20/2674	2.3	11.6	
76G1458 Stockholm B post	†40 2	26/3551	26/3216	-1.7	11.6	
77C DanishBCG 77c post	30 1	120/6920	92/6044	4.8	50.9	
77F3467 UK MCCG 009	†20 0.5	2/413	0/587	1.2	0.5	
77H NATO	20 2	0/6085	0/5391			
77K NSABP B-09	†20 2	27/8116	18/7541	2.8	11.1	
78A2 S Swedish BCG post	30 1	24/2525	16/2211	2.9	9.3	
78B1 Toronto-Edmo. post	30 2	8/1389	4/1060	1.0	2.8	
78C GUN Naples	†30 2	3/1751	7/1688	-2.4	1.8	
78E UK/Asia Collab.	†40 2	7/1402	2/1148	2.1	1.9	
78H Innsbruck ER+	20 1	0/762	3/606	-1.6	0.7	
78J ECOG EST1178 post	20 2	0/744	0/493			
78M NCCTG/Mayo Clinic	†20 1	6/2731	5/2426	0.4	2.7	
78S12345 NKCC Japan	†20 2	3/4887	6/4374	-1.8	2.2	
78V ECOG 5177/6177	†20 1	0/2588	0/2456			
78Y1 Ghent Univ. N-post	20 2	-/518	-/406	(no data)		
79B1 SWOG7827ApoER+	†20 1	13/2613	6/2382	3.4	4.7	
79D1+2 GABG/HD Germany	†30 2	-/232	-/1996	(no data)		
80B2+4 N Sweden BCG	†40 2	17/1745	22/1479	-4.0	9.4	
80D1 CRC2 UK	†20 2	18/9335	18/8361	-0.1	9.0	
80E Toulouse	30 2	3/1139	1/1176	1.6	0.9	
80J Vienna Gyn. post	†20 1	0/667	0/620			
80P GABG 2 Germany post	30 2	-/1912	-/1611	(no data)		
80S Helsinki	†40 2	2/469	1/443	1.0	0.4	
81A Montpellier post	30 2	2/950	4/819	-1.2	1.5	
81B IBBordeaux N+ER+	†30 2	2/1434	1/1244	0.4	0.8	
82S ACETBC-1	†20 2			(no data)		
82B1 DanishBCG 82b pre	†30 1	2/2378	1/2398	0.4	0.7	
82H NBCG 1a ER+	20 2	4/971	4/701	-0.6	1.9	
82L123456 ACETBC-1	†20 1 or 2	27/18239	21/17520	1.3	11.6	
82N Kumamoto	†20 2	0/403	0/414			
82R1+3 Amsterdam C8209 *	30 1 or 3	32/6307	2(23/2757)	-6.5	11.3	
83F1+2 Oita	†20 2	0/500	0/516			
84A1+5 GBSG 02 Germany	†30 2	2/1046	1/1098	0.5	0.7	
84Q4 Austrian BCSC 4	20 2	-/499	-/445	(no data)		
84S1 Kawasaki 2	†20 1	-/51	-/30	(no data)		
84U SE Sweden BCG	40 2	-/412	-/481	(no data)		
85G S Swedish BCG	20 2	4/1618	1/1520	1.6	1.2	
85Hdfrknq ACETBC-2	†30 2	4/2105	1/2006	1.6	1.2	
85J123578 PetrovSiPetersb'g	†20 1	14/3775	9/3652	2.3	5.6	
86F1 Osaka BCSC Japan	40 2	0/617	0/642			
86K Wisconsin U.	20 2	0/568	0/562			
87A ZIPP *	†20 2	0/7793	2(0/4326)			
87B SE Sweden BCG	†?? ??	0/152	0/138			
87E1 Oita	†20 2	0/541	0/547			
88M Osaka	?? ??			(no data)		
89J2 CRCRAMS Moscow	†20 2	0/26	0/36			
90L Stockholm 7 post	40 2	2/968	6/890	-2.0	2.0	
90V Stockholm 5 pre	†?? ??			(no data)		
91J GBSG V Germany	?? ??			(no data)		
91K SITAM-02	†20 2	0/926	0/875			
95D CRC ATAC UK	†?? ??			(no data)		
Kawasaki 1	?? 1			(no data)		

■ (a) subtotal with data § * **403/ 345/ 9.1 171.3**
114849 106807
(0.4%/y) (0.3%/y) **1.05 (SE 0.08)**
increase
2p > 0.1; NS

(b) Tamoxifen for average of 3 or more (mean: 5) years

76G239ab Stockholm B post	†40 2 or 5	65/11812	57/10790	1.1	29.6	
78D1234 Scottish	20 5 or 10+	64/6890	52/5385	-2.6	26.5	
78F CRFB Caen C5 post	40 3	0/708	0/563			
80H2 Marseille post	†30 3	-/139	-/160	(no data)		
82%61 NSABPB-14 N-ER+	†20 5 or 10	45/15230	39/13615	0.8	20.9	
82M Osaka	20 2	0/469	0/492			
83B GROCTA I Italy ER+	†30 5	0/1474	0/1046			
86M2 CRFB Caen 002	30 5	0/2429	0/2223			
86F2 FASG GFEA 02	†30 3	1/2543	1/2099	-0.1	0.5	
89B2 SWOG 8897	†20 5	9/10361	15/10261	-3.3	5.9	
89F ECOG EST5188	†20 5	0/3139	0/2972			
89K Tokyo CIH	20 2 or 5			(no data)		
89L NSABP B-21	20 5	3/1813	1/1710	1.0	1.0	
91C EORTC 10901	†20 3			(no data)		
91F1 ICCG C/9/91 N+pre	†?? 5			(no data)		
91H NSABP B-23 ER-	†20 5	2/4243	4/4266	-0.6	1.4	
93B NCI-C MA.12	†?? 5			(no data)		
93C5+6 GABG 4 Germany post	†?? 5			(no data)		
93N IBCSG 13-93 N+pre	†?? 5			(no data)		

■ (b) subtotal with data § **189/ 169/ -3.8 85.8**
61111 55422
(0.3%/y) (0.3%/y) **0.96 (SE 0.11)**
reduction
2p > 0.1; NS

■ Total (a + b) * **592/ 514/ 5.3 257.1**
175960 162229
(0.3%/y) (0.3%/y) **1.021 (SE 0.063)**
increase
2p > 0.1; NS

■ 99% or ◊ 95% confidence intervals

Difference between treatment effects in 2 subtotals: $\chi^2_1 = 0.5$; $2p > 0.1$; NS

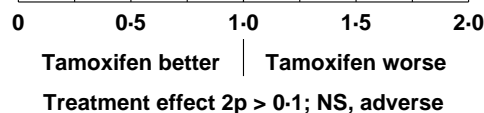
Heterogeneity within subtotals: $\chi^2_{34} = 41.8$; $p > 0.1$; NS

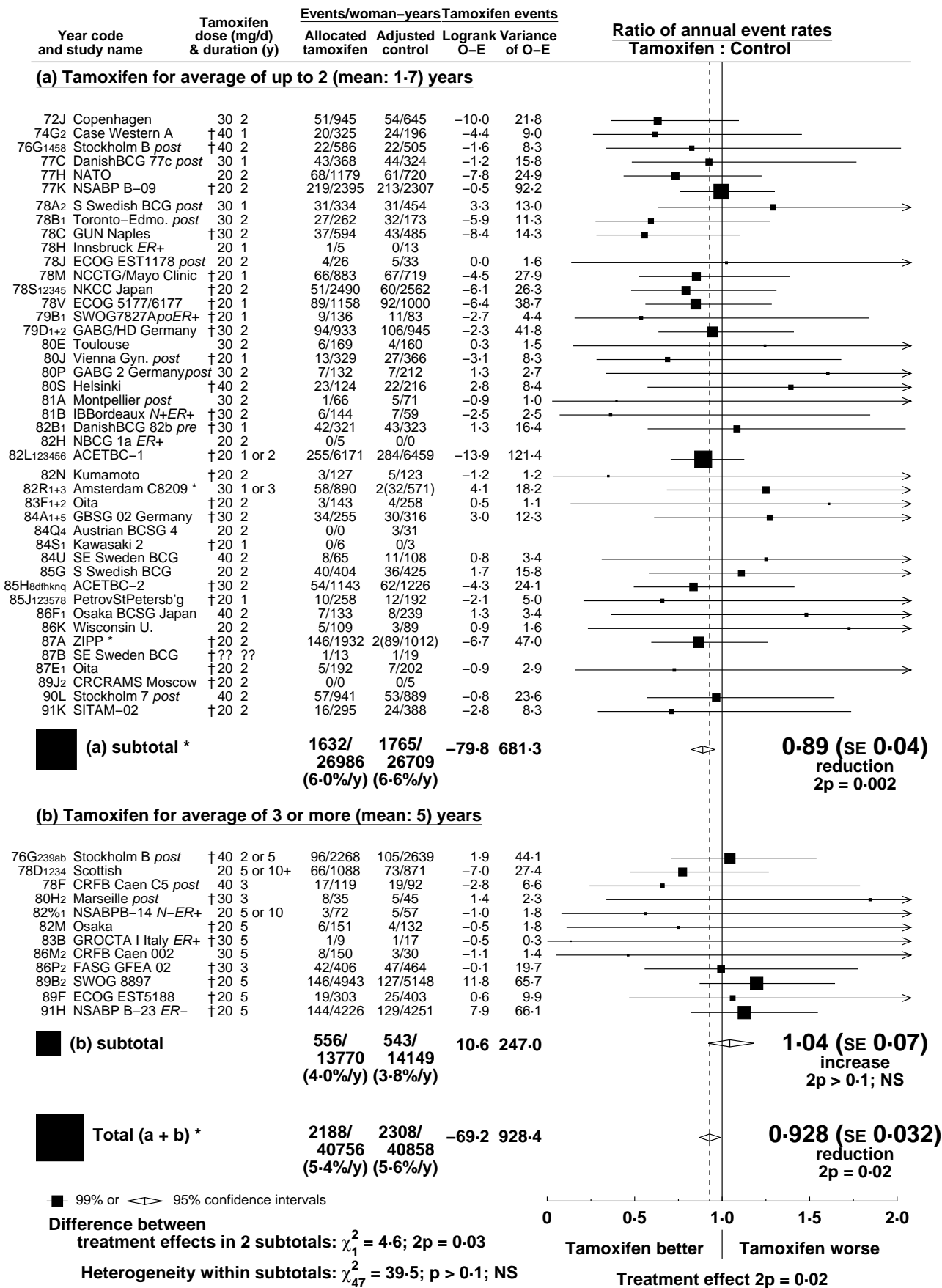
Heterogeneity between 36 trials: $\chi^2_{35} = 42.4$; $p > 0.1$; NS

§ 8 trials with no data do not contribute to subtotals or to the overall total (allocated tamoxifen: 7993; allocated control: 6800)

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

† Tamoxifen plus chemotherapy versus same chemotherapy alone





■ 99% or ◊ 95% confidence intervals

Difference between

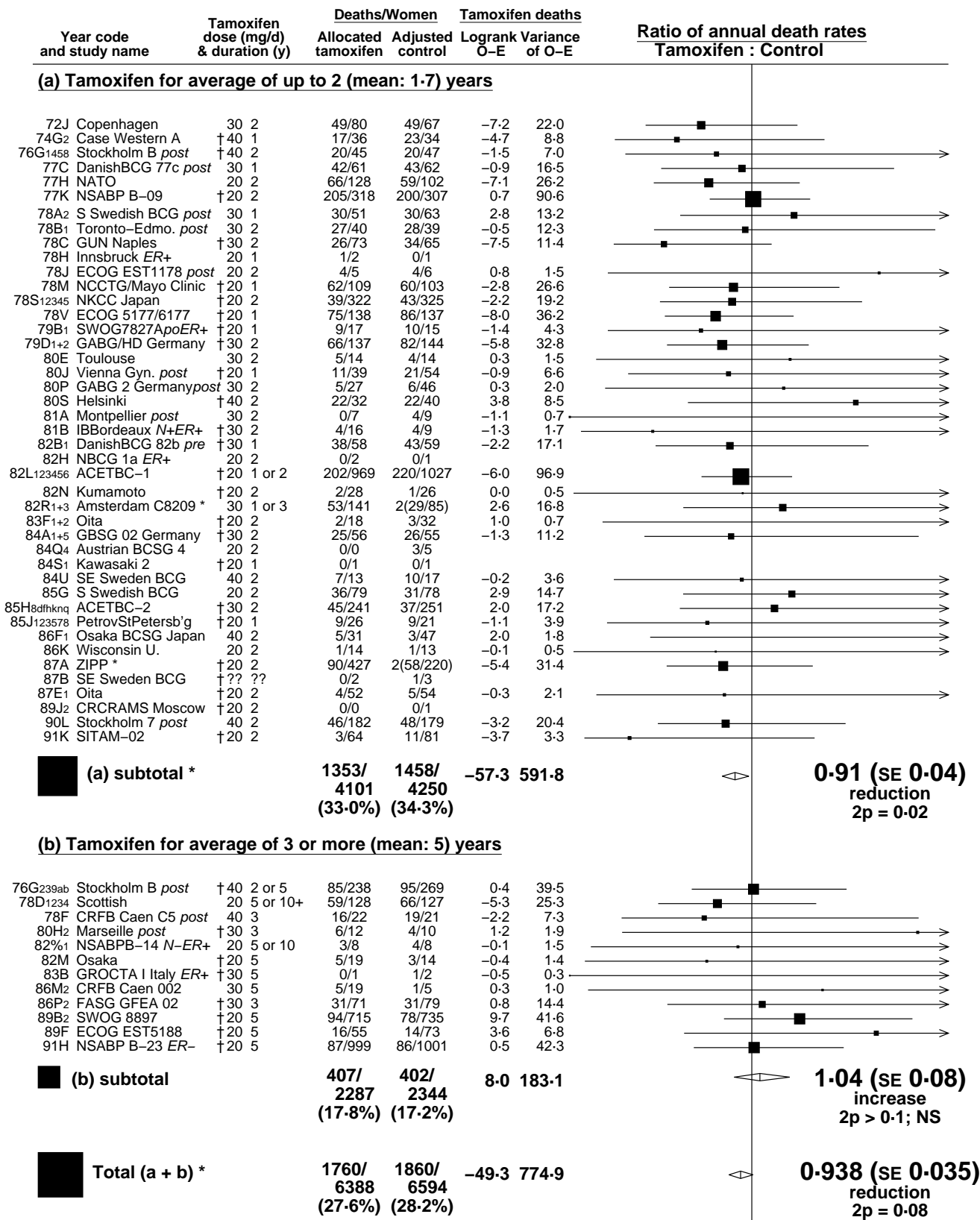
treatment effects in 2 subtotals: $\chi^2_1 = 4.6$; $2p = 0.03$

Heterogeneity within subtotals: $\chi^2_{47} = 39.5$; $p > 0.1$; NS

Heterogeneity between 49 trials: $\chi^2_{48} = 44.1$; $p > 0.1$; NS

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.

† Tamoxifen plus chemotherapy versus same chemotherapy alone



■ 99% or ◊ 95% confidence intervals

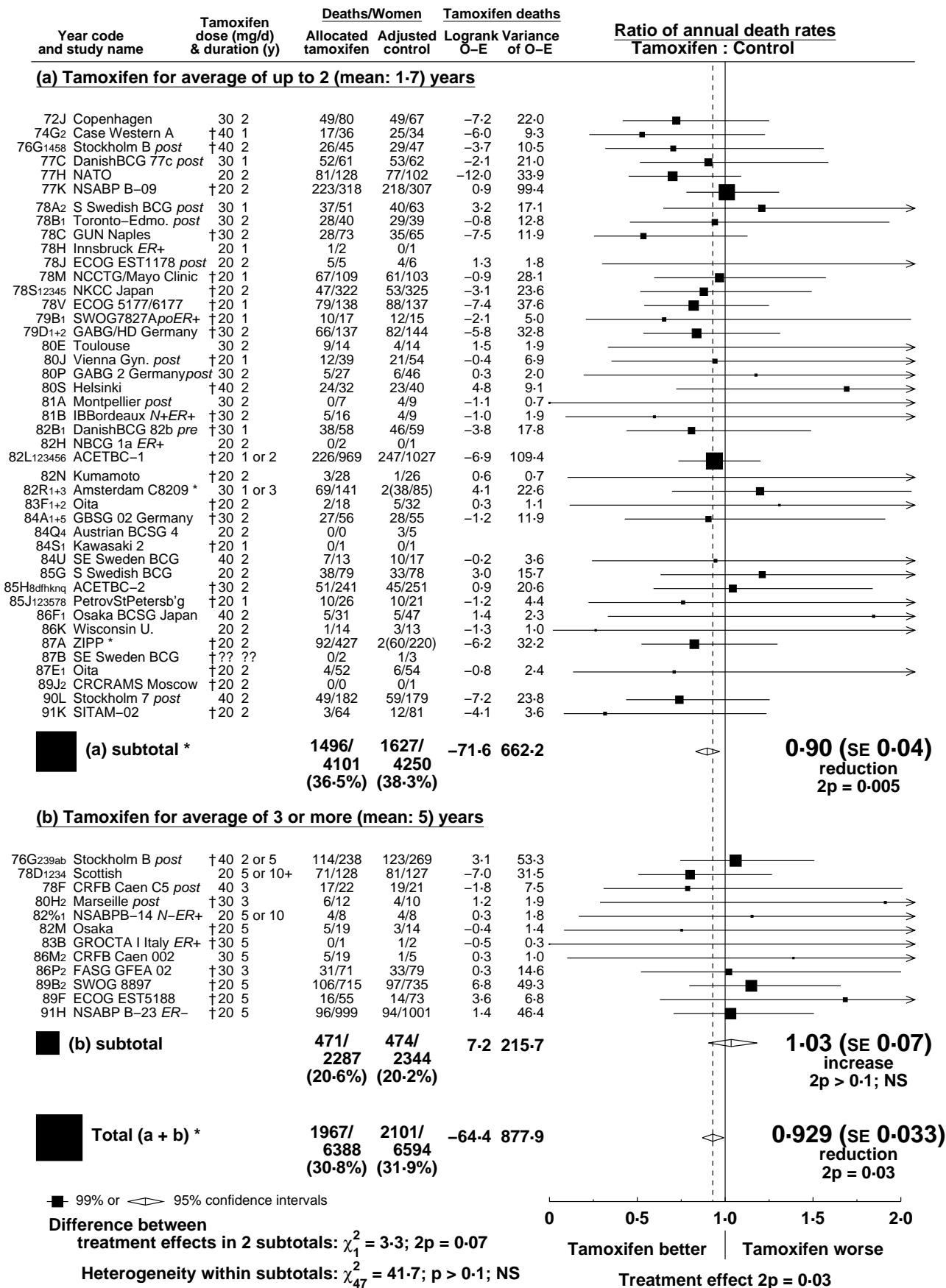
Difference between treatment effects in 2 subtotals: $\chi^2_1 = 2.8$; 2p = 0.10

Heterogeneity within subtotals: $\chi^2_{47} = 35.3$; p > 0.1; NS

Heterogeneity between 49 trials: $\chi^2_{48} = 38.0$; p > 0.1; NS

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

† Tamoxifen plus chemotherapy versus same chemotherapy alone



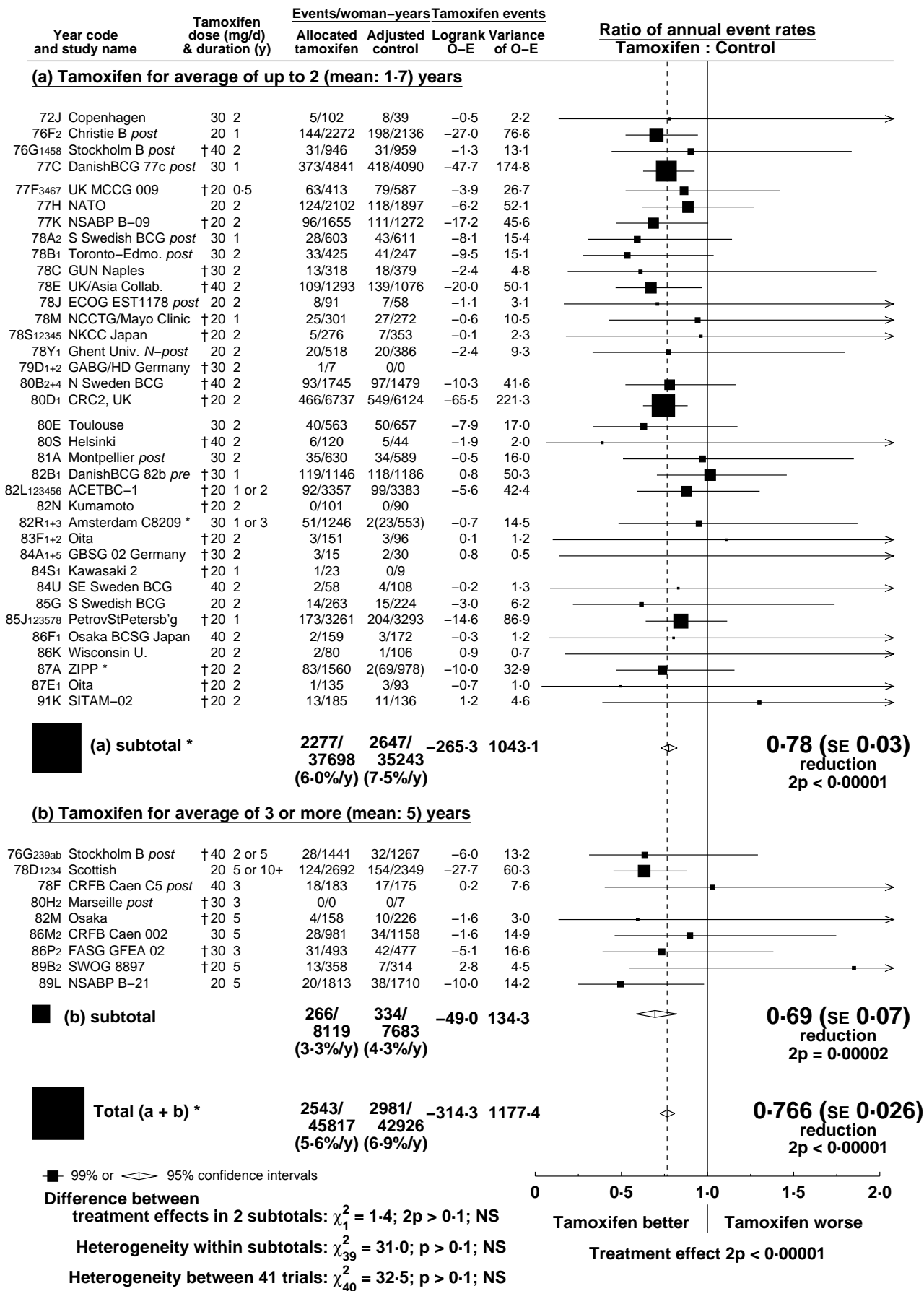
■ 99% or ◁ 95% confidence intervals

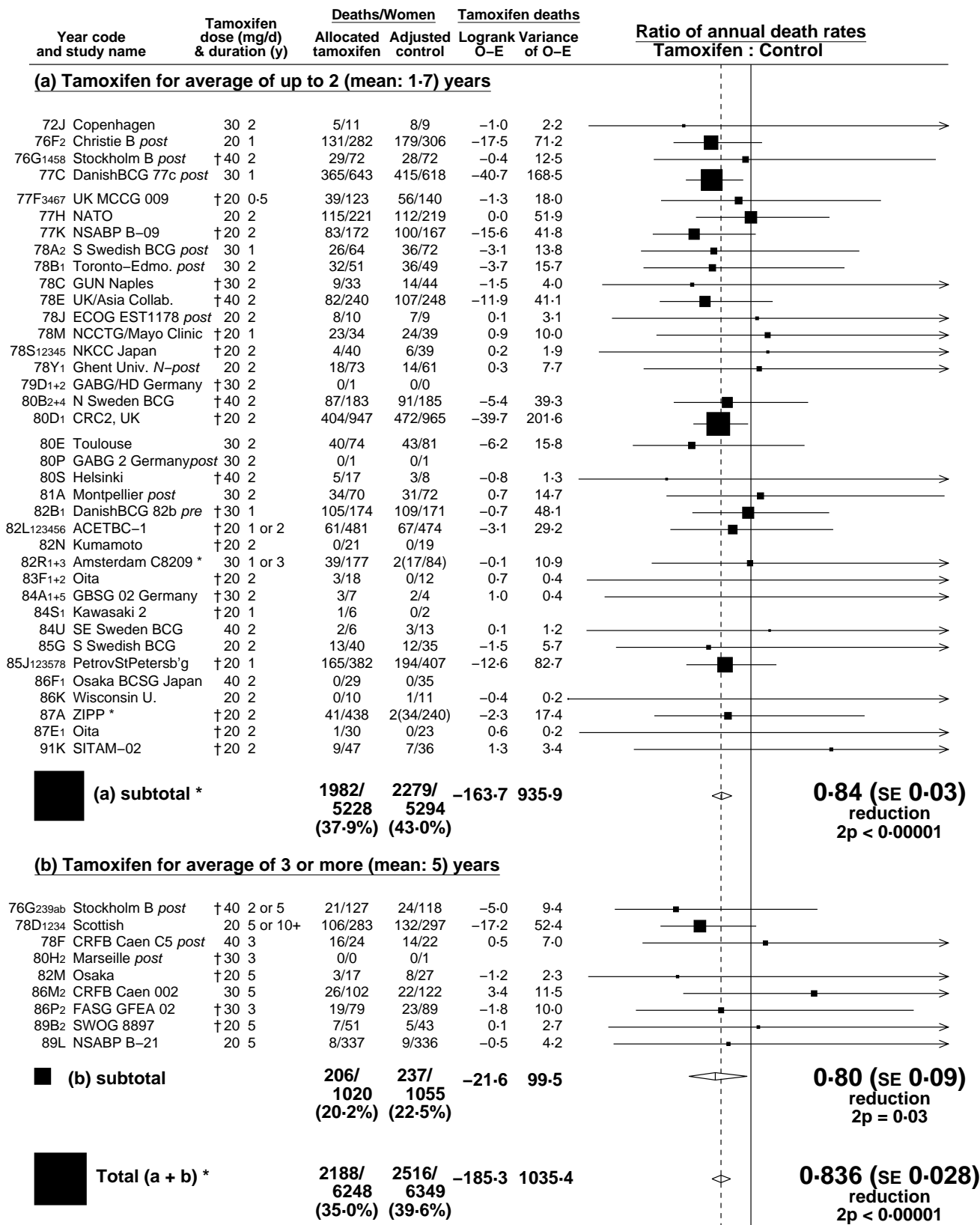
Difference between treatment effects in 2 subtotals: $\chi^2 = 3.3$; $2p = 0.07$

Heterogeneity within subtotals: $\chi^2_{47} = 41.7$; $p > 0.1$; NS

Heterogeneity between 49 trials: $\chi^2_{48} = 45.0$; $p > 0.1$; NS

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.
 † Tamoxifen plus chemotherapy versus same chemotherapy alone



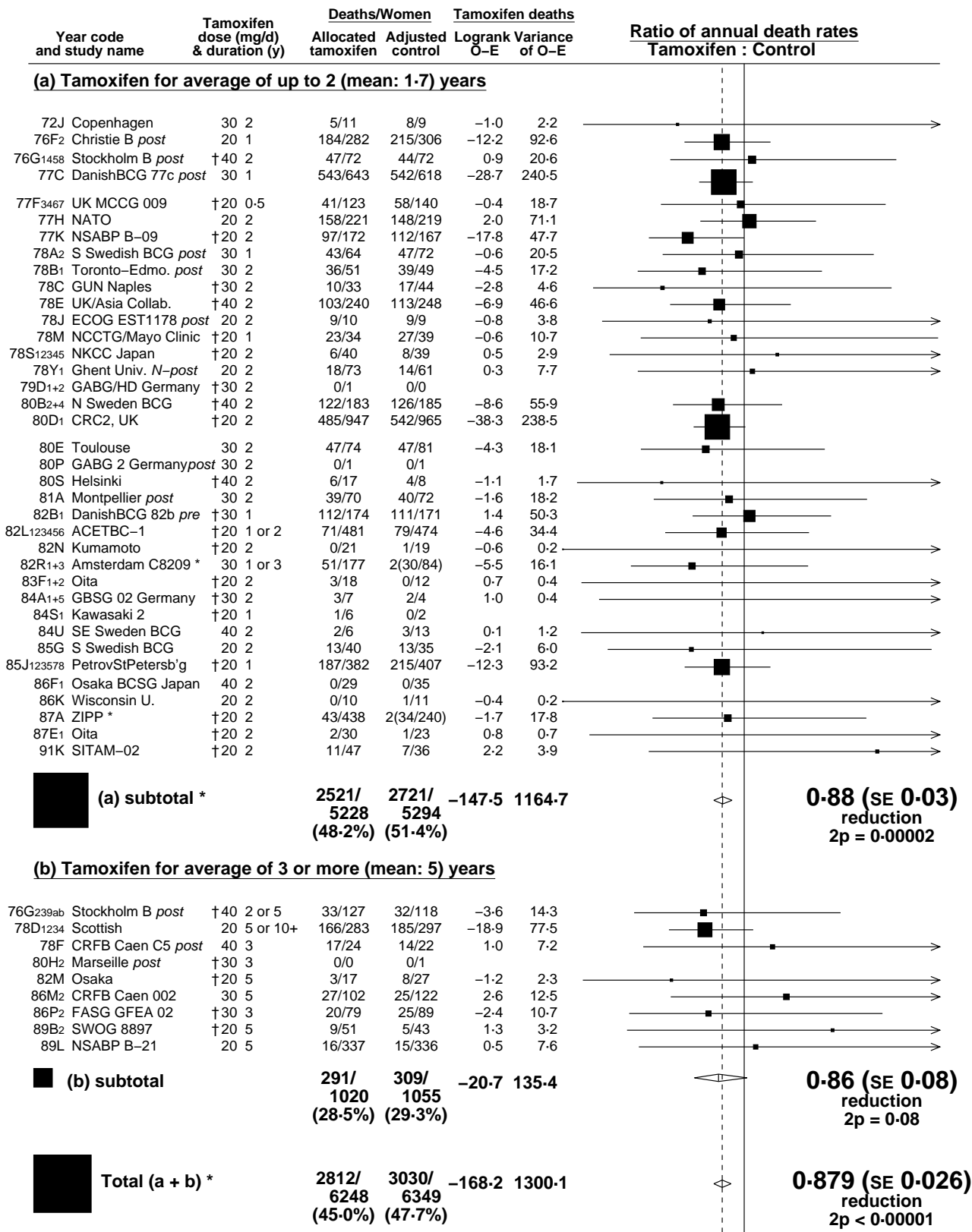


■ 99% or ◊ 95% confidence intervals

Difference between treatment effects in 2 subtotals: $\chi^2_1 = 0.2$; $2p > 0.1$; NS
Heterogeneity within subtotals: $\chi^2_{38} = 24.0$; $p > 0.1$; NS
Heterogeneity between 40 trials: $\chi^2_{39} = 24.1$; $p > 0.1$; NS

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

† Tamoxifen plus chemotherapy versus same chemotherapy alone



■ 99% or ◊ 95% confidence intervals

Difference between treatment effects in 2 subtotals: $\chi^2_1 = 0.1$; $2p > 0.1$; NS

Heterogeneity within subtotals: $\chi^2_{39} = 24.6$; $p > 0.1$; NS

Heterogeneity between 41 trials: $\chi^2_{40} = 24.7$; $p > 0.1$; NS

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

† Tamoxifen plus chemotherapy versus same chemotherapy alone

Year code and study name	Tamoxifen dose (mg/d) & duration (y)	Events/woman-years		Logrank O-E	Variance of O-E	Ratio of annual event rates Tamoxifen : Control
		Allocated tamoxifen	Adjusted control			
72J Copenhagen	30 2	52/1131	57/972	-6.5	24.1	
74G2 Case Western A	†40 1	35/520	43/491	-6.8	16.3	
76G1458 Stockholm B post	†40 2	69/2009	83/1751	-13.9	30.3	
77C DanishBCG 77c post	30 1	137/1711	166/1630	-18.8	64.2	
77H NATO	20 2	118/1943	159/2005	-19.0	56.6	
77K NSABP B-09	†20 2	302/4066	315/3962	-14.1	139.3	
78A2 S Swedish BCG post	30 1	67/1111	64/722	-14.5	26.4	
78B1 Toronto-Edmo. post	30 2	70/702	82/641	-9.5	32.2	
78C GUN Naples	†30 2	52/839	70/824	-10.3	20.7	
78H Innsbruck ER+	20 1	49/757	56/593	-11.6	22.4	
78J ECOG EST1178 post	20 2	56/627	62/402	-14.6	24.6	
78M NCCTG/Mayo Clinic	†20 1	110/1547	121/1435	-8.2	51.0	
78S12345 NKCC Japan	†20 2	39/2121	38/1459	-4.8	17.9	
78V ECOG 5177/6177	†20 1	116/1430	109/1456	4.1	49.0	
78Y1 Ghent Univ. N-post	20 2	0/0	2/20			
79B1 SWOG7827ApoER+	†20 1	175/2477	189/2299	-11.4	82.5	
79D1+2 GABG/HD Germany	†30 2	121/1292	122/1051	-15.4	47.7	
80E Toulouse	30 2	17/407	13/360	-1.6	4.5	
80J Vienna Gyn. post	†20 1	14/338	14/254	-3.2	5.9	
80P GABG 2 Germany post	30 2	64/1780	72/1399	-10.8	31.3	
80S Helsinki	†40 2	14/225	17/183	-3.8	6.6	
81A Montpellier post	30 2	7/254	12/159	-3.3	3.8	
81B IBBordeaux N+ER+	†30 2	73/1290	74/1185	-4.0	33.7	
82B1 DanishBCG 82b pre	†30 1	70/911	77/889	-3.7	31.7	
82H NBCG 1a ER+	20 2	82/966	106/701	-24.3	39.9	
82L123456 ACETBC-1	†20 1 or 2	264/8712	337/7678	-52.4	137.9	
82N Kumamoto	†20 2	6/176	9/201	-1.6	3.1	
82R1+3 Amsterdam C8209 *	30 1 or 3	177/4171	2(98/1634)	-18.4	51.8	
83F1+2 Oita	†20 2	5/207	5/162	1.5	1.0	
84A1+5 GBSG 02 Germany	†30 2	67/778	84/753	-12.1	30.3	
84Q4 Austrian BCSG 4	20 2	36/499	45/414	-8.2	17.7	
84S1 Kawasaki 2	†20 1	1/22	0/18			
84U SE Sweden BCG	40 2	11/289	17/265	-1.7	6.2	
85G S Swedish BCG	20 2	37/640	47/577	-5.3	18.0	
85H8dfhknq ACETBC-2	†30 2	93/962	82/781	-4.9	33.2	
85J123578 PetrovStPetersb'g	†20 1	8/256	11/167	-3.1	2.4	
86F1 Osaka BCSG Japan	40 2	8/325	6/231	0.0	3.2	
86K Wisconsin U.	20 2	6/379	11/367	-2.3	4.2	
87A ZIPP *	†20 2	219/4301	2(160/2336)	-27.8	79.9	
87B SE Sweden BCG	†?? ??	6/139	5/120	-0.1	2.6	
87E1 Oita	†20 2	3/214	7/252	-1.6	2.4	
89J2 CRCRAMS Moscow	†20 2	0/26	3/31	-0.4	0.2	
90L Stockholm 7 post	40 2	1/27	1/1			
91K SITAM-02	†20 2	18/447	27/351	-7.9	10.2	

(a) subtotal *

2875/ 53024 3336/ 47152 -376.2 1266.8
(5.4%/y) (7.1%/y)

0.74 (SE 0.02)
reduction
2p < 0.00001

(b) Tamoxifen for average of 3 or more (mean: 5) years

76G239ab Stockholm B post	†40 2 or 5	220/8062	286/6829	-52.5	113.1	
78D1234 Scottish	20 5 or 10+	95/2644	127/1834	-33.2	46.3	
78F CRFB Caen C5 post	40 3	28/407	37/297	-8.2	13.0	
80H2 Marseille post	†30 3	12/105	9/108	1.6	3.8	
82%1 NSABPB-14 N-ER+	20 5 or 10	350/15158	547/13558	-117.9	215.8	
82M Osaka	†20 5	5/160	4/134	1.1	1.3	
83B GROCTA I Italy ER+	†30 5	99/1465	115/1029	-23.6	47.2	
86M2 CRFB Caen 002	30 5	24/1298	44/1035	-15.5	15.5	
86P2 FASG GFEA 02	†30 3	83/1644	126/1158	-36.1	46.5	
89B2 SWOG 8897	†20 5	111/5060	157/4799	-26.5	64.6	
89F ECOG EST5188	†20 5	118/2836	155/2569	-24.8	64.2	
91H NSABP B-23 ER-	†20 5	1/17	0/15			

(b) subtotal

1146/ 38856 1607/ 33365 -335.5 631.2
(2.9%/y) (4.8%/y)

0.59 (SE 0.03)
reduction
2p < 0.00001

Total (a + b) *

4021/ 91880 4943/ 80517 -711.7 1898.0
(4.4%/y) (6.1%/y)

0.687 (SE 0.019)
reduction
2p < 0.00001

■ 99% or ◊ 95% confidence intervals

Difference between treatment effects in 2 subtotals: $\chi^2_1 = 23.2$; 2p < 0.00001

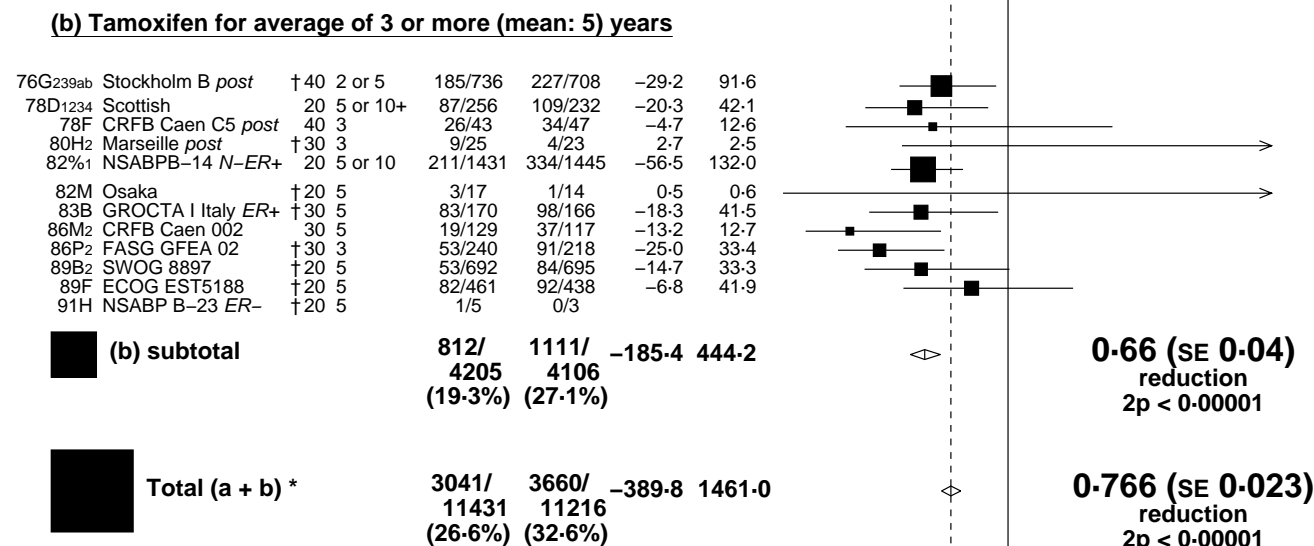
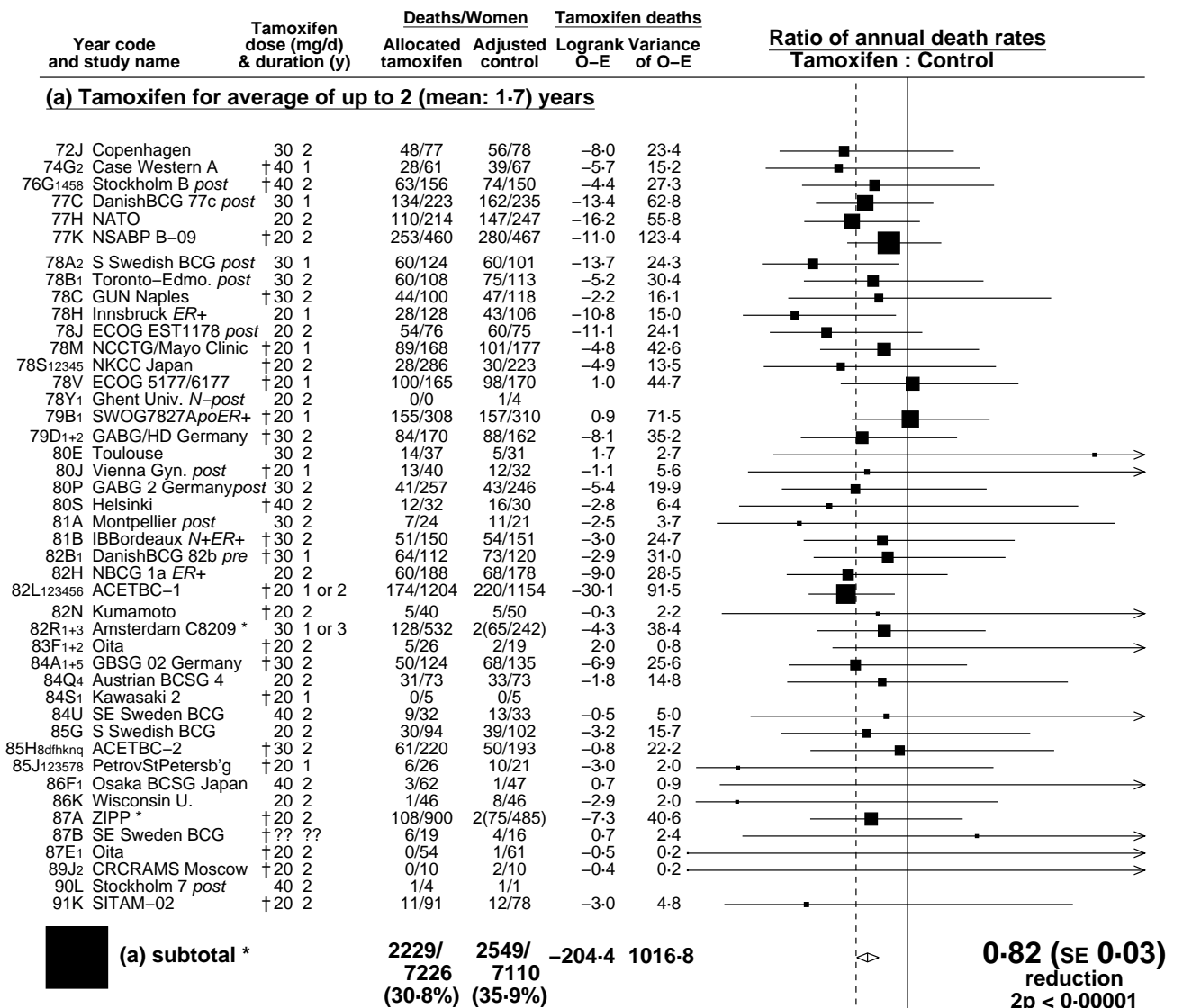
Heterogeneity within subtotals: $\chi^2_{50} = 59.5$; p > 0.1; NS

Heterogeneity between 52 trials: $\chi^2_{51} = 82.7$; p = 0.003

0 0.5 1.0 1.5 2.0
Tamoxifen better | Tamoxifen worse
Treatment effect 2p < 0.00001

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.

† Tamoxifen plus chemotherapy versus same chemotherapy alone



■ 99% or ◁ 95% confidence intervals

Difference between treatment effects in 2 subtotals: $\chi^2_1 = 14.5$; $2p = 0.0001$

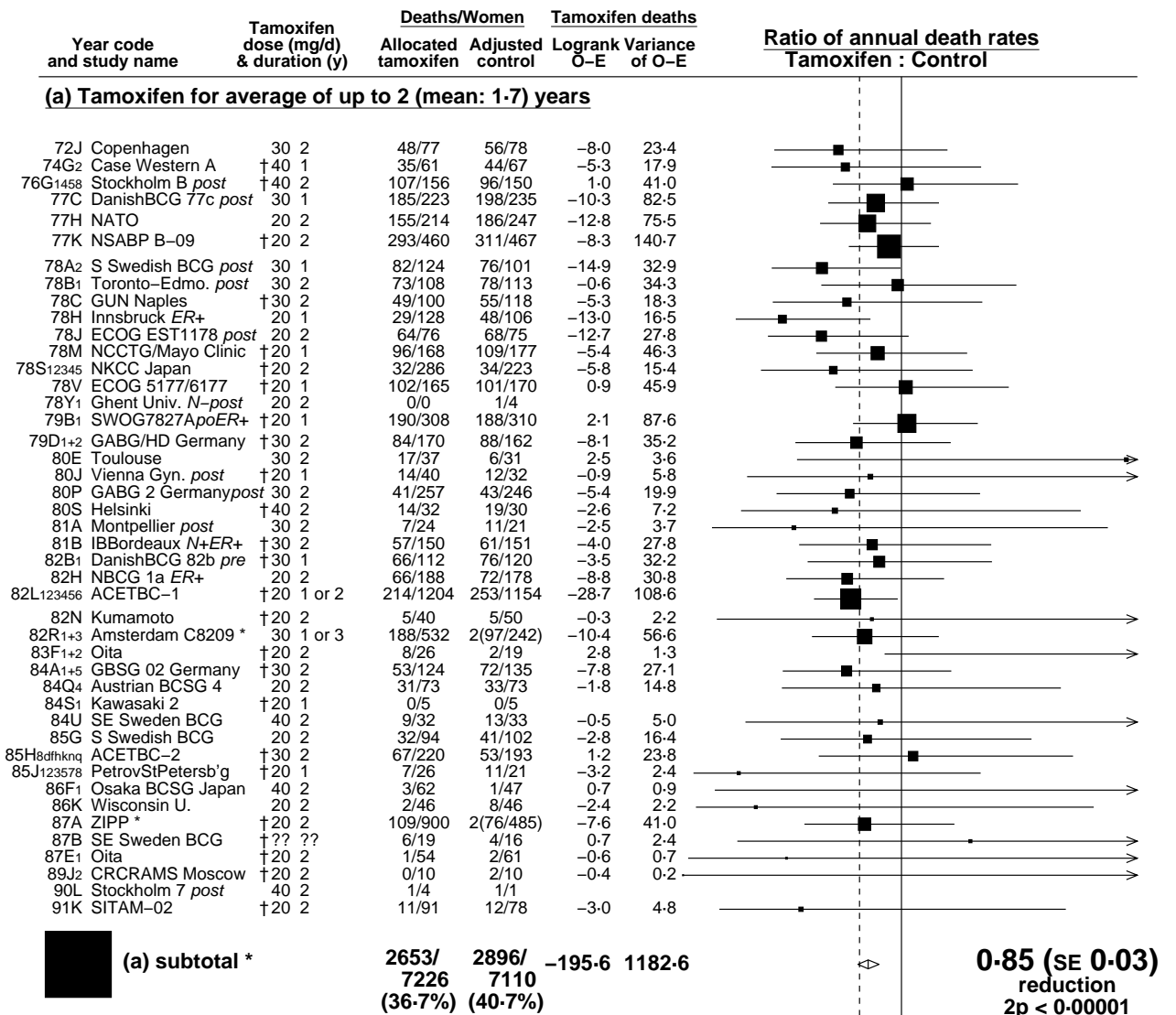
Heterogeneity within subtotals: $\chi^2_{50} = 59.5$; $p > 0.1$; NS

Heterogeneity between 52 trials: $\chi^2_{51} = 74.0$; $p = 0.02$

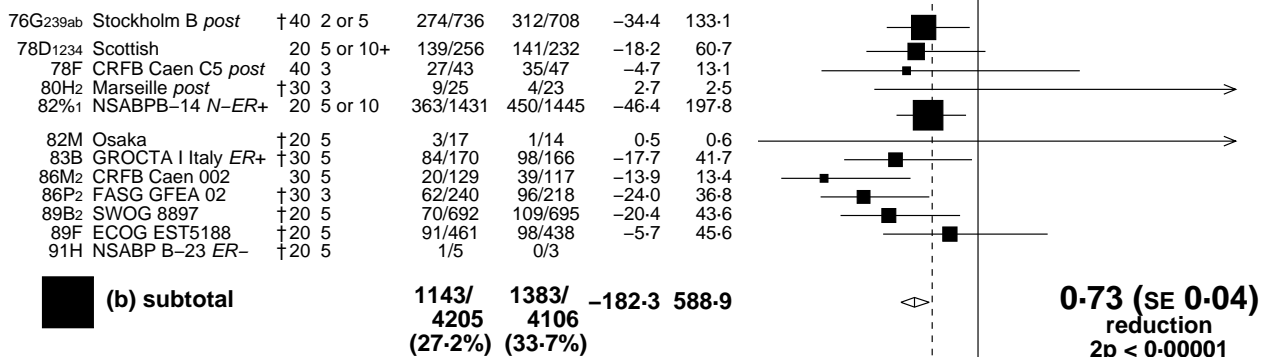
* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

† Tamoxifen plus chemotherapy versus same chemotherapy alone

0 0.5 1.0 1.5 2.0
Tamoxifen better | Tamoxifen worse
Treatment effect $2p < 0.00001$



(b) Tamoxifen for average of 3 or more (mean: 5) years



Total (a + b) *

3796/ 11431	4279/ 11216	-377.9	1771.5	0.808 (SE 0.021) reduction 2p < 0.00001
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■ 99% or ◁▷ 95% confidence intervals

Difference between treatment effects in 2 subtotals: $\chi^2_1 = 8.2$; $2p = 0.004$

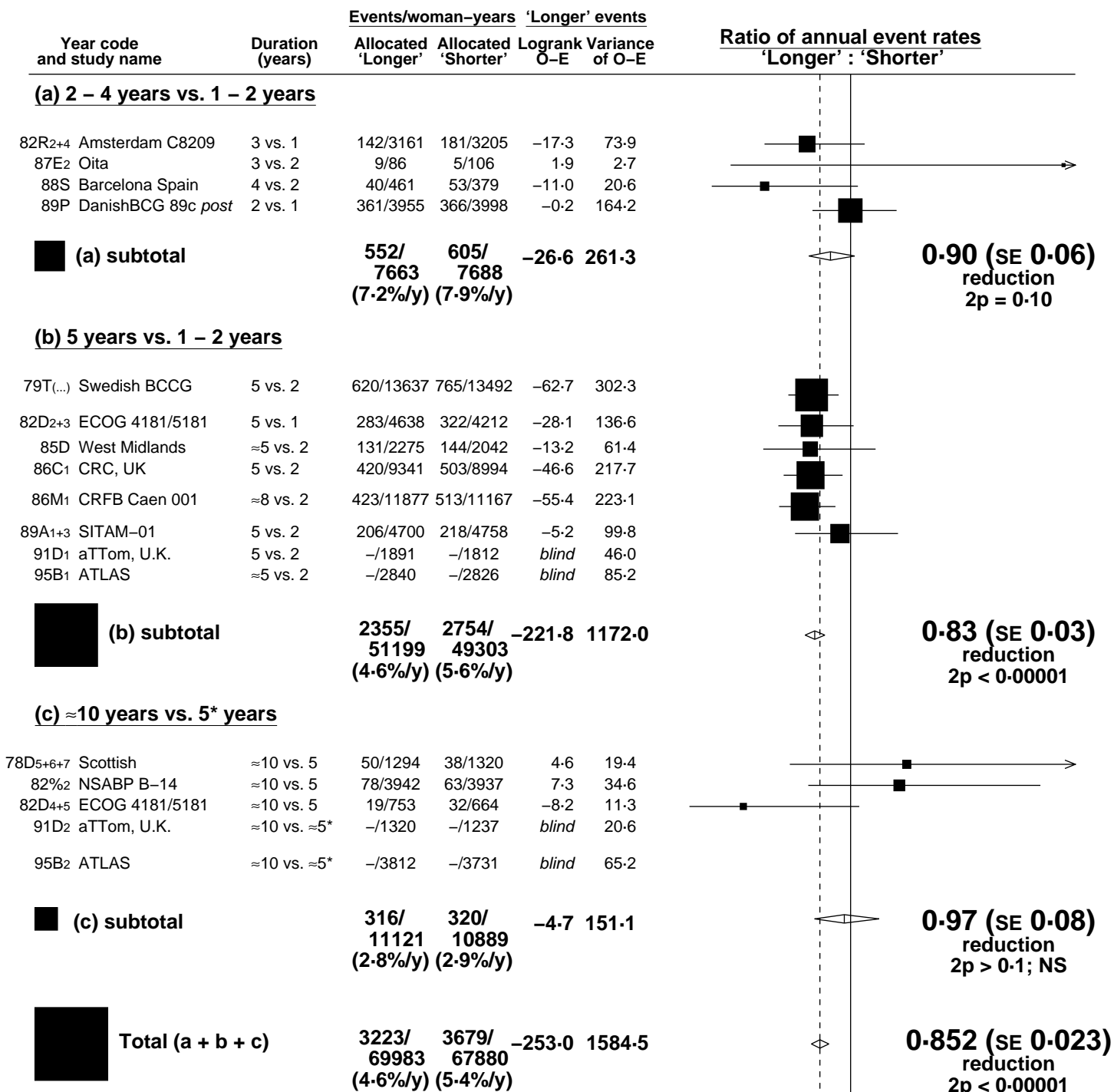
Heterogeneity within subtotals: $\chi^2_{50} = 66.8$; $p = 0.06$

Heterogeneity between 52 trials: $\chi^2_{51} = 75.0$; $p = 0.02$

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

† Tamoxifen plus chemotherapy versus same chemotherapy alone

0 0.5 1.0 1.5 2.0
Tamoxifen better | Tamoxifen worse
Treatment effect $2p < 0.00001$



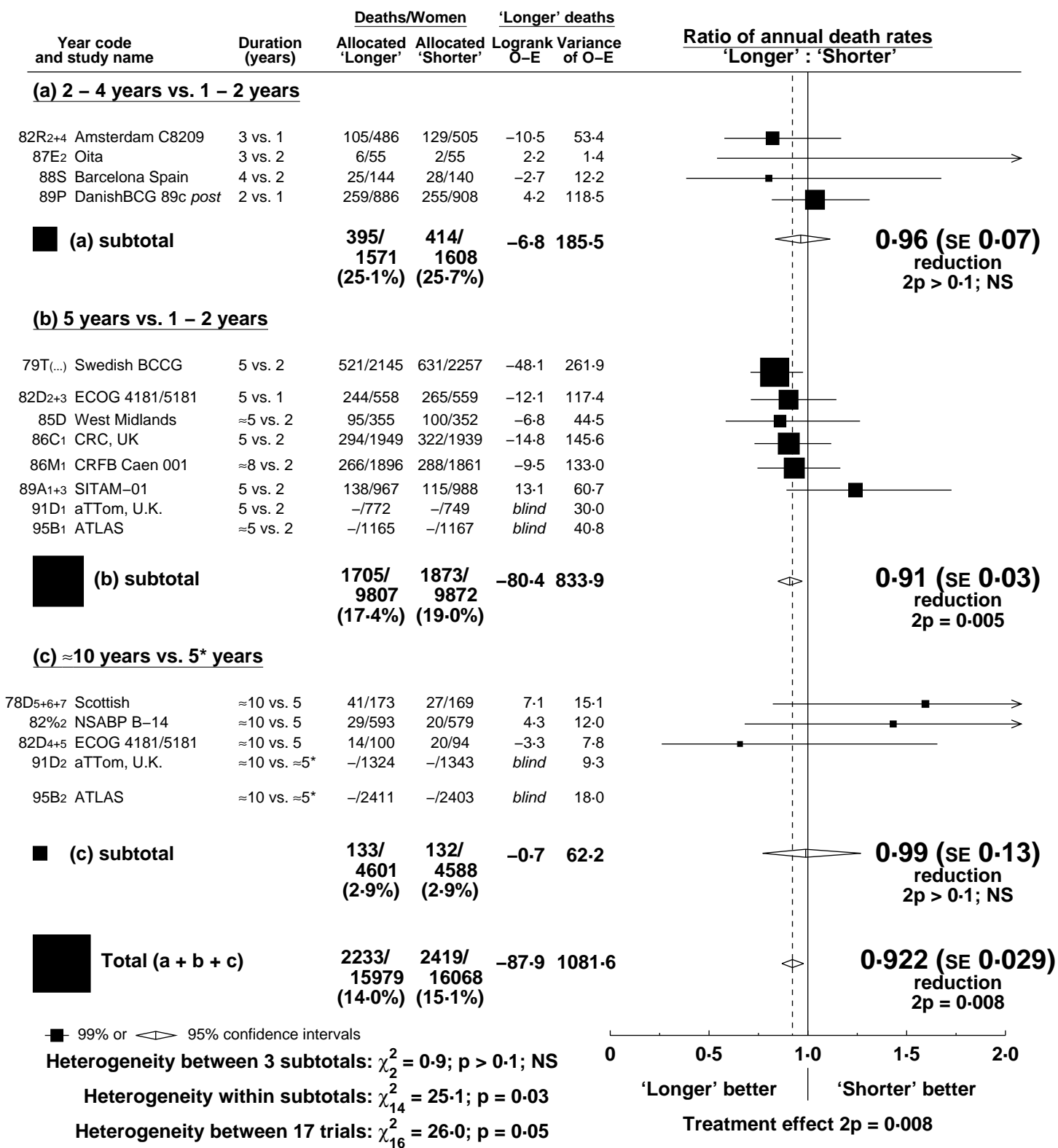
■ 99% or ◊ 95% confidence intervals

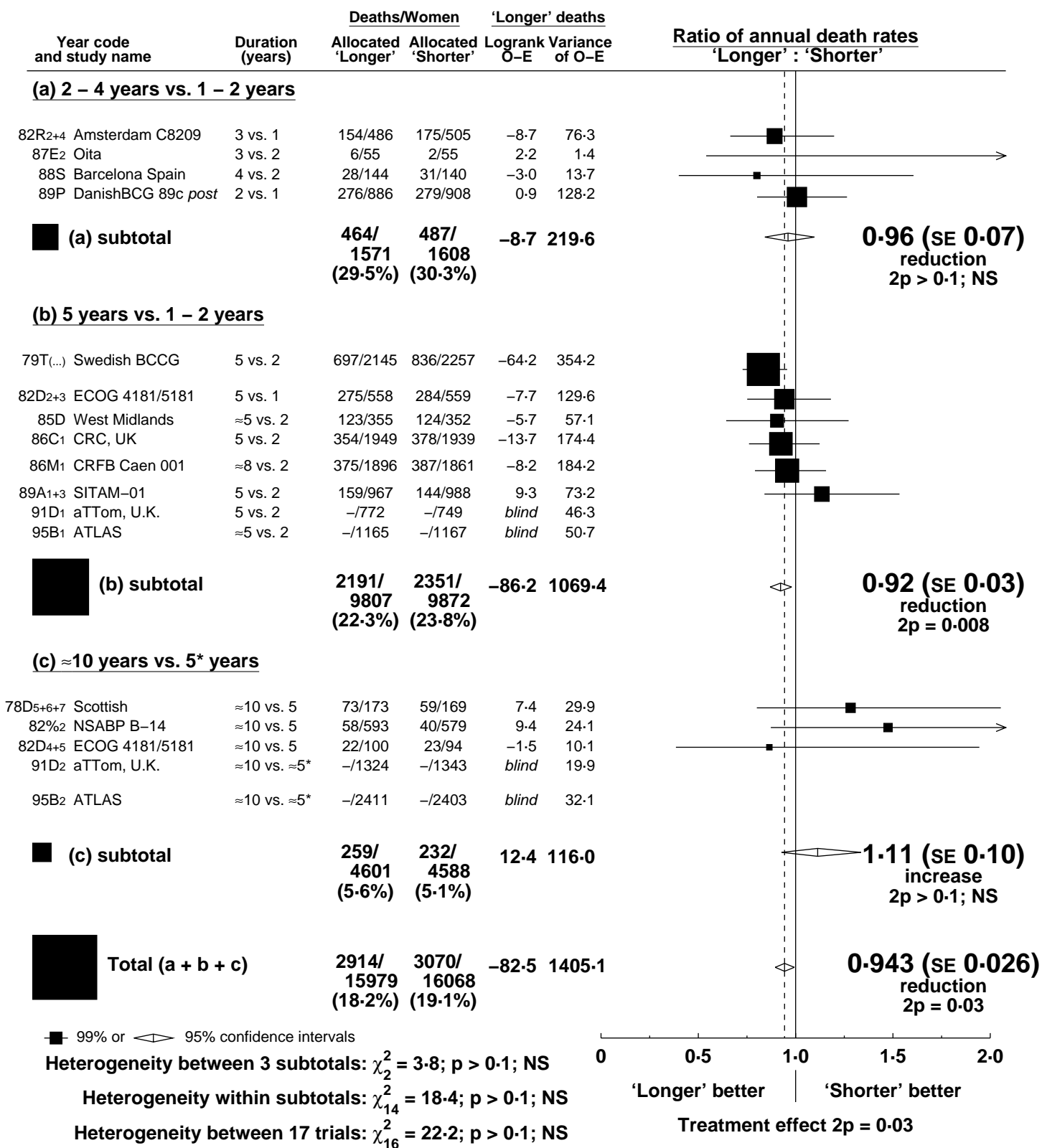
Heterogeneity between 3 subtotals: $\chi^2_2 = 4.4$; $p > 0.1$; NS

Heterogeneity within subtotals: $\chi^2_{14} = 24.9$; $p = 0.04$

Heterogeneity between 17 trials: $\chi^2_{16} = 29.3$; $p = 0.02$

* More than 4 years of tamoxifen at randomisation.





■ 99% or ◊ 95% confidence intervals

Heterogeneity between 3 subtotals: $\chi^2_2 = 3.8$; p > 0.1; NS

Heterogeneity within subtotals: $\chi^2_{14} = 18.4$; p > 0.1; NS

Heterogeneity between 17 trials: $\chi^2_{16} = 22.2$; p > 0.1; NS

* More than 4 years of tamoxifen at randomisation.

Year code and study name	Duration (years)	Deaths/woman-years		'Longer' deaths		Logrank O-E Variance of O-E		Ratio of annual death rates	
		Allocated 'Longer'	Allocated 'Shorter'	'Longer' : 'Shorter'	95% CI				
(a) 2 – 4 years vs. 1 – 2 years									
82R2+4 Amsterdam C8209	3 vs. 1	0/3160	0/3205						
87E2 Oita	3 vs. 2	0/86	0/106						
88S Barcelona Spain	4 vs. 2	1/461	0/379	0.5	0.3				
89P DanishBCG 89c post	2 vs. 1	0/3955	0/3998						
(a) subtotal		1/ 7662 (0.0%/y)	0/ 7688 (0.0%/y)	0.5	0.3				6.82 (SE 6.06) increase 2p > 0.1; NS
(b) 5 years vs. 1 – 2 years									
79T(...) Swedish BCCG	5 vs. 2	3/15376	3/15134	0.6	1.3				
82D2+3 ECOG 4181/5181	5 vs. 1	0/4638	0/4212						
85D West Midlands	≈5 vs. 2	0/2275	0/2042						
86C1 CRC, UK	5 vs. 2	0/9341	0/8994						
86M1 CRFB Caen 001	≈8 vs. 2	0/11877	0/11167						
89A1+3 SITAM-01	5 vs. 2	1/4700	0/4758	0.5	0.3				
91D1 aTTom, U.K.	5 vs. 2	2/1891	1/1812	0.6	0.7				
95B1 ATLAS	≈5 vs. 2	-/2836	-/2824	<i>blind</i>	0.3				
(b) subtotal		6/ 52934 (0.0%/y)	5/ 50943 (0.0%/y)	1.2	2.5				1.65 (SE 0.82) increase 2p > 0.1; NS
(c) ≈10 years vs. 5* years									
78D5+6+7 Scottish	≈10 vs. 5	2/1418	0/1510	1.1	0.5				
82%2 NSABP B-14	≈10 vs. 5	1/3942	0/3937	0.5	0.3				
82D4+5 ECOG 4181/5181	≈10 vs. 5	0/753	0/664						
91D2 aTTom, U.K.	≈10 vs. ≈5*	1/1320	0/1237	0.5	0.3				
95B2 ATLAS	≈10 vs. ≈5*	-/3808	-/3732	<i>blind</i>	0.3				
(c) subtotal		5/ 11241 (0.0%/y)	0/ 11080 (0.0%/y)	2.5	1.3				7.51 (SE 2.89) increase 2p = 0.02
Total (a + b + c)		12/ 71837 (0.0%/y)	5/ 69711 (0.0%/y)	4.2	4.0				2.894 (SE 0.892) increase 2p = 0.03

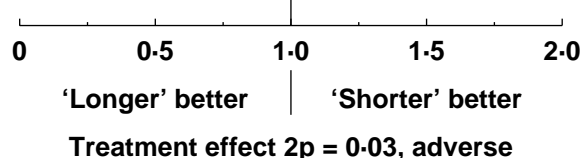
■ 99% or ◁▷ 95% confidence intervals

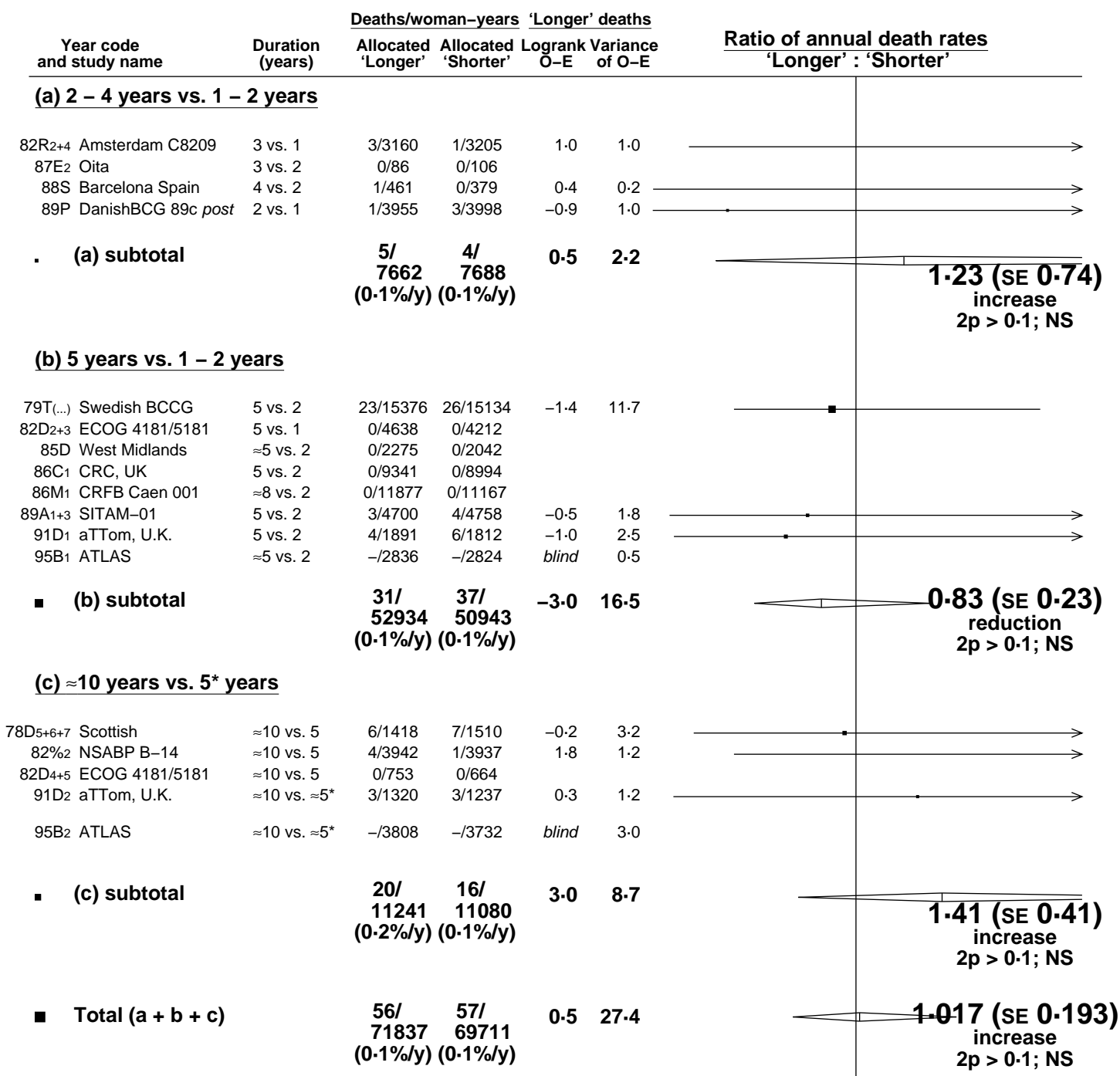
Heterogeneity between 3 subtotals: $\chi^2_2 = 2.1$; $p > 0.1$; NS

Heterogeneity within subtotals: $\chi^2_6 = 2.0$; $p > 0.1$; NS

Heterogeneity between 9 trials: $\chi^2_8 = 4.1$; $p > 0.1$; NS

* More than 4 years of tamoxifen at randomisation.





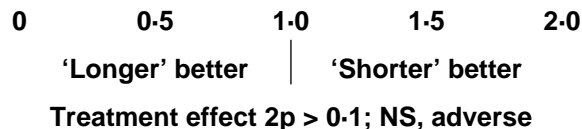
■ 99% or ◊ 95% confidence intervals

Heterogeneity between 3 subtotals: $\chi^2_2 = 1.6$; $p > 0.1$; NS

Heterogeneity within subtotals: $\chi^2_8 = 4.8$; $p > 0.1$; NS

Heterogeneity between 11 trials: $\chi^2_{10} = 6.5$; $p > 0.1$; NS

* More than 4 years of tamoxifen at randomisation.



Year code and study name	Duration (years)	Deaths/woman-years		'Longer' deaths		Logrank Variance O-E of O-E		Ratio of annual death rates 'Longer' : 'Shorter'	
		Allocated 'Longer'	Allocated 'Shorter'						
(a) 2 – 4 years vs. 1 – 2 years									
82R2+4 Amsterdam C8209	3 vs. 1	24/3160	13/3205	5.3	9.0				
87E2 Oita	3 vs. 2	0/86	0/106						
88S Barcelona Spain	4 vs. 2	2/461	0/379	0.9	0.5				
89P DanishBCG 89c post	2 vs. 1	9/3956	5/3998	1.6	3.2				
■ (a) subtotal		35/ 7663	18/ 7688	7.7	12.8	1.83 (SE 0.38) increase 2p = 0.03			
(b) 5 years vs. 1 – 2 years									
79T(...) Swedish BCCG	5 vs. 2	88/15376	105/15134	-8.8	46.9				
82D2+3 ECOG 4181/5181	5 vs. 1	0/4638	0/4212						
85D West Midlands	≈5 vs. 2	0/2275	0/2042						
86C1 CRC, UK	5 vs. 2	0/9341	0/8994						
86M1 CRFB Caen 001	≈8 vs. 2	0/11877	1/11167	-0.5	0.3				
89A1+3 SITAM-01	5 vs. 2	7/4700	11/4758	-1.9	4.5				
91D1 aTTom, U.K.	5 vs. 2	19/1891	10/1812	4.2	7.1				
95B1 ATLAS	≈5 vs. 2	-2836	-2824	<i>blind</i>	4.0				
■ (b) subtotal		121/ 52934	136/ 50943	-8.1	62.8	0.88 (SE 0.12) reduction 2p > 0.1; NS			
(c) ≈10 years vs. 5* years									
78D5+6+7 Scottish	≈10 vs. 5	14/1418	17/1510	-1.2	7.5				
82%2 NSABP B-14	≈10 vs. 5	11/3942	4/3937	3.8	3.7				
82D4+5 ECOG 4181/5181	≈10 vs. 5	0/753	0/664						
91D2 aTTom, U.K.	≈10 vs. ≈5*	11/1320	11/1237	-0.4	5.0				
95B2 ATLAS	≈10 vs. ≈5*	-3808	-3732	<i>blind</i>	8.9				
■ (c) subtotal		60/ 11241	44/ 11080	8.1	25.2	1.38 (SE 0.24) increase 2p > 0.1; NS			
■ Total (a + b + c)		216/ 71838	198/ 69711	7.8	100.7	1.080 (SE 0.104) increase 2p > 0.1; NS			

■ 99% or ◊ 95% confidence intervals

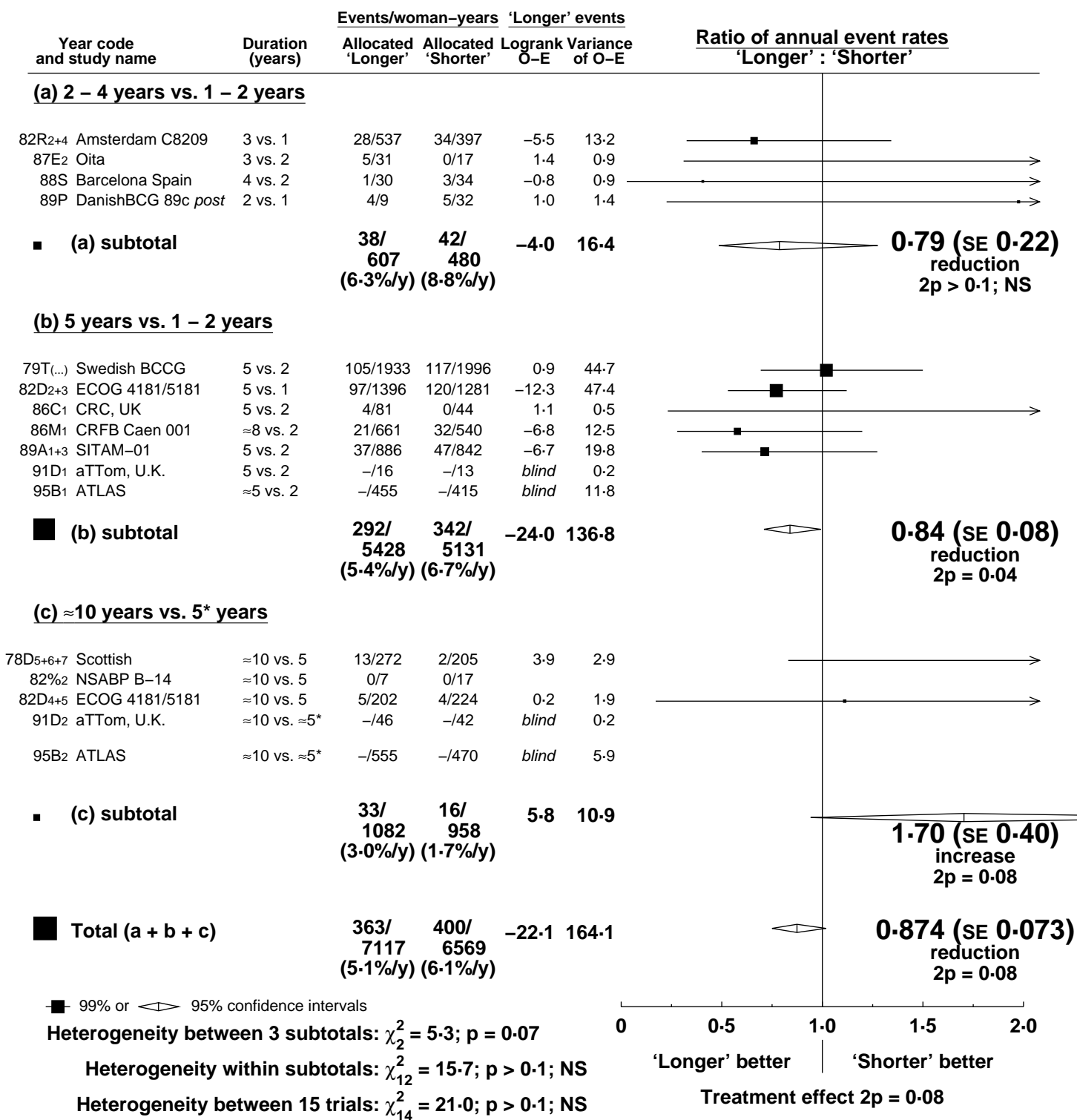
Heterogeneity between 3 subtotals: $\chi^2_2 = 7.8$; p = 0.02

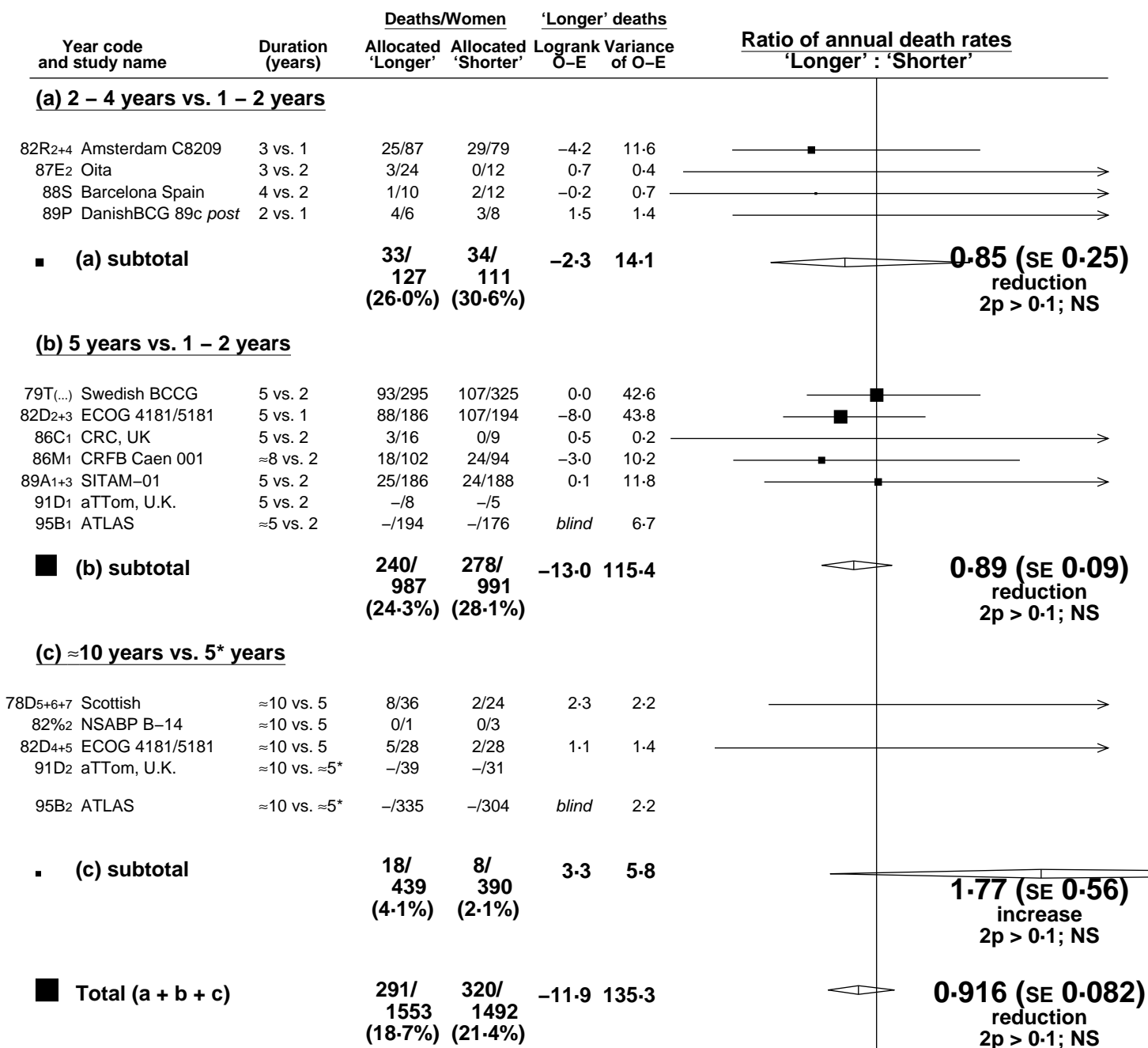
Heterogeneity within subtotals: $\chi^2_9 = 11.5$; p > 0.1; NS

Heterogeneity between 12 trials: $\chi^2_{11} = 19.2$; p = 0.06

* More than 4 years of tamoxifen at randomisation.

0 0.5 1.0 1.5 2.0
 'Longer' better | 'Shorter' better
 Treatment effect 2p > 0.1; NS, adverse





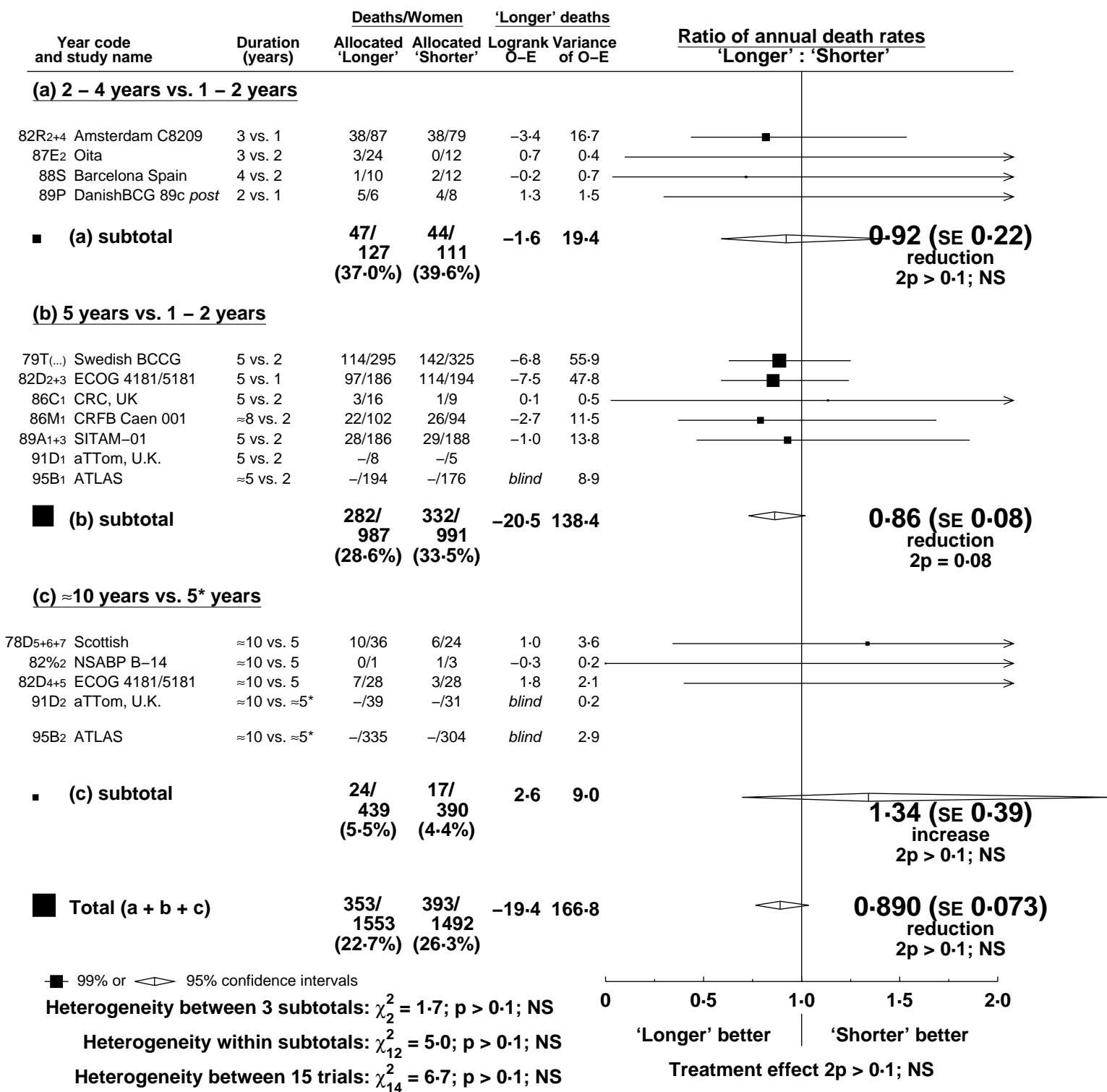
■ 99% or ◊ 95% confidence intervals

Heterogeneity between 3 subtotals: $\chi^2 = 2.6$; $p > 0.1$; NS

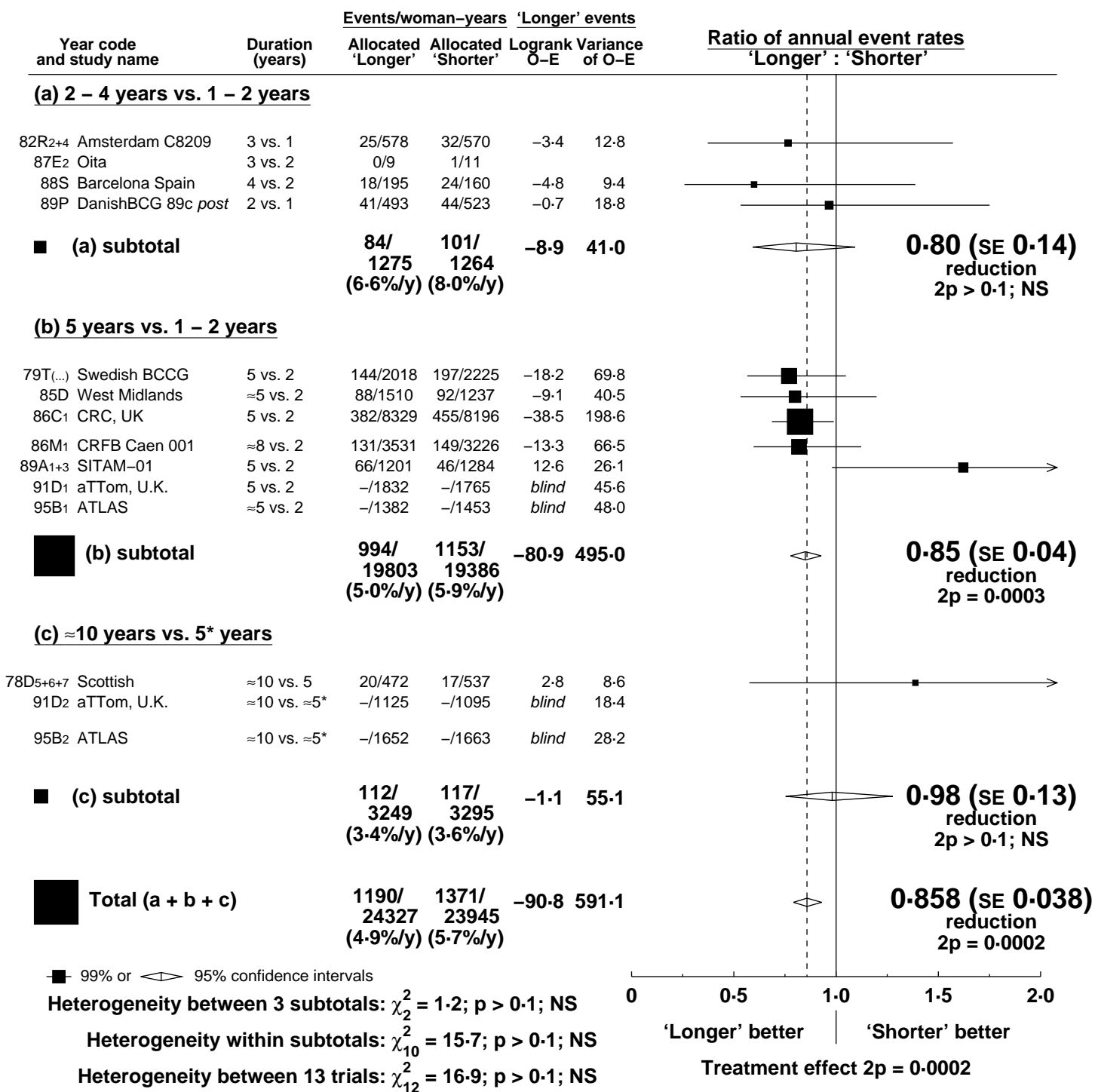
Heterogeneity within subtotals: $\chi^2_{10} = 8.3$; $p > 0.1$; NS

Heterogeneity between 13 trials: $\chi^2_{12} = 10.9$; $p > 0.1$; NS

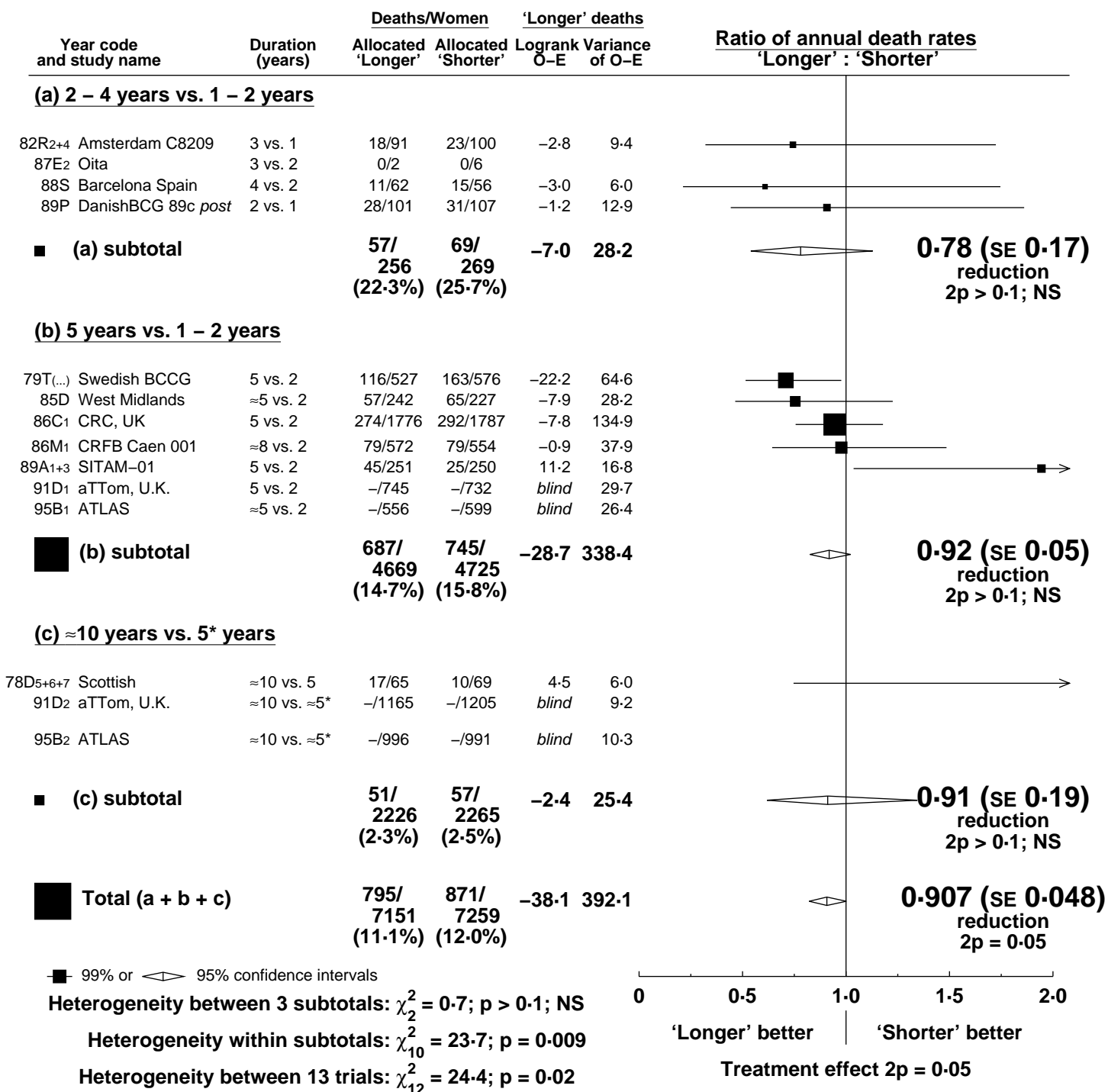
* More than 4 years of tamoxifen at randomisation.



* More than 4 years of tamoxifen at randomisation.

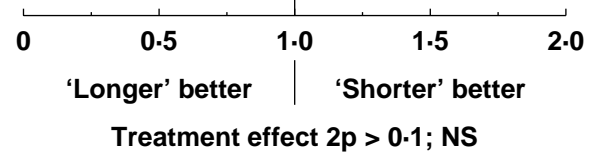


* More than 4 years of tamoxifen at randomisation.



* More than 4 years of tamoxifen at randomisation.

Year code and study name	Duration (years)	Deaths/Women		'Longer' deaths		Logrank O-E	Variance of O-E	Ratio of annual death rates 'Longer' : 'Shorter'
		Allocated 'Longer'	Allocated 'Shorter'	O-E	O-E			
(a) 2 – 4 years vs. 1 – 2 years								
82R2+4 Amsterdam C8209	3 vs. 1	21/91	29/100	-4.6	11.6			
87E2 Oita	3 vs. 2	0/2	0/6					
88S Barcelona Spain	4 vs. 2	13/62	17/56	-3.2	7.0			
89P DanishBCG 89c post	2 vs. 1	30/101	37/107	-2.8	14.8			
■ (a) subtotal		64/ 256 (25.0%)	83/ 269 (30.9%)	-10.6	33.4			0.73 (SE 0.15) reduction 2p = 0.07
(b) 5 years vs. 1 – 2 years								
79T(...) Swedish BCCG	5 vs. 2	155/527	197/576	-18.5	82.5			
85D West Midlands	≈5 vs. 2	76/242	81/227	-7.4	36.7			
86C1 CRC, UK	5 vs. 2	326/1776	341/1787	-6.6	160.0			
86M1 CRFB Caen 001	≈8 vs. 2	114/572	105/554	2.0	52.9			
89A1+3 SITAM-01	5 vs. 2	49/251	29/250	11.3	18.8			
91D1 aTTom, U.K.	5 vs. 2	-745	-732	<i>blind</i>	45.2			
95B1 ATLAS	≈5 vs. 2	-556	-599	<i>blind</i>	30.3			
■ (b) subtotal		884/ 4669 (18.9%)	905/ 4725 (19.2%)	-12.1	426.3			0.97 (SE 0.05) reduction 2p > 0.1; NS
(c) ≈10 years vs. 5* years								
78D5+6+7 Scottish	≈10 vs. 5	29/65	26/69	3.1	12.5			
91D2 aTTom, U.K.	≈10 vs. ≈5*	-1165	-1205	<i>blind</i>	18.0			
95B2 ATLAS	≈10 vs. ≈5*	-996	-991	<i>blind</i>	17.0			
■ (c) subtotal		98/ 2226 (4.4%)	101/ 2265 (4.5%)	-0.5	47.4			0.99 (SE 0.14) reduction 2p > 0.1; NS
■ Total (a + b + c)		1046/ 7151 (14.6%)	1089/ 7259 (15.0%)	-23.2	507.1			0.955 (SE 0.043) reduction 2p > 0.1; NS



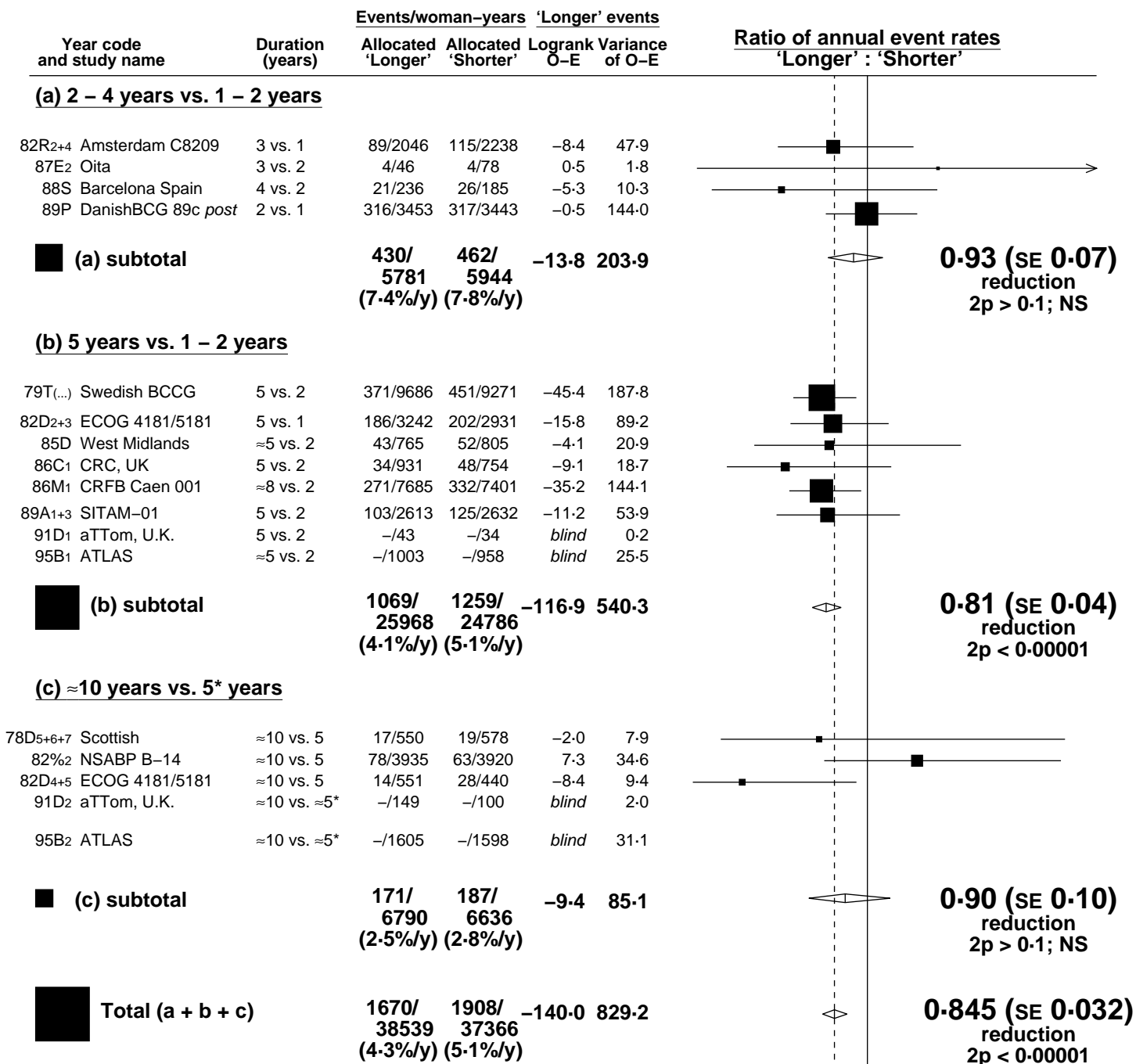
■ 99% or ◊ 95% confidence intervals

Heterogeneity between 3 subtotals: $\chi^2_2 = 2.7$; $p > 0.1$; NS

Heterogeneity within subtotals: $\chi^2_{10} = 17.0$; $p = 0.07$

Heterogeneity between 13 trials: $\chi^2_{12} = 19.7$; $p = 0.07$

* More than 4 years of tamoxifen at randomisation.



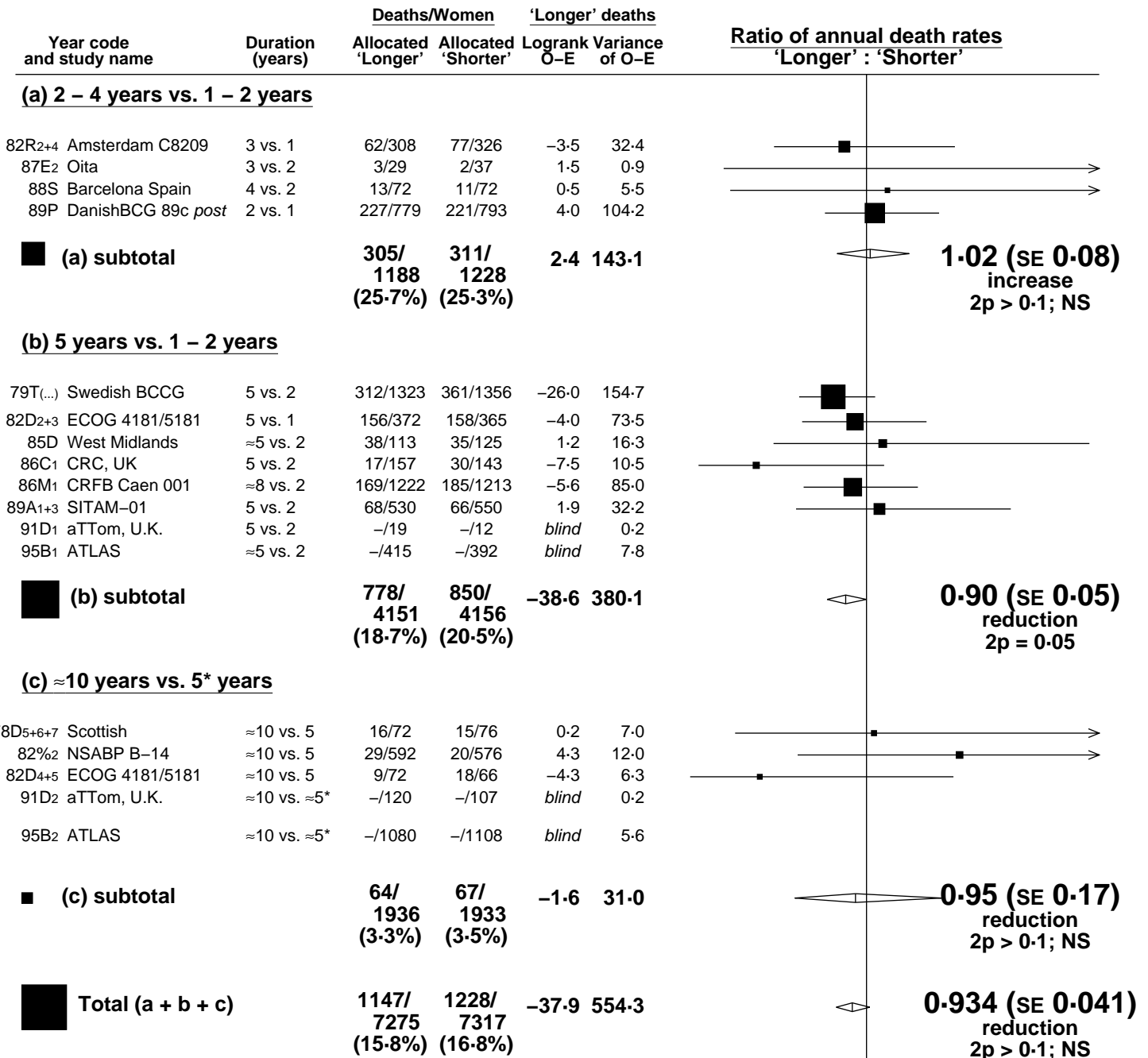
■ 99% or ◊ 95% confidence intervals

Heterogeneity between 3 subtotals: $\chi^2_2 = 3.6$; $p > 0.1$; NS

Heterogeneity within subtotals: $\chi^2_{14} = 20.6$; $p > 0.1$; NS

Heterogeneity between 17 trials: $\chi^2_{16} = 24.2$; $p = 0.08$

* More than 4 years of tamoxifen at randomisation.



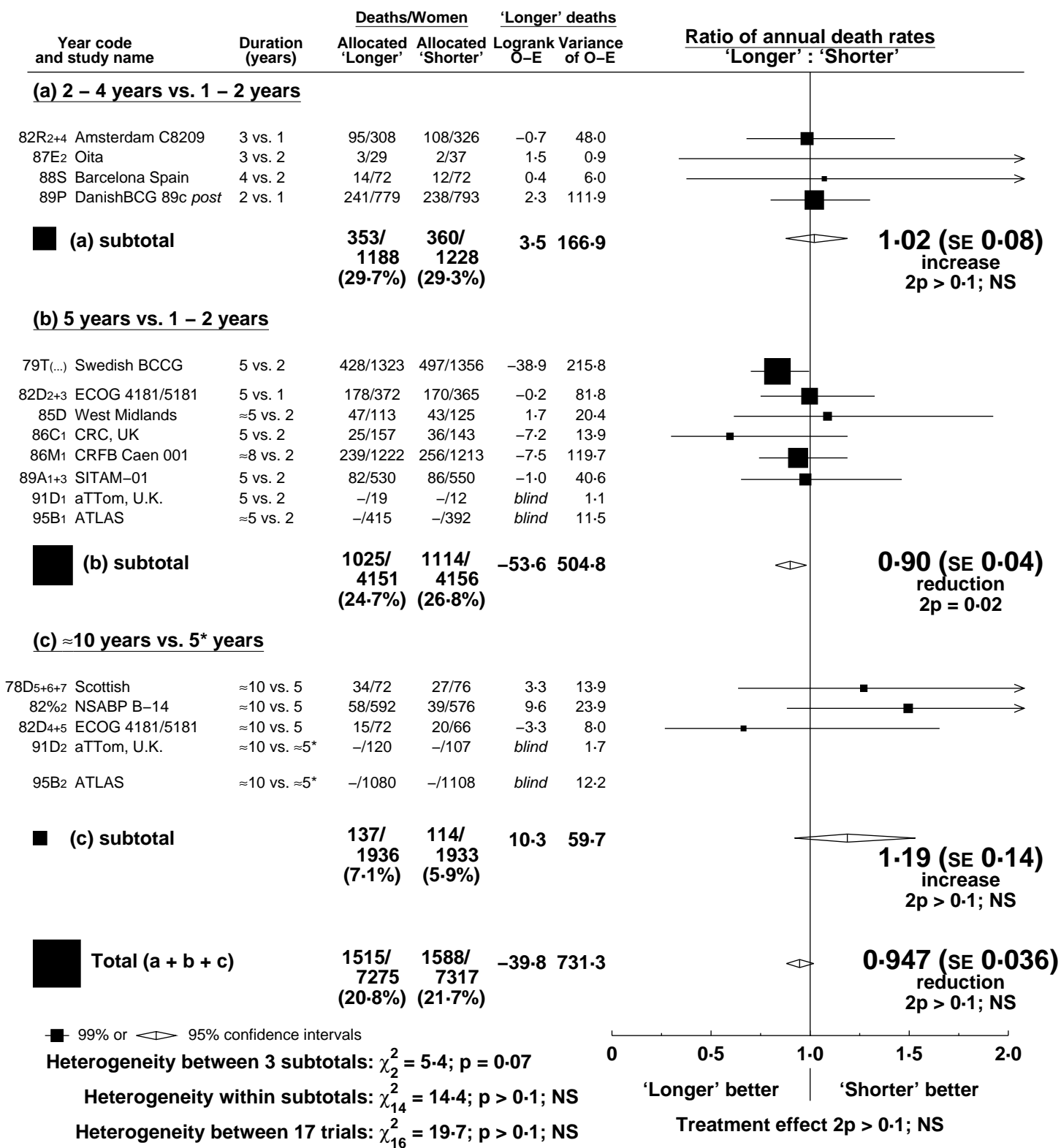
■ 99% or ◊ 95% confidence intervals

Heterogeneity between 3 subtotals: $\chi^2_2 = 1.5$; $p > 0.1$; NS

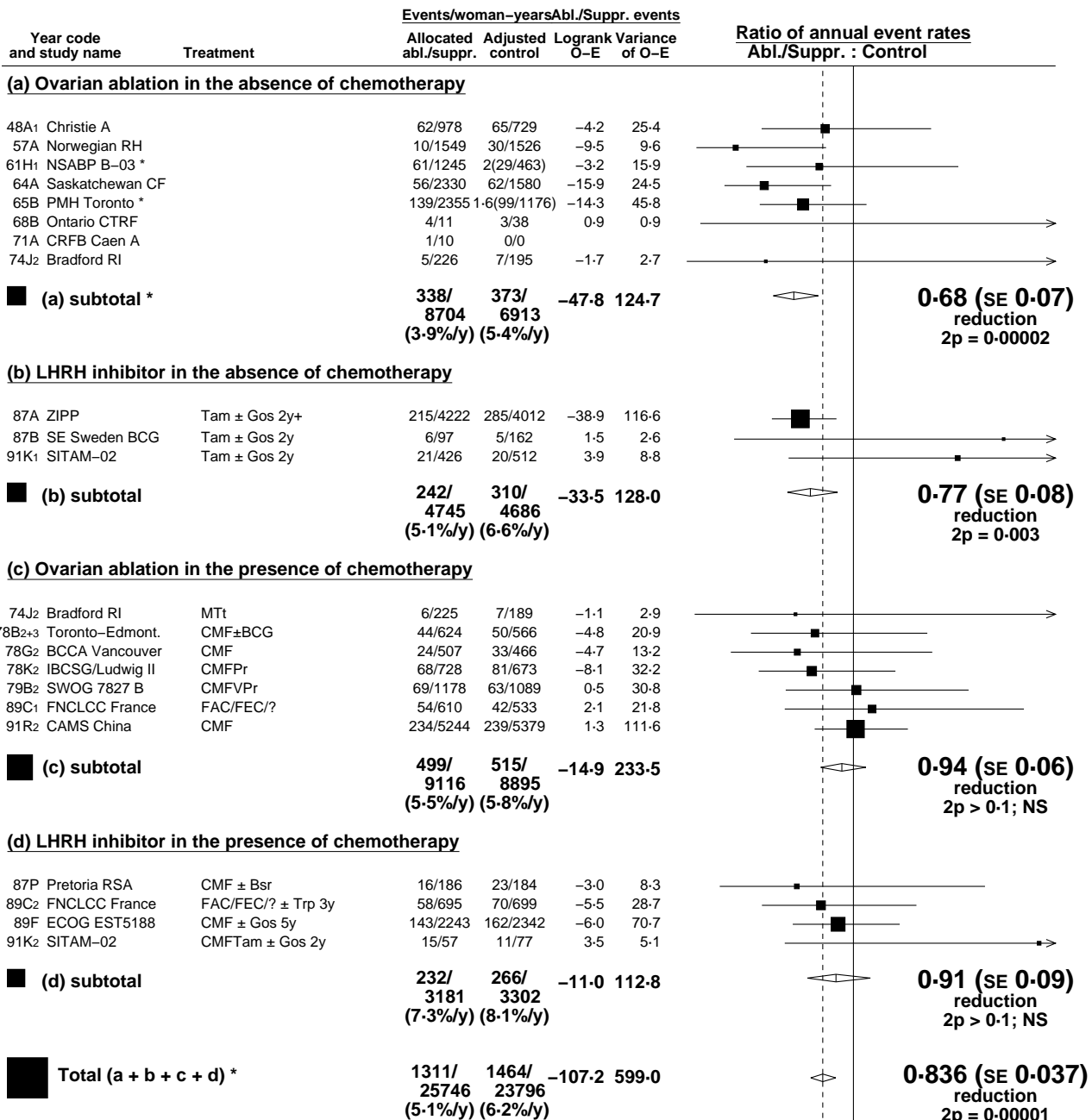
Heterogeneity within subtotals: $\chi^2_{14} = 16.0$; $p > 0.1$; NS

Heterogeneity between 17 trials: $\chi^2_{16} = 17.5$; $p > 0.1$; NS

* More than 4 years of tamoxifen at randomisation.



* More than 4 years of tamoxifen at randomisation.



■ 99% or ◊ 95% confidence intervals

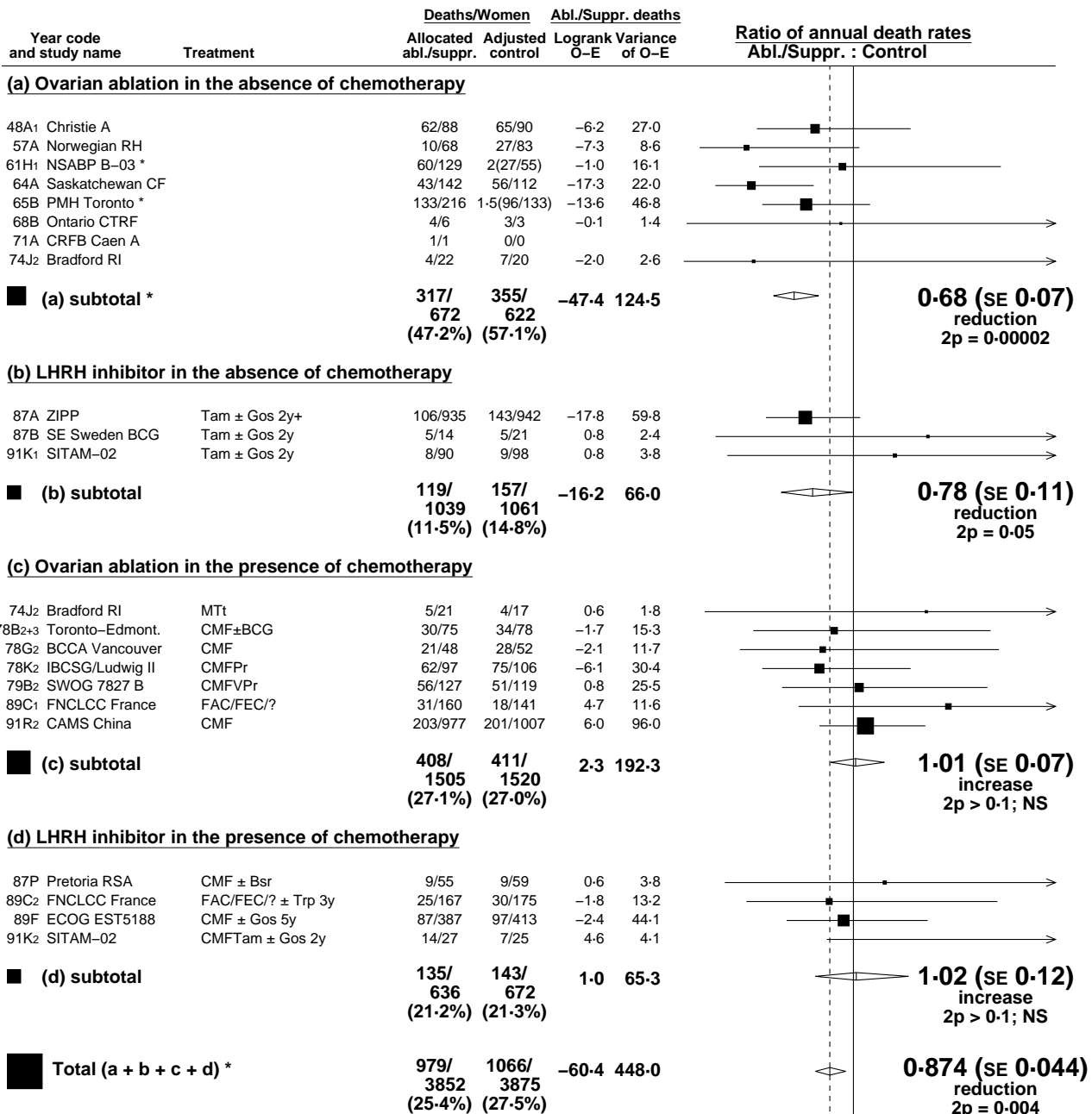
Heterogeneity between 4 subtotals: $\chi^2_3 = 9.9$; $p = 0.02$

Heterogeneity within subtotals: $\chi^2_{17} = 24.4$; $p > 0.1$; NS

Heterogeneity between 21 trials: $\chi^2_{20} = 34.3$; $p = 0.02$

0 0.5 1.0 1.5 2.0
Abl./Suppr. better | Abl./Suppr. worse
Treatment effect 2p = 0.00001

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.

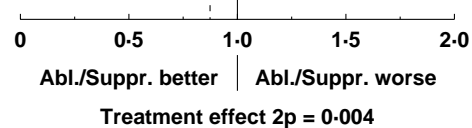


■ 99% or ◁▷ 95% confidence intervals

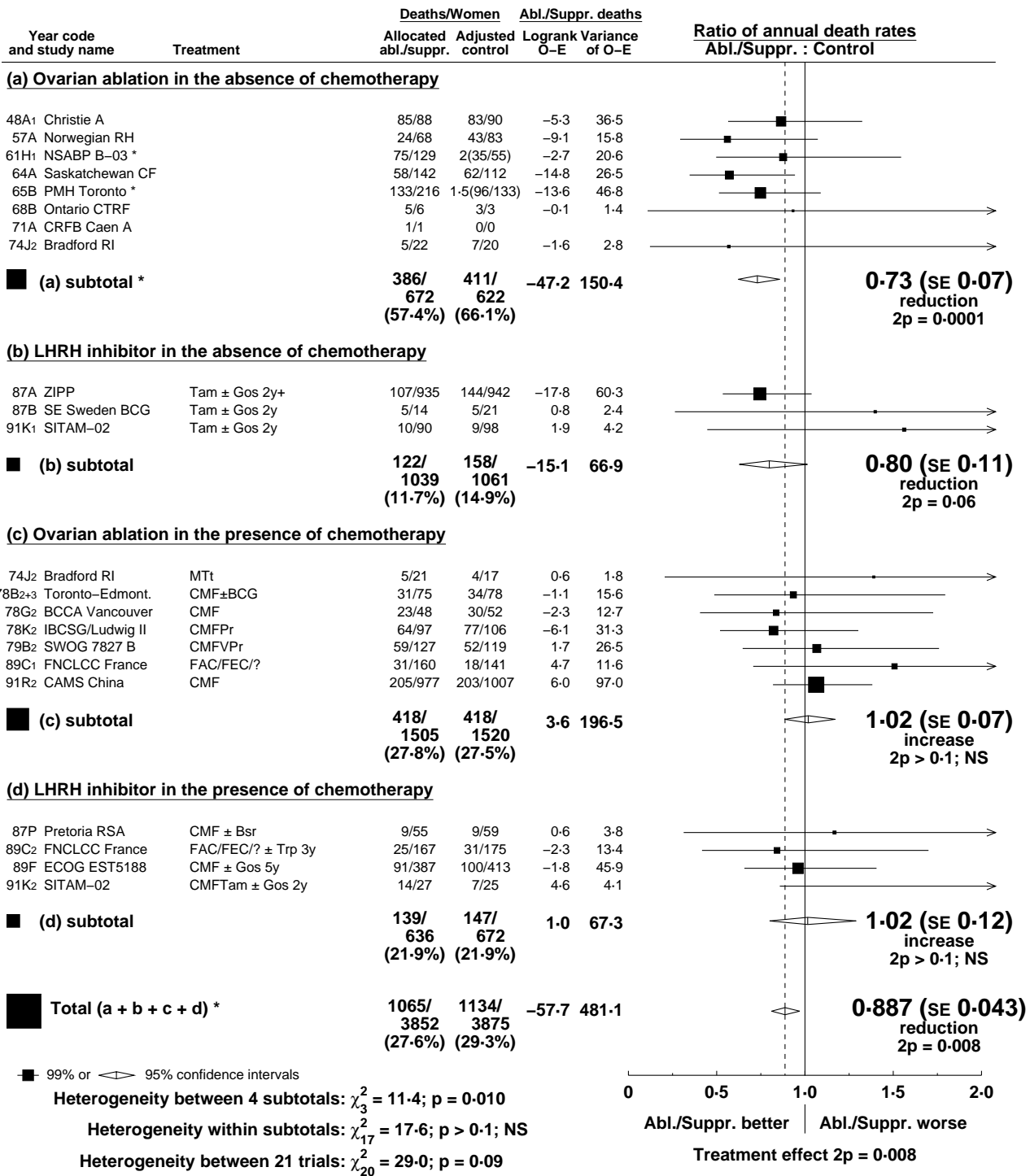
Heterogeneity between 4 subtotals: $\chi^2_3 = 14.0$; $p = 0.003$

Heterogeneity within subtotals: $\chi^2_{17} = 20.3$; $p > 0.1$; NS

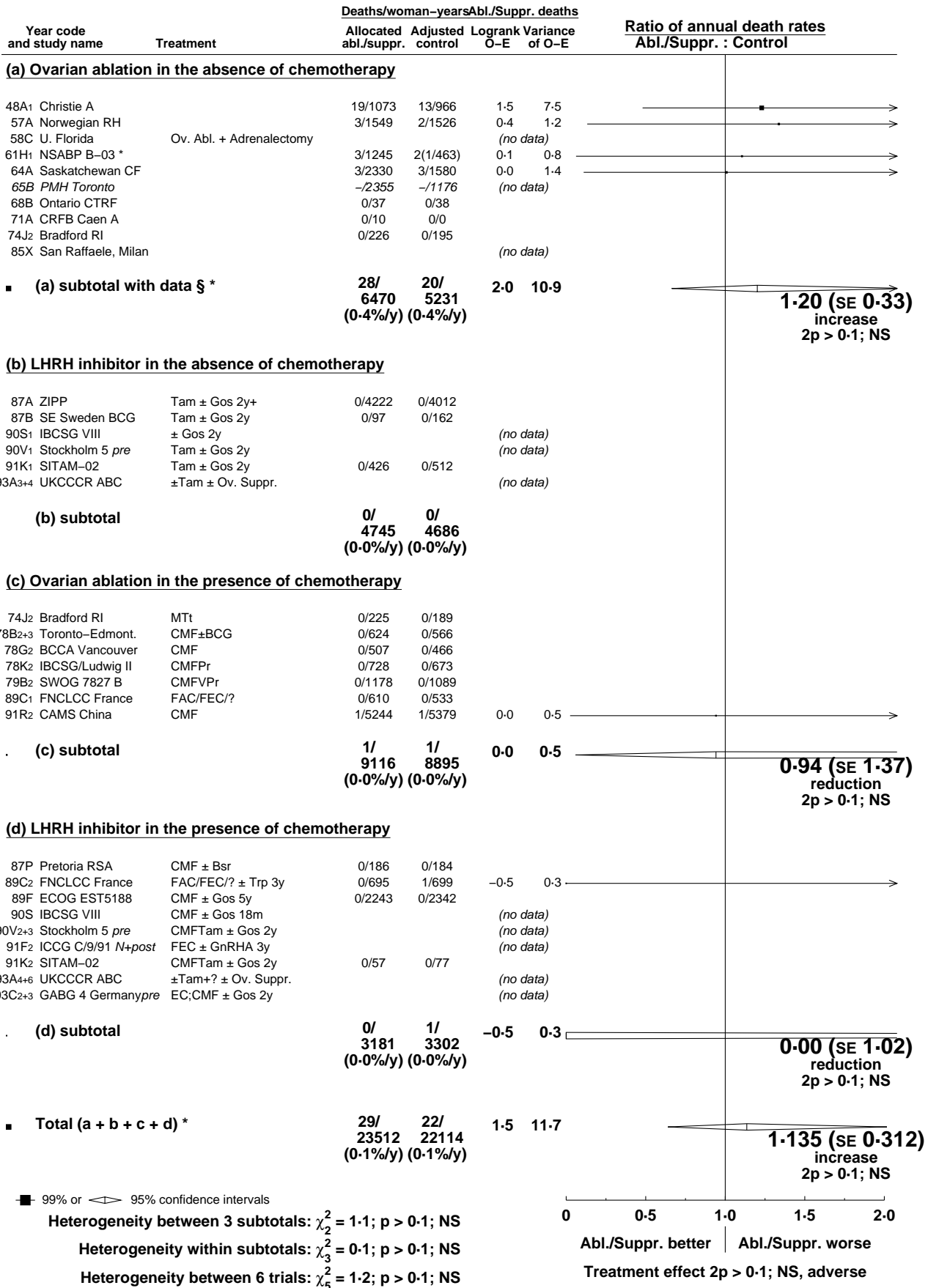
Heterogeneity between 21 trials: $\chi^2_{20} = 34.2$; $p = 0.02$



* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.

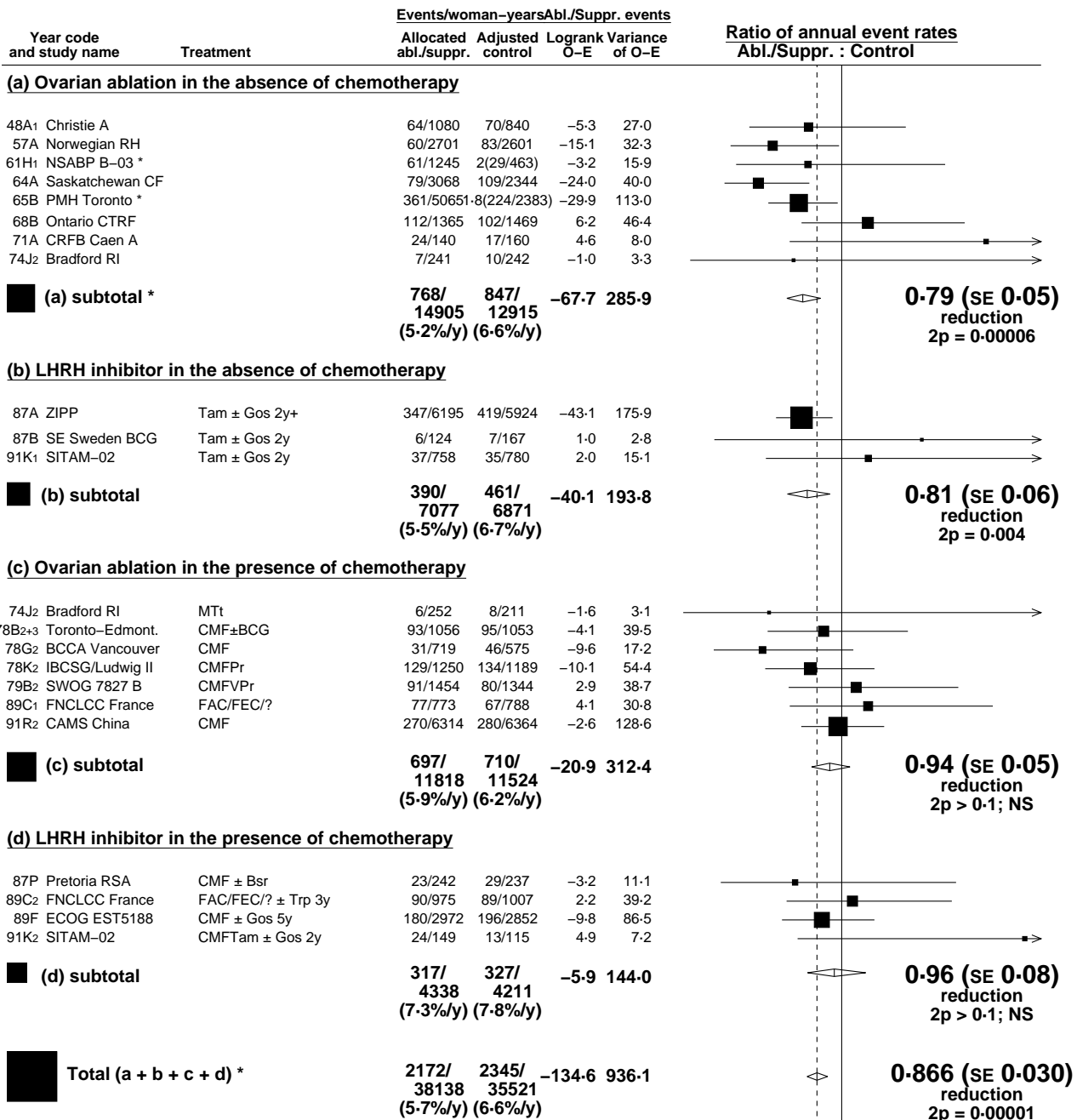


* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.



§ 1 trial with no data does not contribute to subtotals or to the overall total (allocated abl./suppr.: 2355; allocated control: 1176)

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.



■ 99% or ◊ 95% confidence intervals

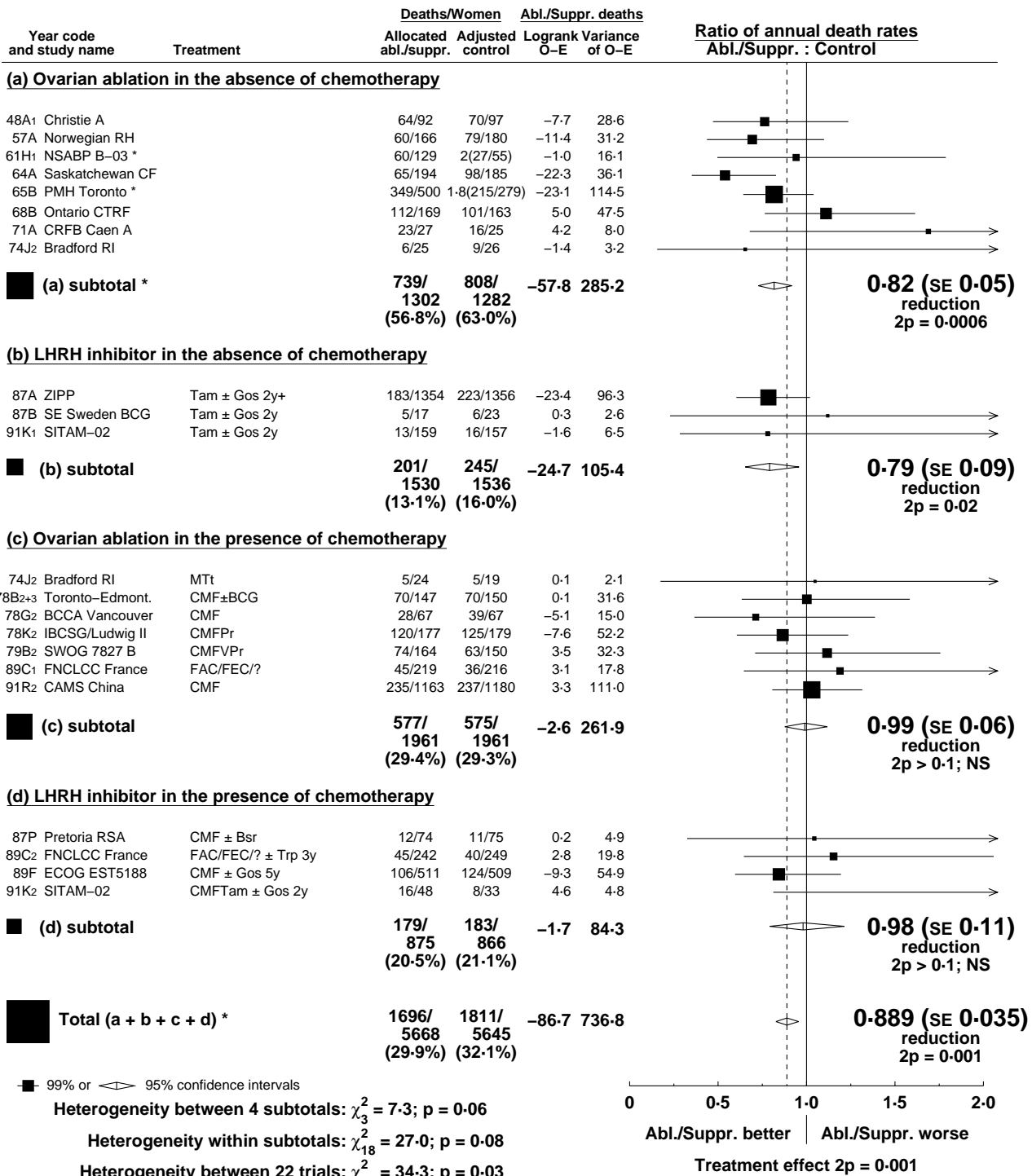
Heterogeneity between 4 subtotals: $\chi^2_3 = 6.6$; $p = 0.09$

Heterogeneity within subtotals: $\chi^2_{18} = 35.0$; $p = 0.009$

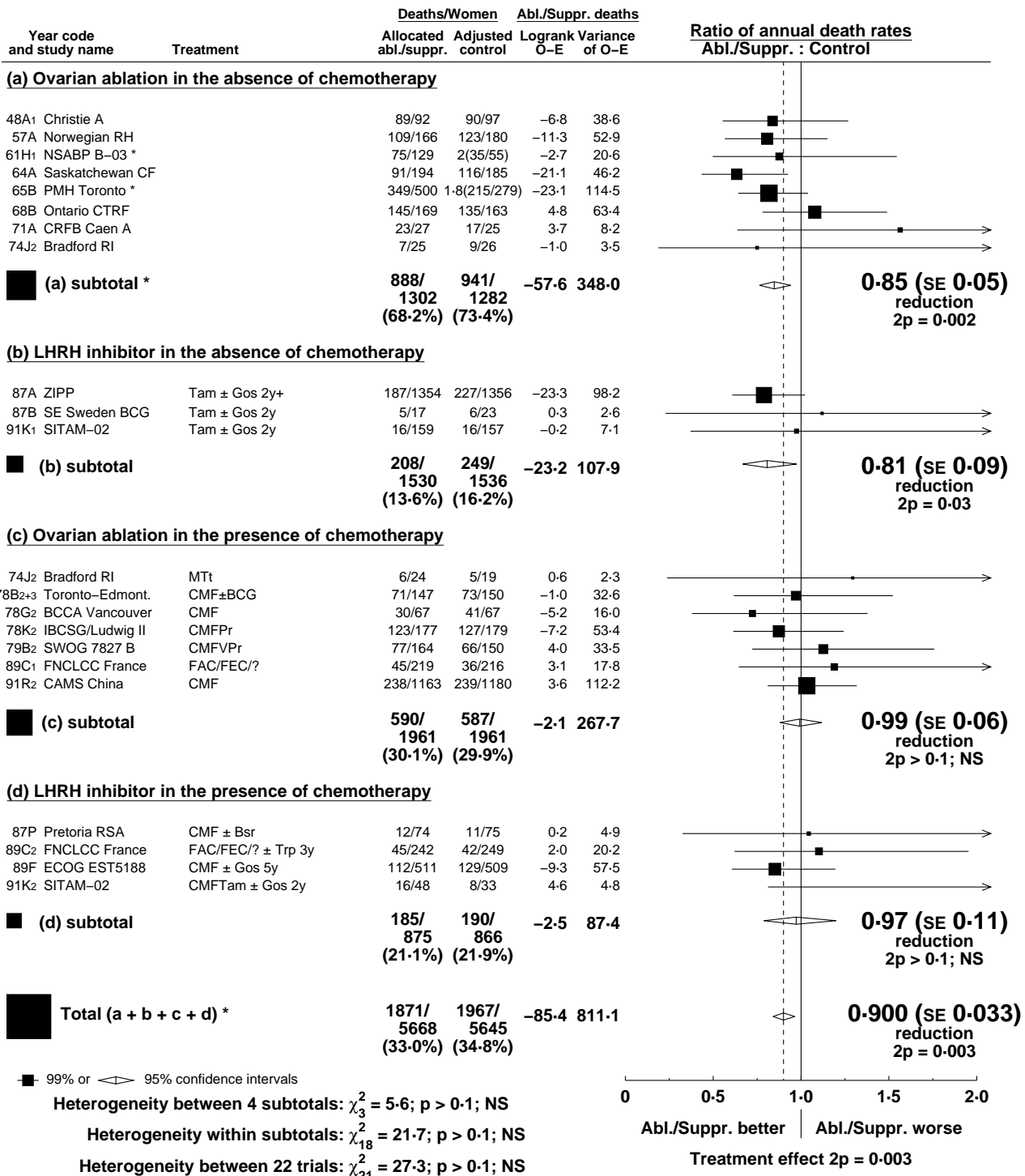
Heterogeneity between 22 trials: $\chi^2_{21} = 41.6$; $p = 0.005$

* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/women.

0 0.5 1.0 1.5 2.0
Abl./Suppr. better | Abl./Suppr. worse
Treatment effect 2p = 0.00001



* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/women.



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