

THE LANCET

Supplementary webappendix

This webappendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

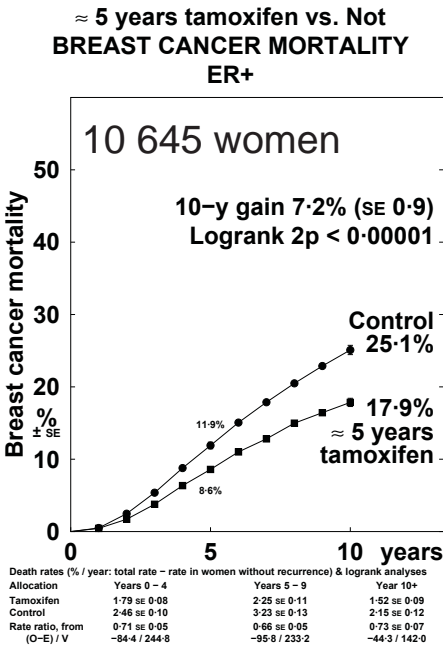
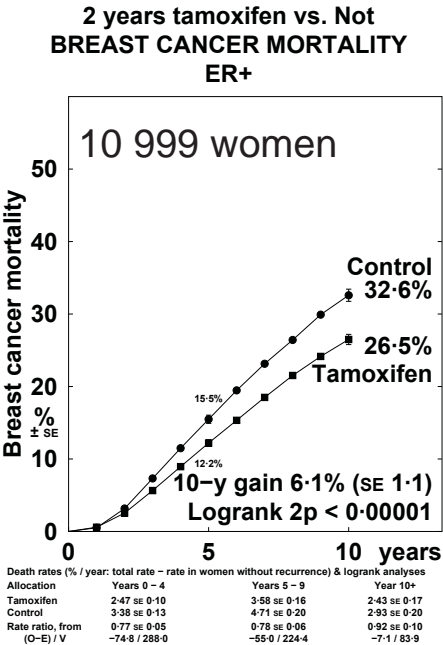
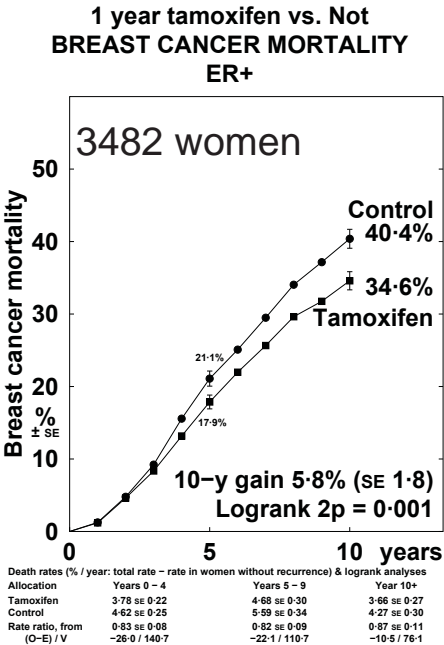
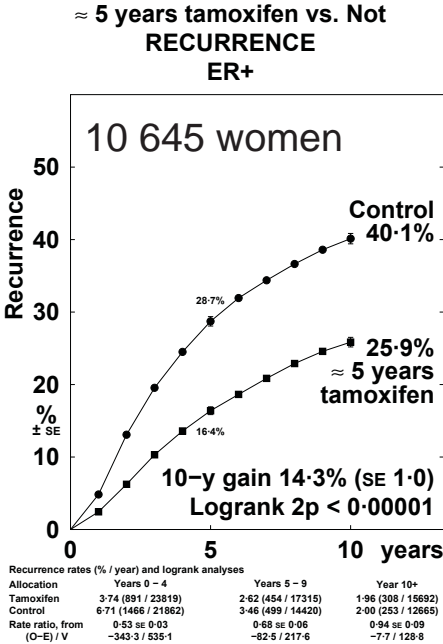
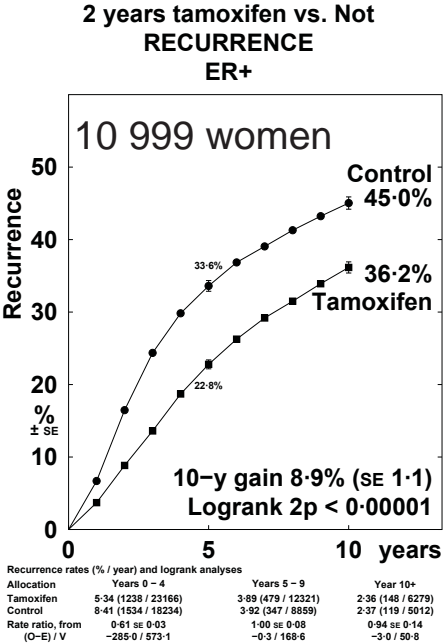
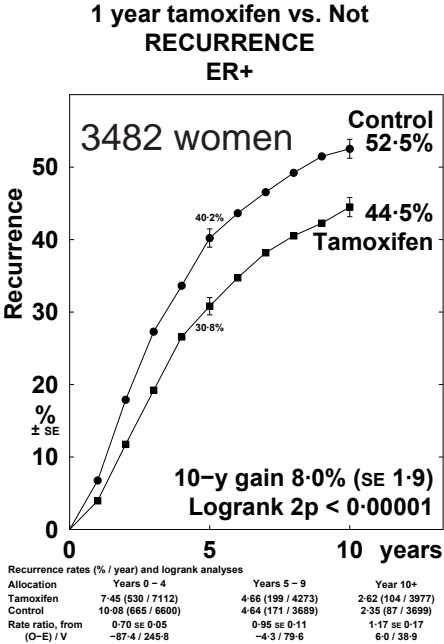
Supplement to: Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. *Lancet* 2011; published online July 29. DOI:10.1016/S0140-6736(11)60993-8.

Webappendix: Supplementary figures and tables for “Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials” *Analyses are by allocated treatment: tamoxifen vs control (no adjuvant tam.)*

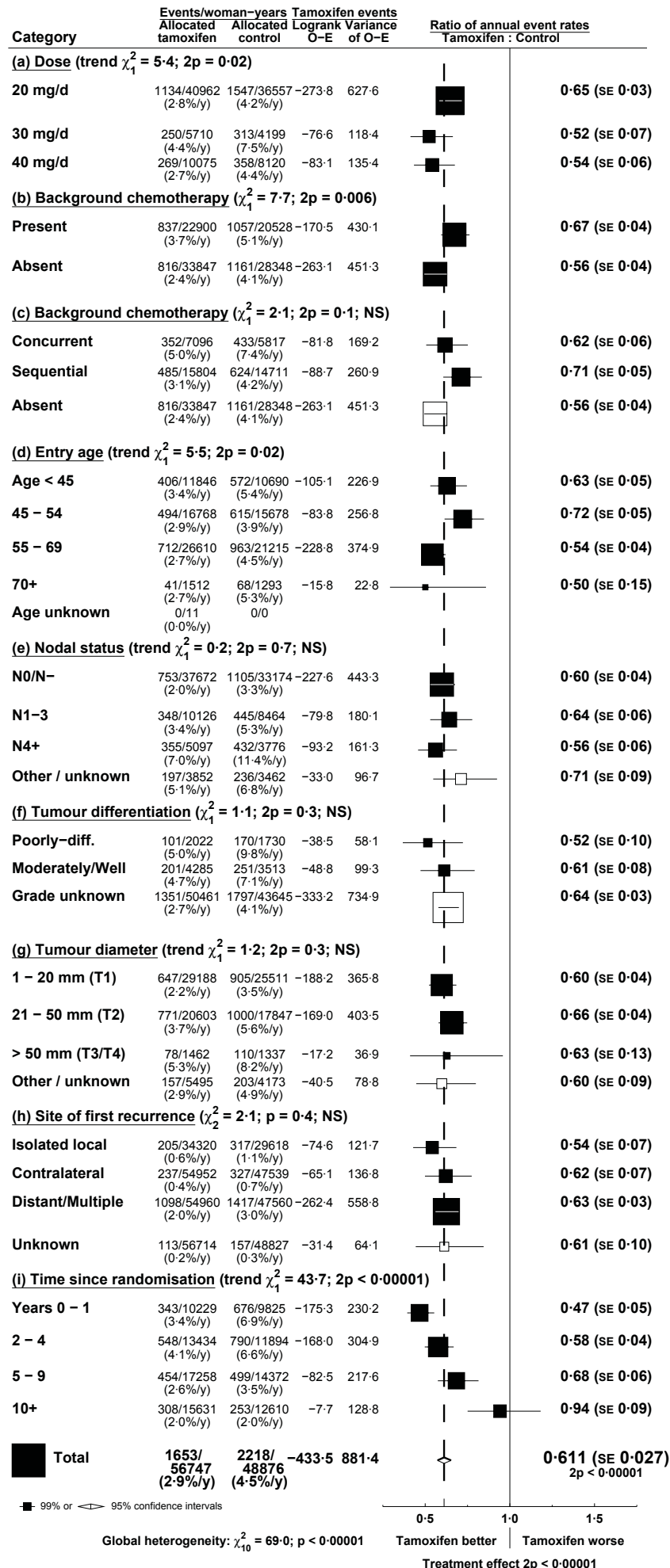
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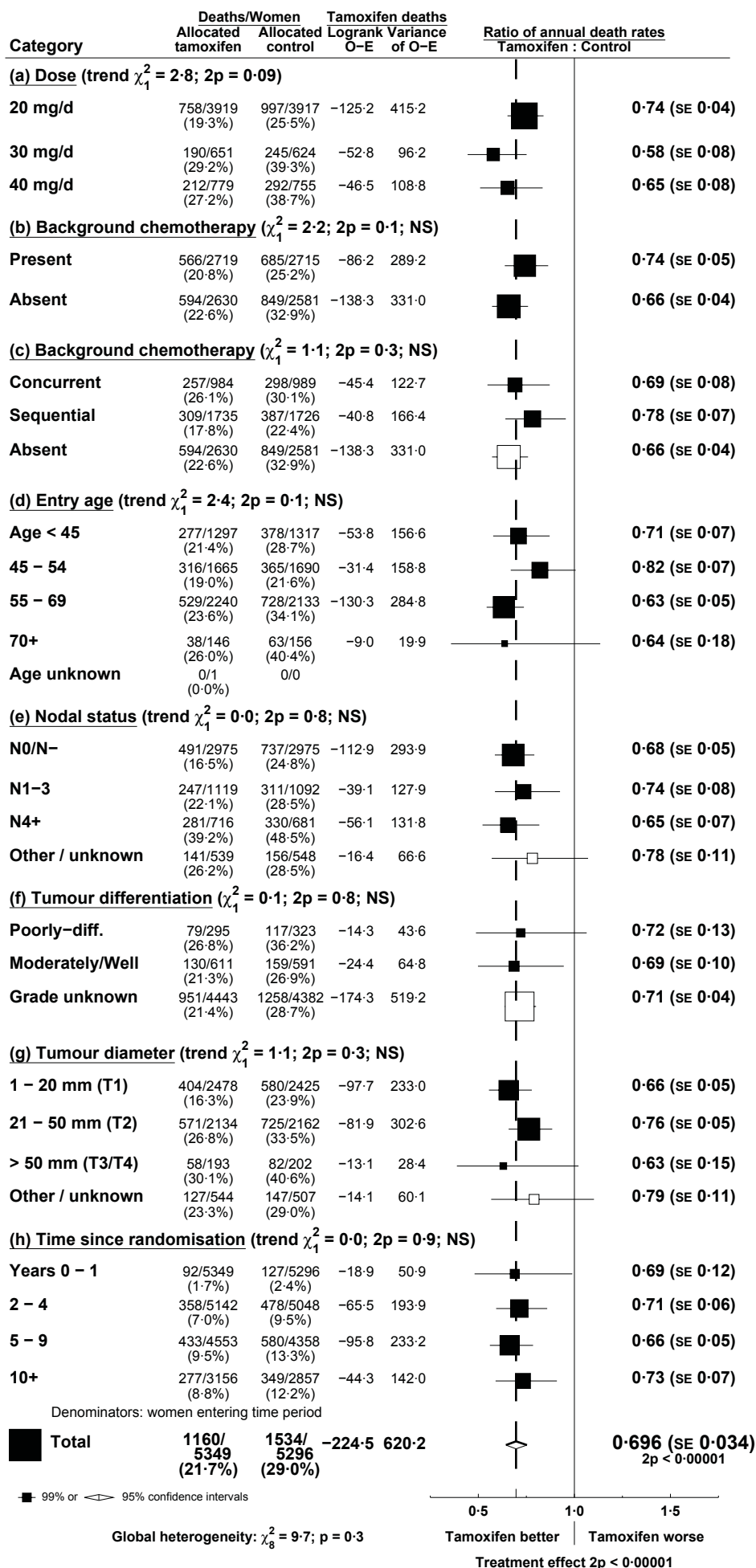
p 2: 10-year recurrence & breast cancer mortality, ER+ disease: 1, 2 or 5 years tam.



p 3: RRs for recurrence, multiple subgroup analyses, ER+ disease: ~5 years tam.



p 4: RRs for death with recurrence, multiple subgroup analyses, ER+ disease: ~5 years tam.

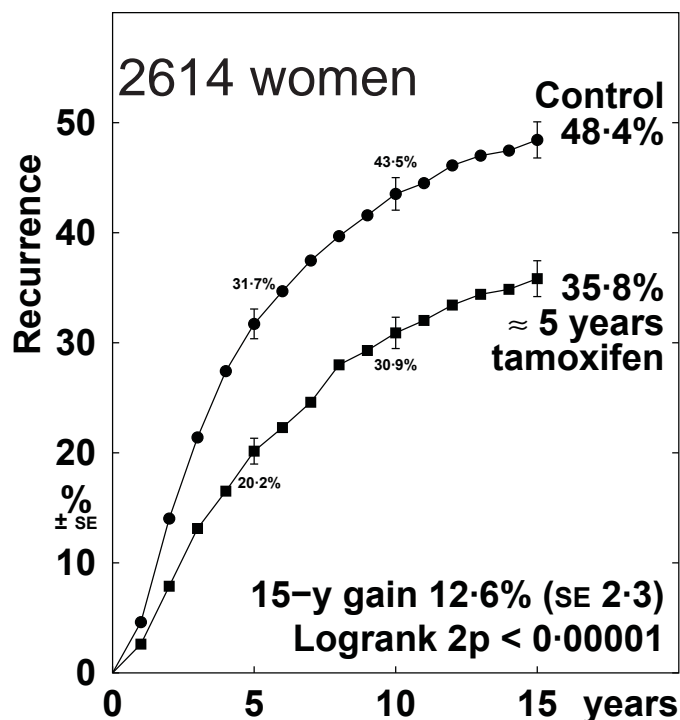


p 5: 15-year outcomes, age at entry <45 years, ER+ disease: ~5 years tam.

≈ 5 years tamoxifen vs. Not

RECURRENCE

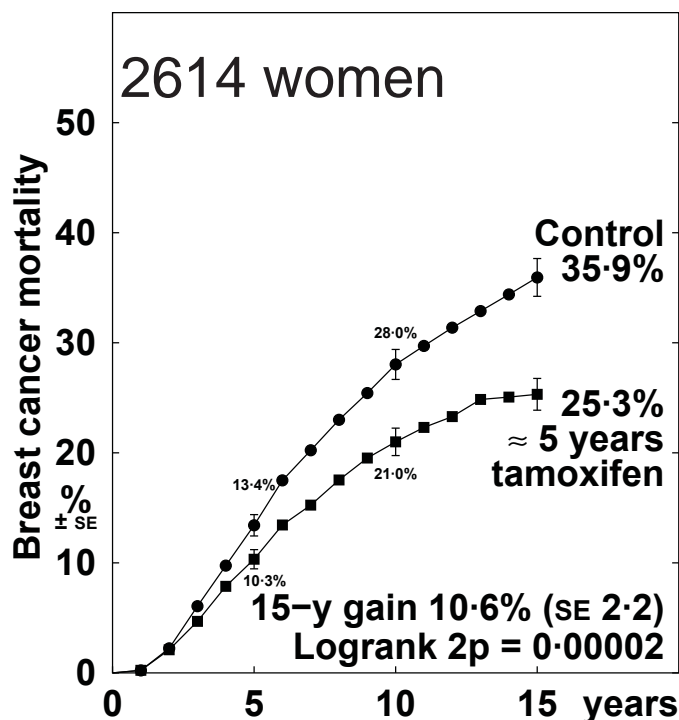
Entry age < 45, ER+



≈ 5 years tamoxifen vs. Not

BREAST CANCER MORTALITY

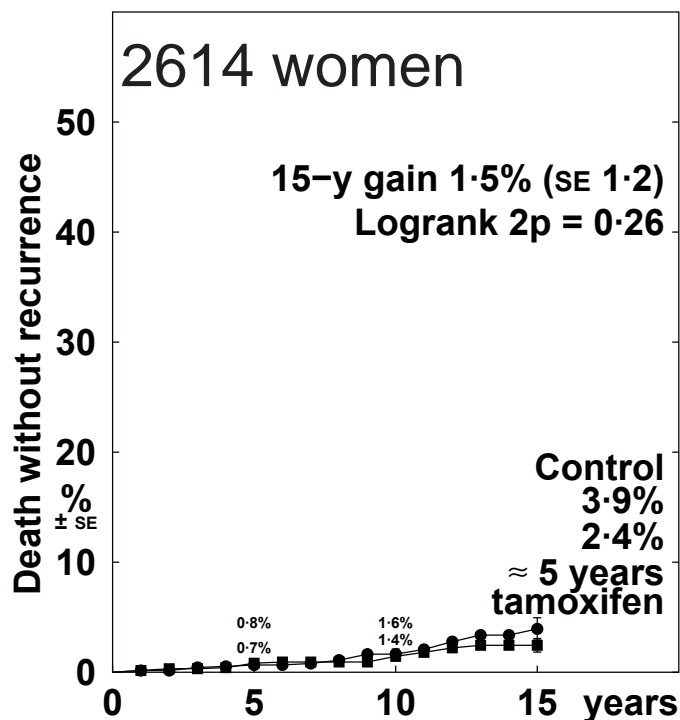
Entry age < 45, ER+



≈ 5 years tamoxifen vs. Not

DEATH WITHOUT RECURRENCE

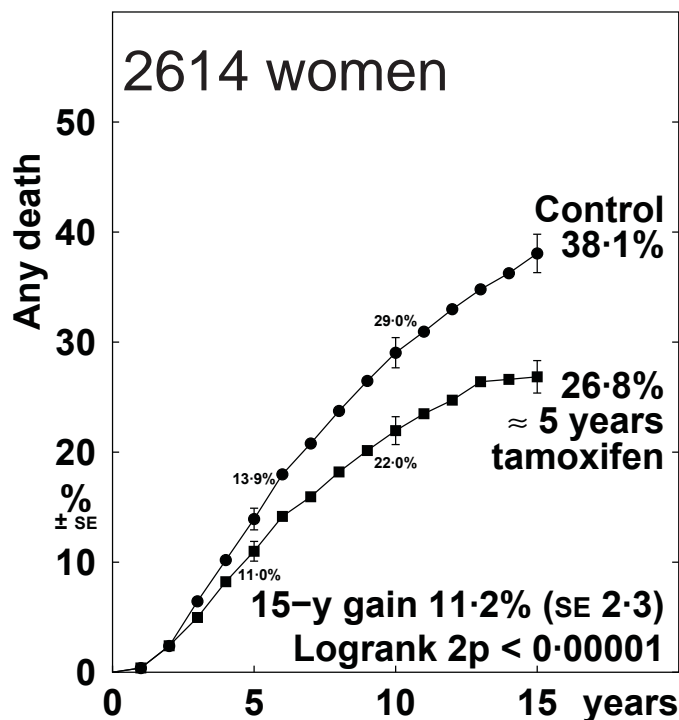
Entry age < 45, ER+



≈ 5 years tamoxifen vs. Not

ANY DEATH

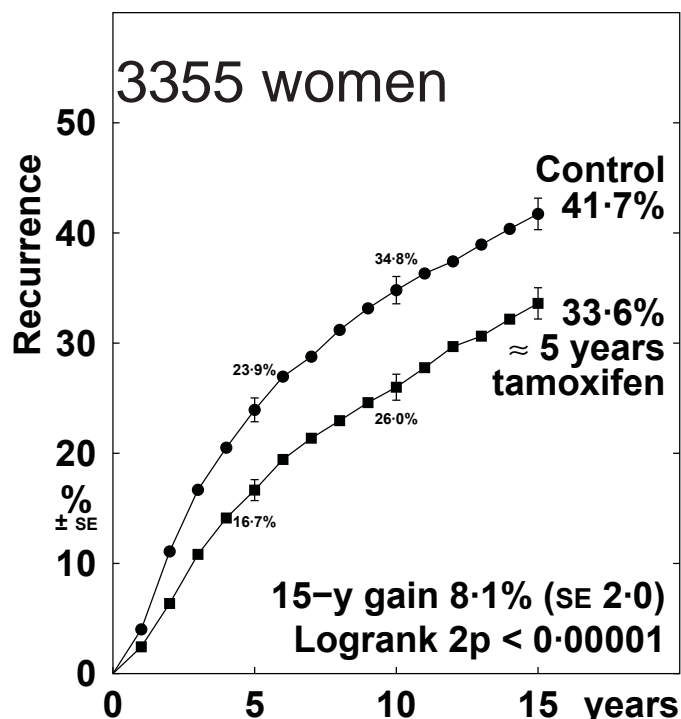
Entry age < 45, ER+



≈ 5 years tamoxifen vs. Not

RECURRENCE

Entry age 45-54, ER+



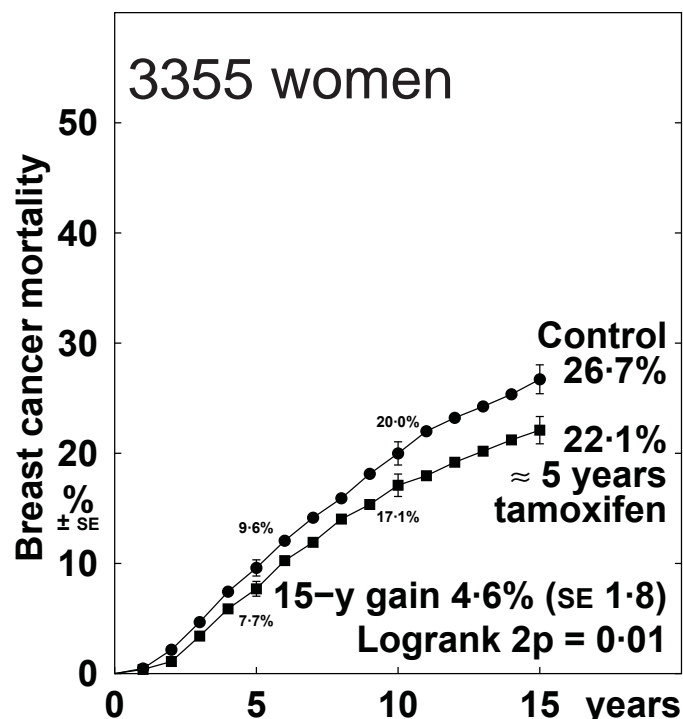
Recurrence rates (% / year) and logrank analyses

Allocation	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
Tamoxifen	3.69 (274 / 7420)	2.60 (135 / 5200)	2.18 (62 / 2849)	1.74 (23 / 1322)
Control	5.47 (392 / 7170)	3.00 (143 / 4763)	2.25 (58 / 2573)	1.84 (22 / 1196)
Rate ratio, from (O-E) / V	0.66 SE 0.07 -64.0 / 153.3	0.78 SE 0.11 -16.3 / 64.3	0.99 SE 0.18 -0.4 / 29.0	0.74 SE 0.27 -3.1 / 10.2

≈ 5 years tamoxifen vs. Not

BREAST CANCER MORTALITY

Entry age 45-54, ER+



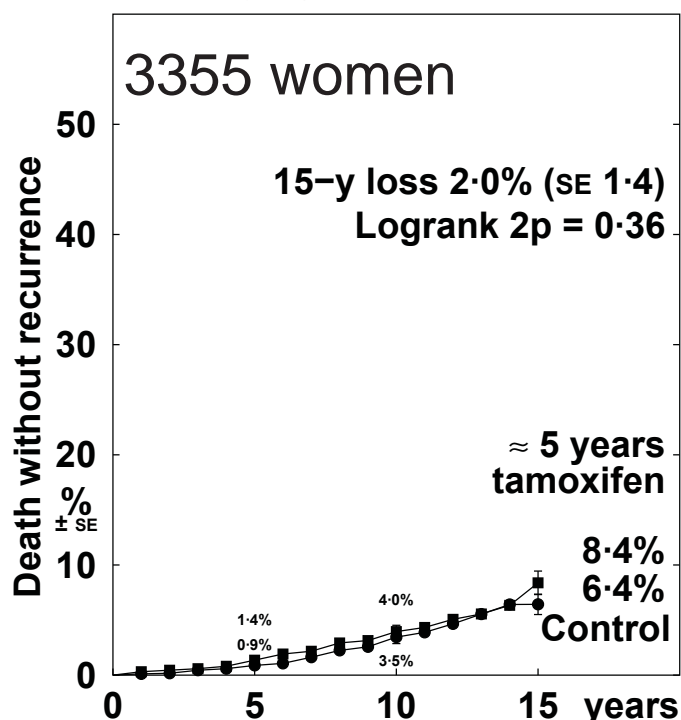
Death rates (% / year: total rate - rate in women without recurrence) & logrank analyses

Allocation	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
Tamoxifen	1.59 SE 0.14	2.27 SE 0.20	1.26 SE 0.20	1.11 SE 0.26
Control	1.97 SE 0.16	2.37 SE 0.20	1.79 SE 0.24	1.02 SE 0.26
Rate ratio, from (O-E) / V	0.79 SE 0.11 -15.2 / 65.7	0.89 SE 0.12 -7.2 / 62.4	0.69 SE 0.17 -8.5 / 23.1	0.93 SE 0.35 -0.5 / 7.6

≈ 5 years tamoxifen vs. Not

DEATH WITHOUT RECURRENCE

Entry age 45-54, ER+



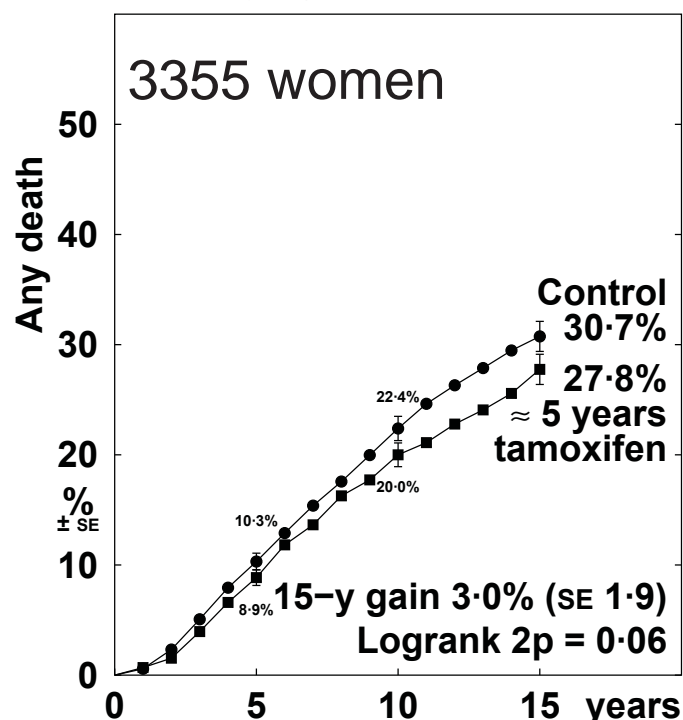
Death-without-recurrence rates (% / year) and logrank analyses

Allocation	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
Tamoxifen	0.26 (19 / 7420)	0.52 (27 / 5200)	0.81 (23 / 2854)	0.72 (10 / 1395)
Control	0.18 (13 / 7170)	0.50 (24 / 4763)	0.66 (17 / 2574)	0.89 (11 / 1235)
Rate ratio, from (O-E) / V	1.54 SE 0.45 3.4 / 7.9	1.04 SE 0.29 0.5 / 12.6	1.26 SE 0.36 2.3 / 9.9	0.86 SE 0.42 -0.7 / 4.9

≈ 5 years tamoxifen vs. Not

ANY DEATH

Entry age 45-54, ER+



Death rates (% / year) and logrank analyses

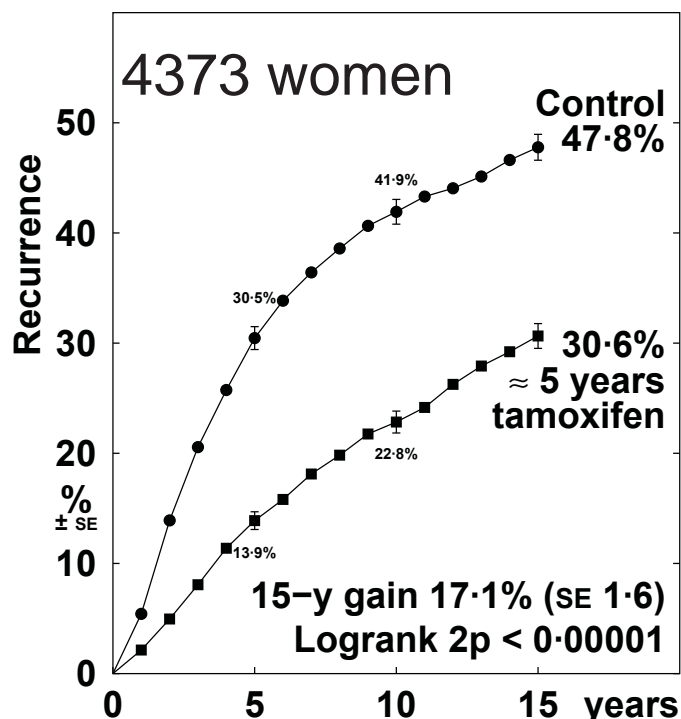
Allocation	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
Tamoxifen	1.83 (144 / 7862)	2.73 (159 / 5823)	1.97 (64 / 3256)	1.73 (28 / 1623)
Control	2.14 (169 / 7900)	2.79 (160 / 5732)	2.33 (74 / 3179)	1.72 (27 / 1568)
Rate ratio, from (O-E) / V	0.85 SE 0.11 -11.8 / 73.6	0.92 SE 0.11 -6.7 / 75.0	0.83 SE 0.16 -6.2 / 33.0	0.90 SE 0.27 -1.3 / 12.5

p 7: 15-year outcomes, age at entry 55-69 years, ER+ disease: ~5 years tam.

≈ 5 years tamoxifen vs. Not

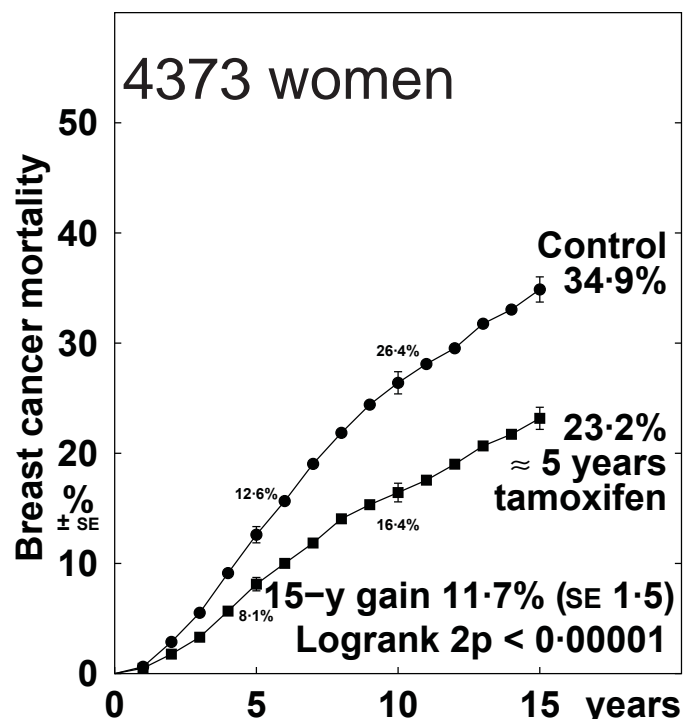
RECURRENCE

Entry age 55-69, ER+



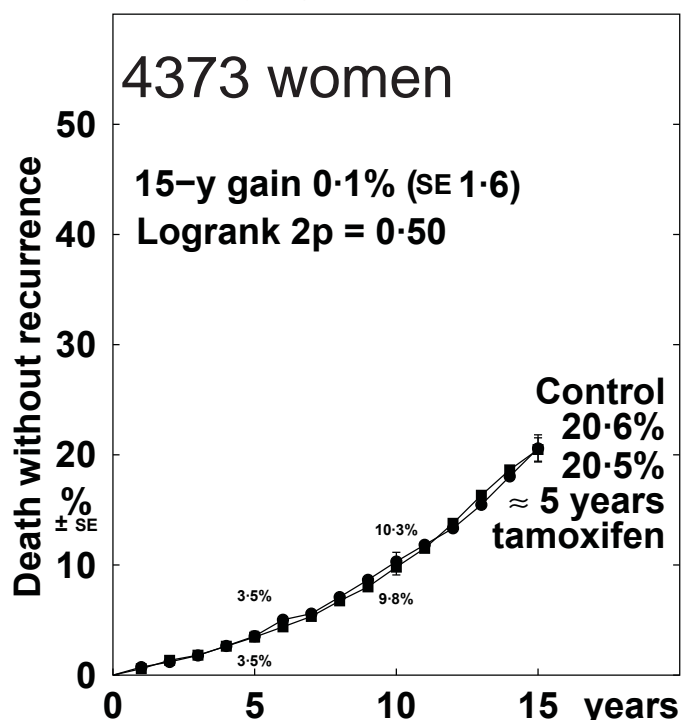
≈ 5 years tamoxifen vs. Not
BREAST CANCER MORTALITY

Entry age 55-69, ER+



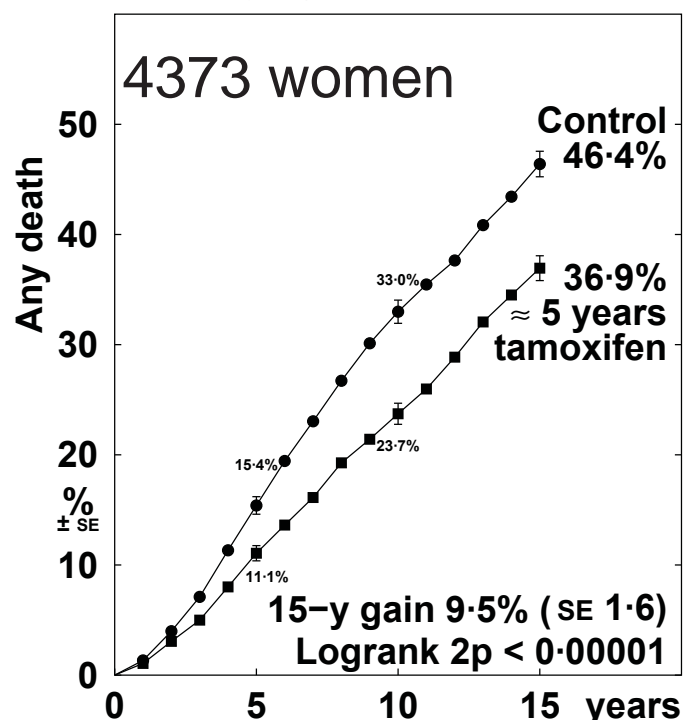
≈ 5 years tamoxifen vs. Not
DEATH WITHOUT RECURRENCE

Entry age 55-69, ER+



≈ 5 years tamoxifen vs. Not
ANY DEATH

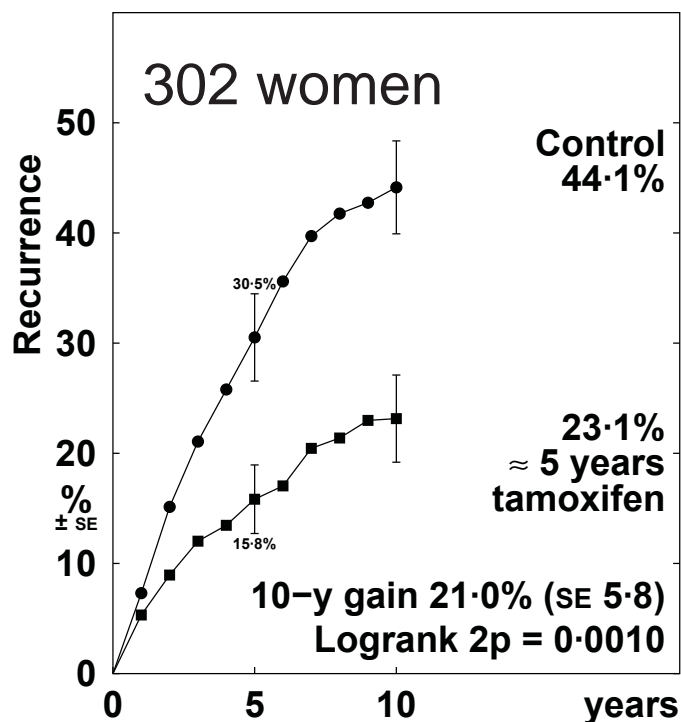
Entry age 55-69, ER+



≈ 5 years tamoxifen vs. Not

RECURRENCE

Entry age 70+, ER+



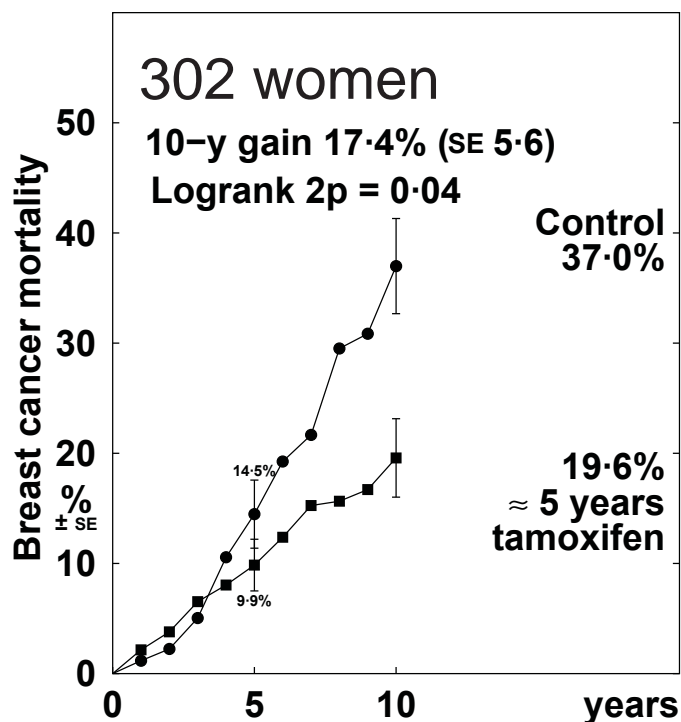
Recurrence rates (% / year) and logrank analyses

Allocation	Years 0 - 4	Years 5 - 9	Year 10+
Tamoxifen	3.46 (22 / 635)	2.52 (12 / 476)	1.71 (7 / 409)
Control	7.49 (46 / 614)	4.08 (16 / 392)	2.03 (6 / 296)
Rate ratio, from (O-E) / V	0.49 SE 0.18 -10.7 / 14.9	0.45 SE 0.29 -4.4 / 5.5	0.74 SE 0.55 -0.7 / 2.4

≈ 5 years tamoxifen vs. Not

BREAST CANCER MORTALITY

Entry age 70+, ER+



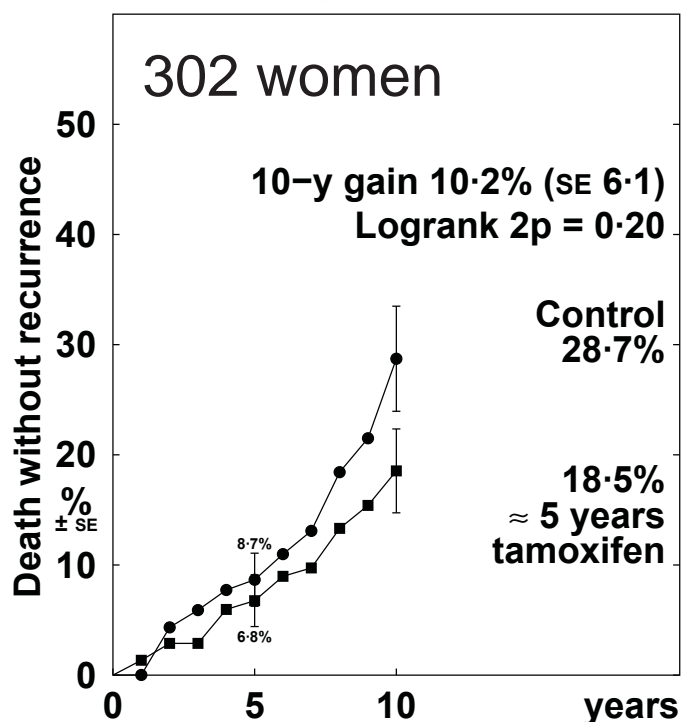
Death rates (% / year: total rate - rate in women without recurrence) & logrank analyses

Allocation	Years 0 - 4	Years 5 - 9	Year 10+
Tamoxifen	1.79 SE 0.52	2.68 SE 0.72	2.68 SE 0.77
Control	3.27 SE 0.68	5.65 SE 1.07	3.17 SE 0.92
Rate ratio, from (O-E) / V	0.67 SE 0.31 -2.9 / 7.3	0.41 SE 0.23 -7.3 / 8.2	1.28 SE 0.54 1.1 / 4.5

≈ 5 years tamoxifen vs. Not

DEATH WITHOUT RECURRENCE

Entry age 70+, ER+



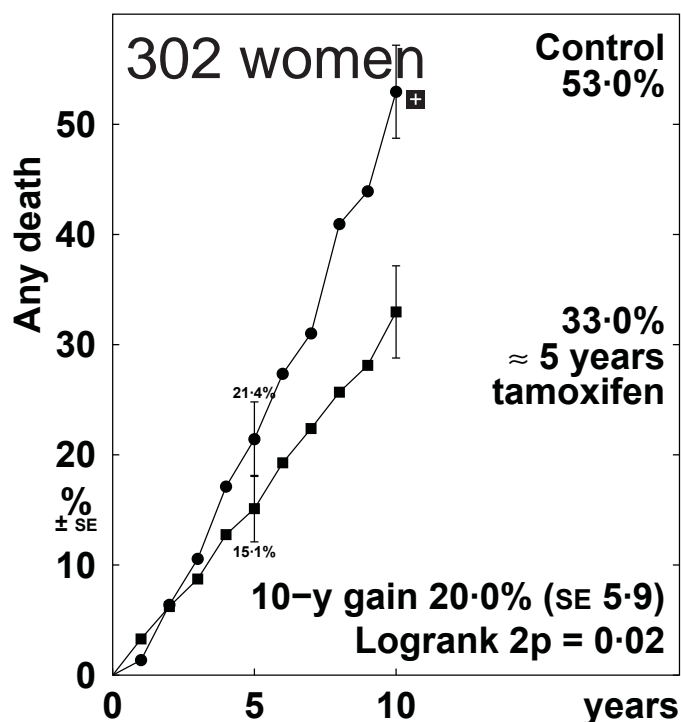
Death-without-recurrence rates (% / year) and logrank analyses

Allocation	Years 0 - 4	Years 5 - 9	Year 10+
Tamoxifen	1.57 (10 / 635)	2.73 (13 / 476)	9.25 (38 / 411)
Control	1.63 (10 / 614)	4.85 (19 / 392)	8.79 (27 / 307)
Rate ratio, from (O-E) / V	0.69 SE 0.41 -1.6 / 4.3	0.56 SE 0.29 -4.0 / 6.9	0.96 SE 0.29 -0.5 / 11.0

≈ 5 years tamoxifen vs. Not

ANY DEATH

Entry age 70+, ER+

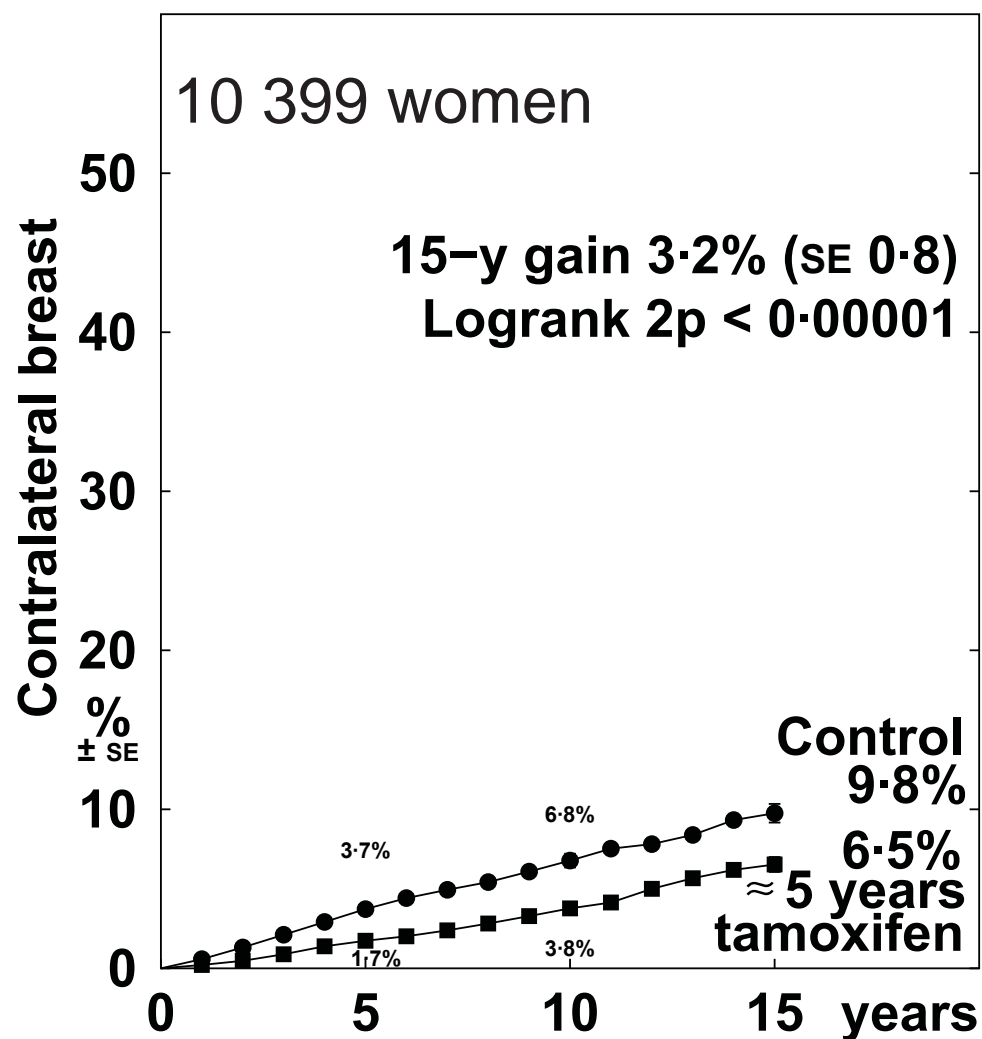


Death rates (% / year) and logrank analyses

Allocation	Years 0 - 4	Years 5 - 9	Year 10+
Tamoxifen	3.28 (22 / 670)	5.17 (27 / 522)	11.19 (50 / 447)
Control	4.69 (33 / 704)	9.48 (47 / 496)	10.32 (39 / 378)
Rate ratio, from (O-E) / V	0.68 SE 0.24 -4.5 / 11.5	0.47 SE 0.18 -11.3 / 15.0	1.04 SE 0.26 0.6 / 15.5

p 9: 15-year contralateral breast cancer incidence, all ages, by ER status: ~5 years tam.

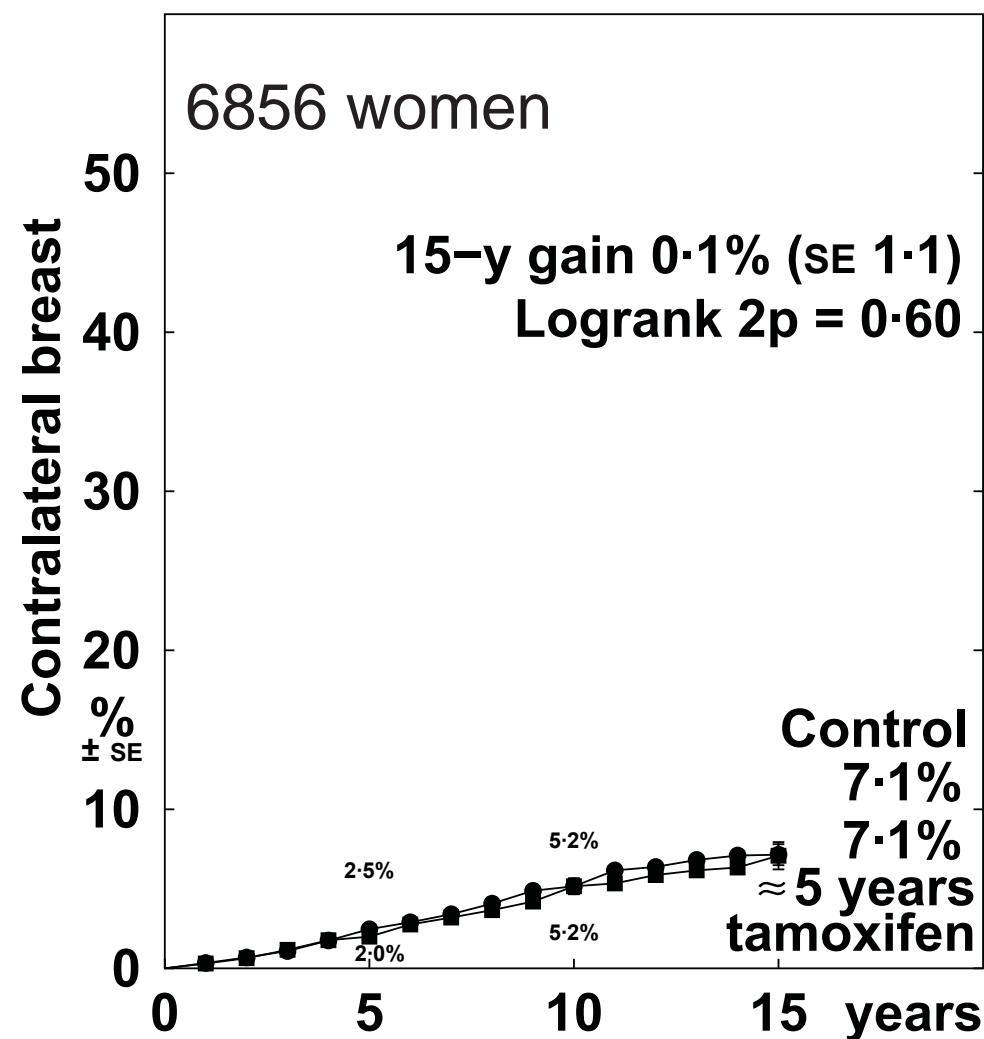
≈ 5 years tamoxifen vs. Not CONTRALATERAL BREAST ER+



Contralateral breast cancer rates (% / year) and logrank analyses

Allocation	Years 0 – 4	Years 5 – 9	Years 10 – 14	Year 15+
Tamoxifen	0.35 (80 / 23136)	0.42 (70 / 16704)	0.61 (62 / 10200)	0.52 (25 / 4812)
Control	0.77 (163 / 21301)	0.65 (91 / 13959)	0.64 (53 / 8321)	0.51 (20 / 3938)
Rate ratio, from (O-E) / V	0.47 SE 0.09 -44.9 / 59.9	0.64 SE 0.13 -17.1 / 38.8	0.91 SE 0.18 -2.5 / 27.5	0.95 SE 0.30 -0.5 / 10.6

≈ 5 years tamoxifen vs. Not CONTRALATERAL BREAST ER-poor

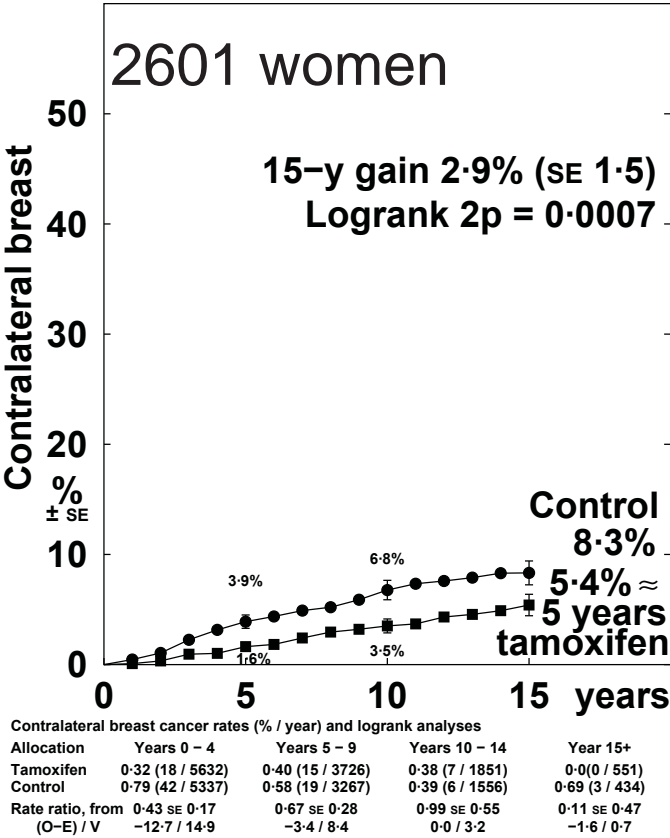


Contralateral breast cancer rates (% / year) and logrank analyses

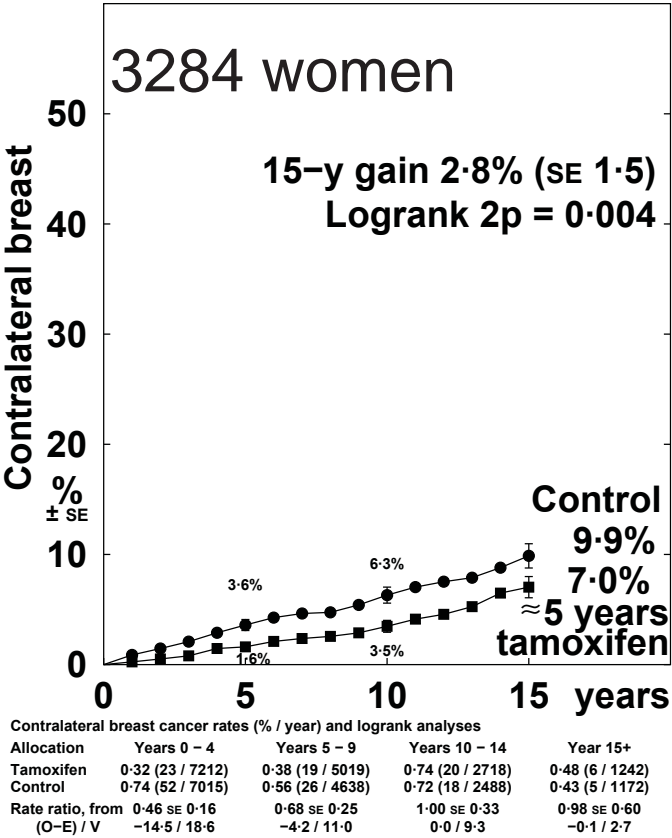
Allocation	Years 0 – 4	Years 5 – 9	Years 10 – 14	Year 15+
Tamoxifen	0.41 (58 / 14091)	0.64 (55 / 8601)	0.37 (12 / 3209)	0.58 (4 / 687)
Control	0.47 (66 / 14044)	0.56 (49 / 8702)	0.53 (18 / 3369)	0.26 (2 / 770)
Rate ratio, from (O-E) / V	0.84 SE 0.17 -5.2 / 29.3	1.15 SE 0.21 3.5 / 25.1	0.64 SE 0.30 -3.2 / 7.2	1.94 SE 1.30 0.8 / 1.2

p 10: 15-year contralateral breast cancer incidence, ER+ disease, by age: ~5 years tam.

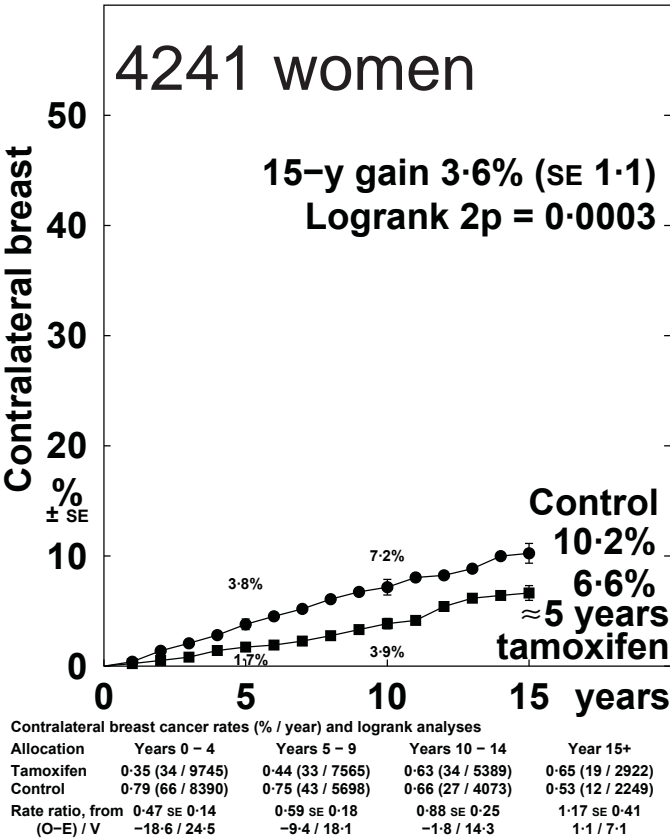
≈ 5 years tamoxifen vs. Not
CONTRALATERAL BREAST
Entry age < 45, ER+



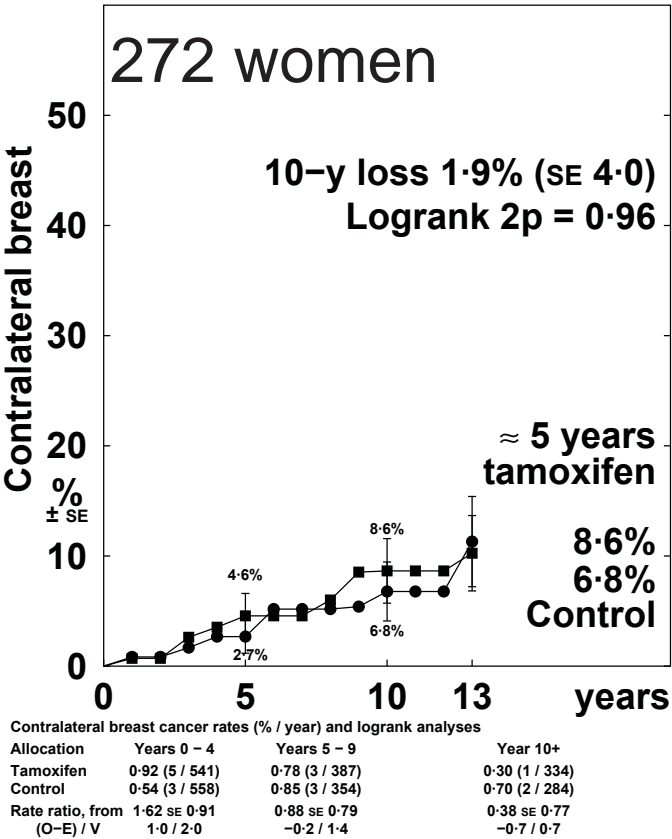
≈ 5 years tamoxifen vs. Not
CONTRALATERAL BREAST
Entry age 45-54, ER+



≈ 5 years tamoxifen vs. Not
CONTRALATERAL BREAST
Entry age 55-69, ER+

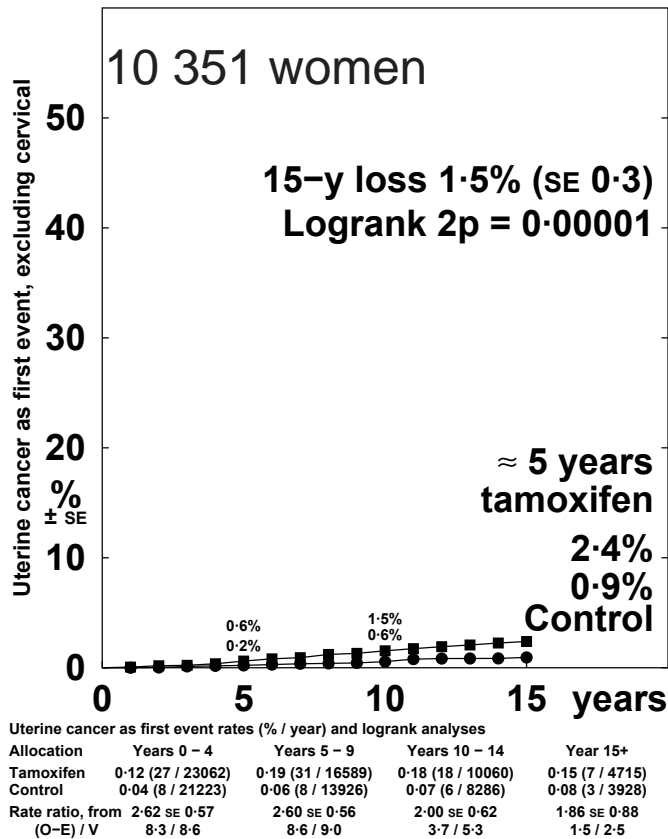


≈ 5 years tamoxifen vs. Not
CONTRALATERAL BREAST
Entry age 70+, ER+

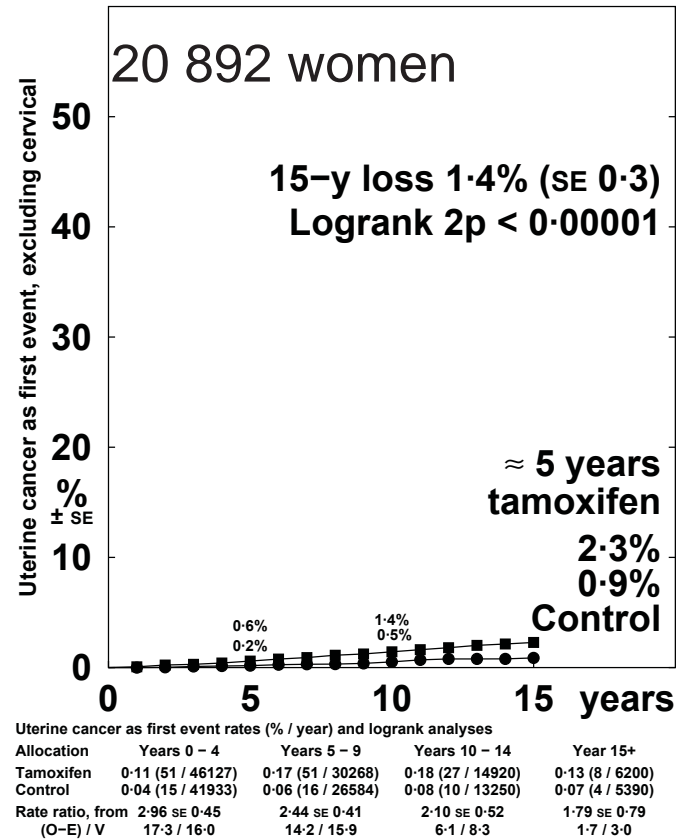


p 11: 15-year uterus (excl. cervix) ca. incidence & mortality, ER+ and all ER: ~5 years tam.

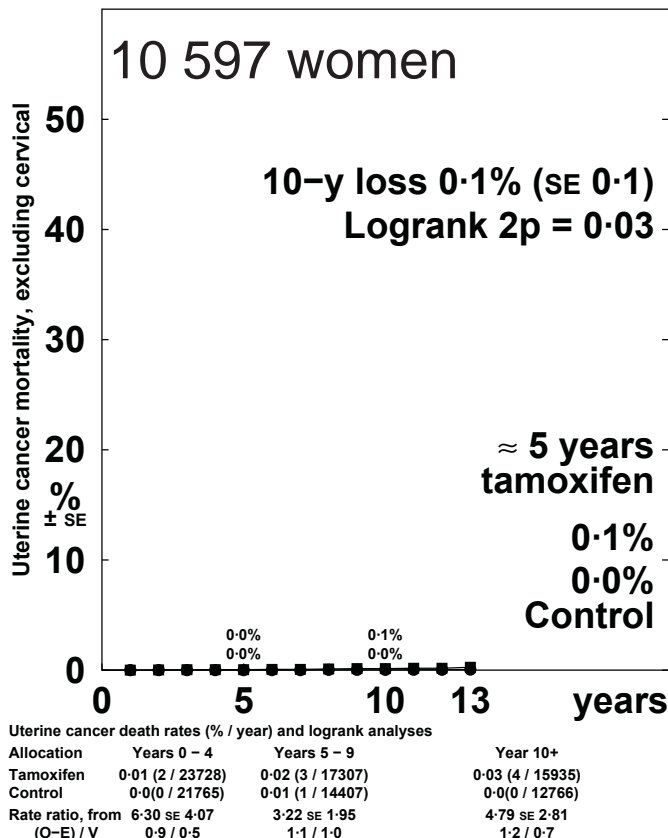
≈ 5 years tamoxifen vs. Not
UTERUS (not cervix) cancer INCIDENCE
ER+



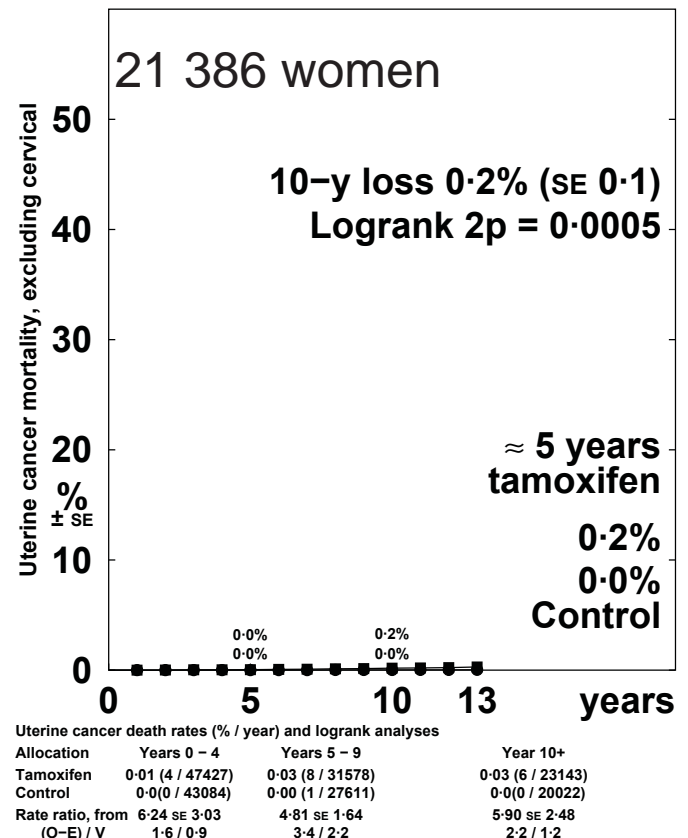
≈ 5 years tamoxifen vs. Not
UTERUS (not cervix) cancer INCIDENCE



≈ 5 years tamoxifen vs. Not
UTERUS (not cervix) cancer MORTALITY
ER+



≈ 5 years tamoxifen vs. Not
UTERUS (not cervix) cancer MORTALITY

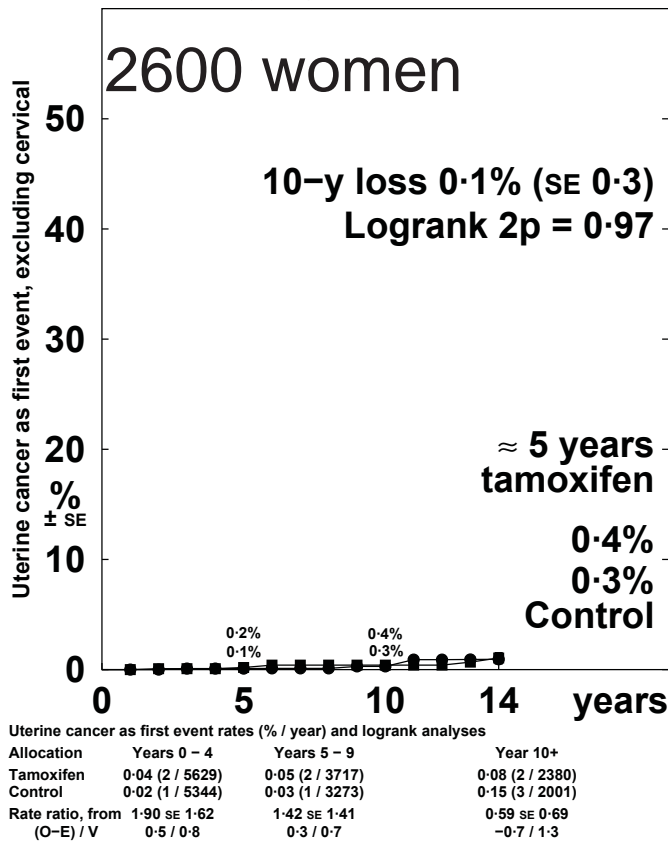


p 12: 15-year uterus (excl. cervix) ca. incidence, ER+ disease, by age: ~5 years tam.

≈ 5 years tamoxifen vs. Not

UTERUS (not cervix) cancer INCIDENCE

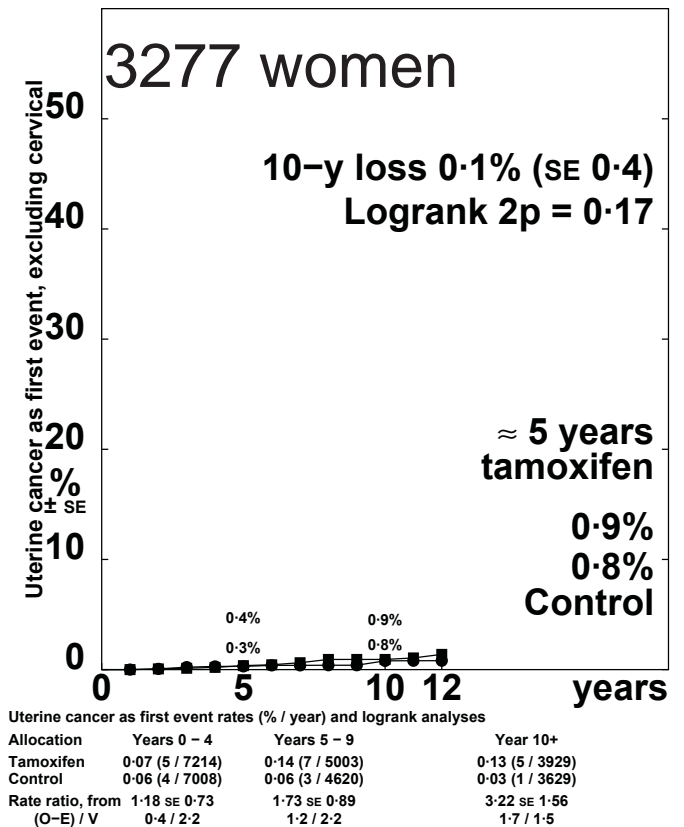
Entry age < 45, ER+



≈ 5 years tamoxifen vs. Not

UTERUS (not cervix) cancer INCIDENCE

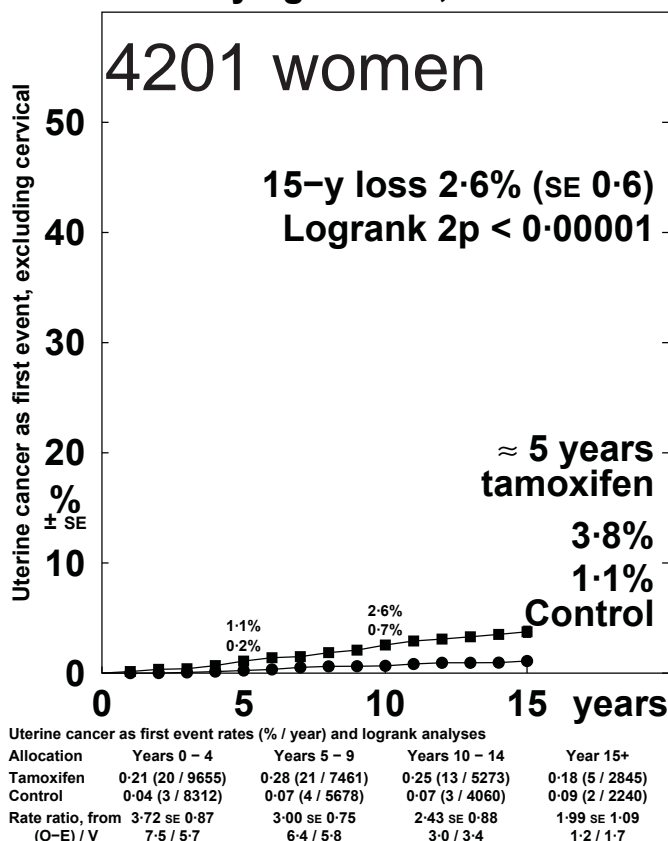
Entry age 45-54, ER+



≈ 5 years tamoxifen vs. Not

UTERUS (not cervix) cancer INCIDENCE

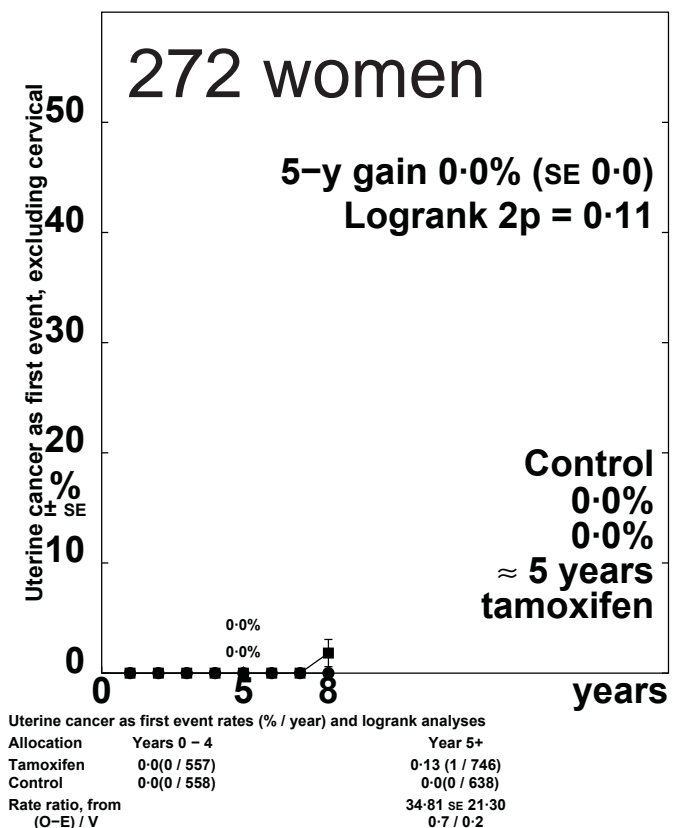
Entry age 55-69, ER+



≈ 5 years tamoxifen vs. Not

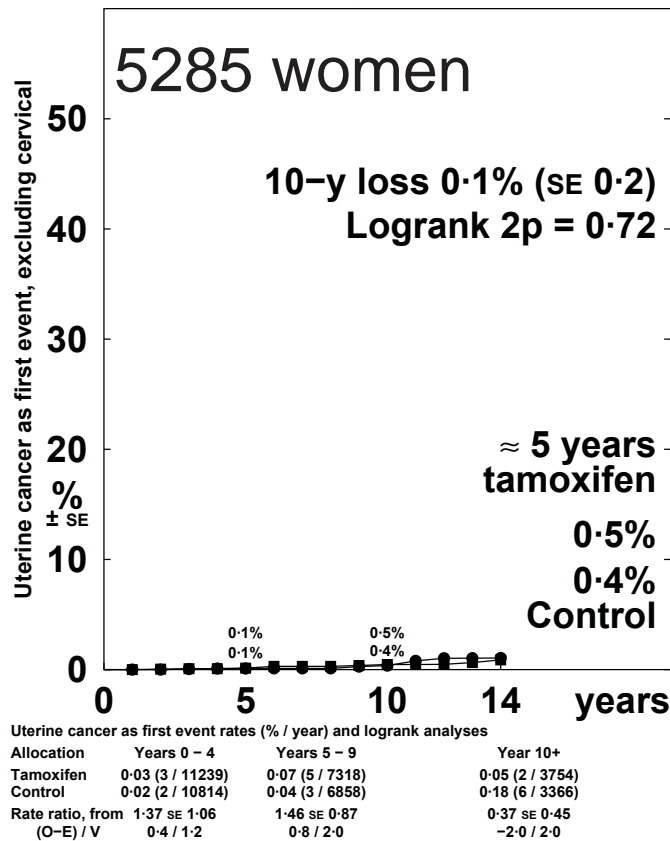
UTERUS (not cervix) cancer INCIDENCE

Entry age 70+, ER+

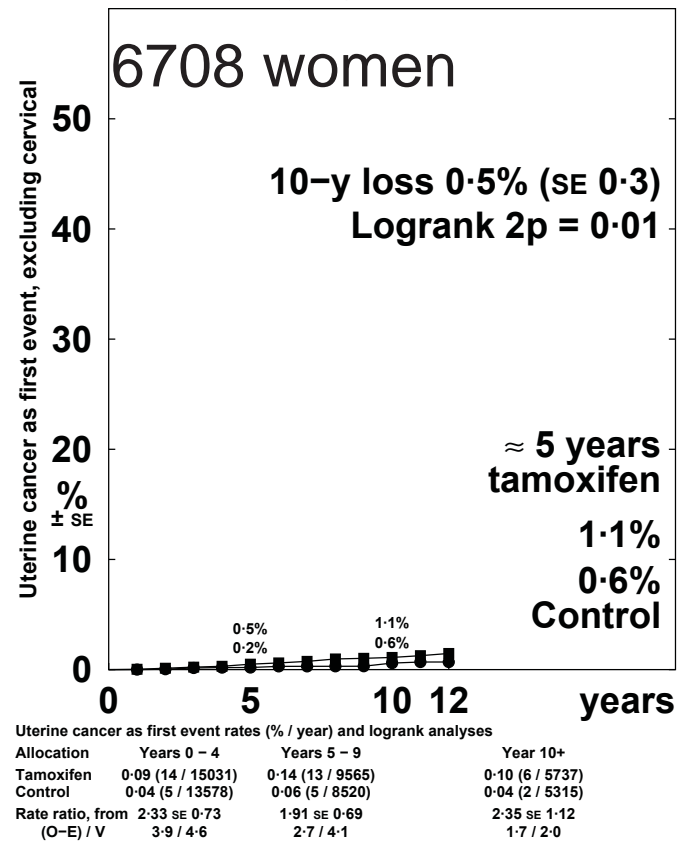


p 13: 15-year uterus (excl. cervix) ca. incidence, all ER, by age: ~5 years tam.

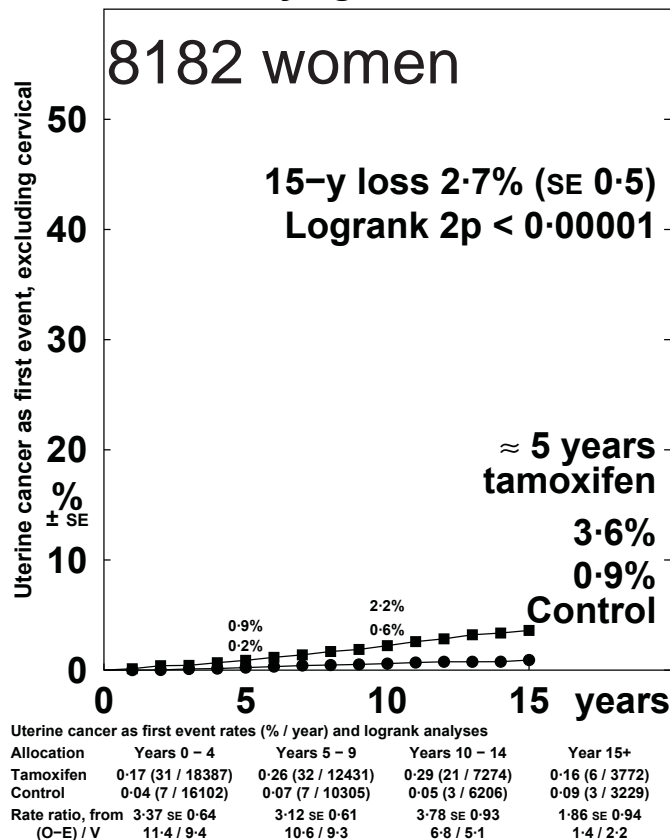
≈ 5 years tamoxifen vs. Not
UTERUS (not cervix) cancer INCIDENCE
Entry age < 45



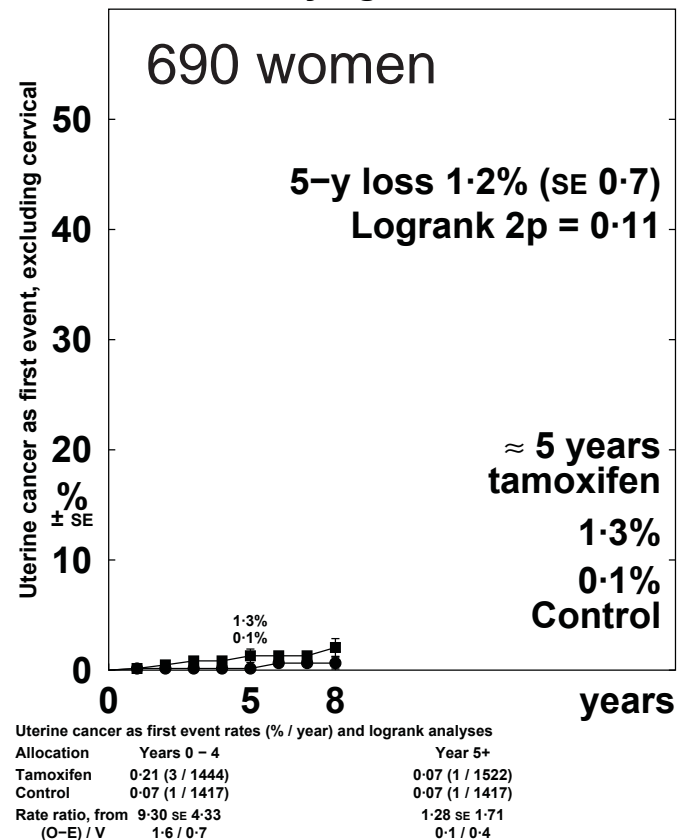
≈ 5 years tamoxifen vs. Not
UTERUS (not cervix) cancer INCIDENCE
Entry age 45-54



≈ 5 years tamoxifen vs. Not
UTERUS (not cervix) cancer INCIDENCE
Entry age 55-69

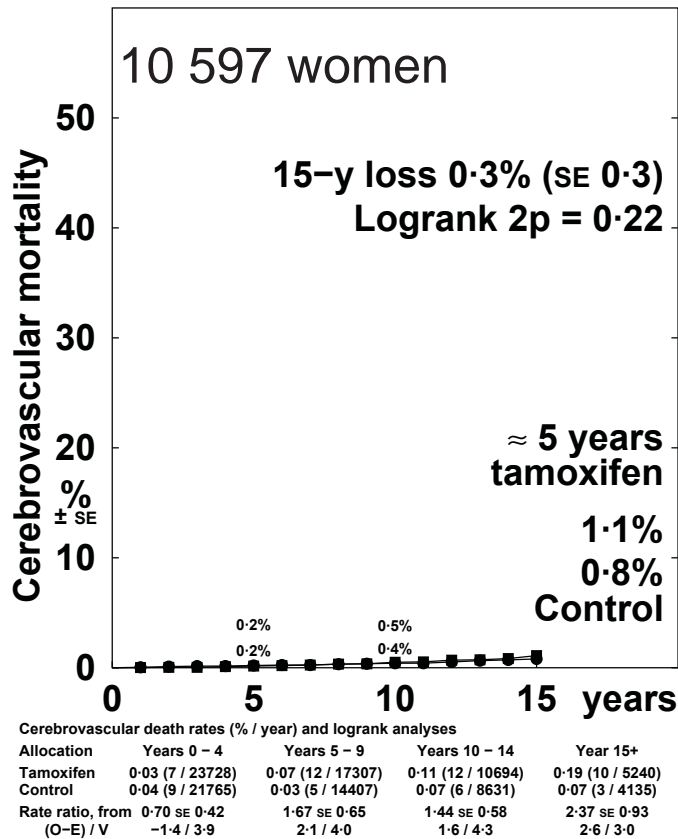


≈ 5 years tamoxifen vs. Not
UTERUS (not cervix) cancer INCIDENCE
Entry age 70+

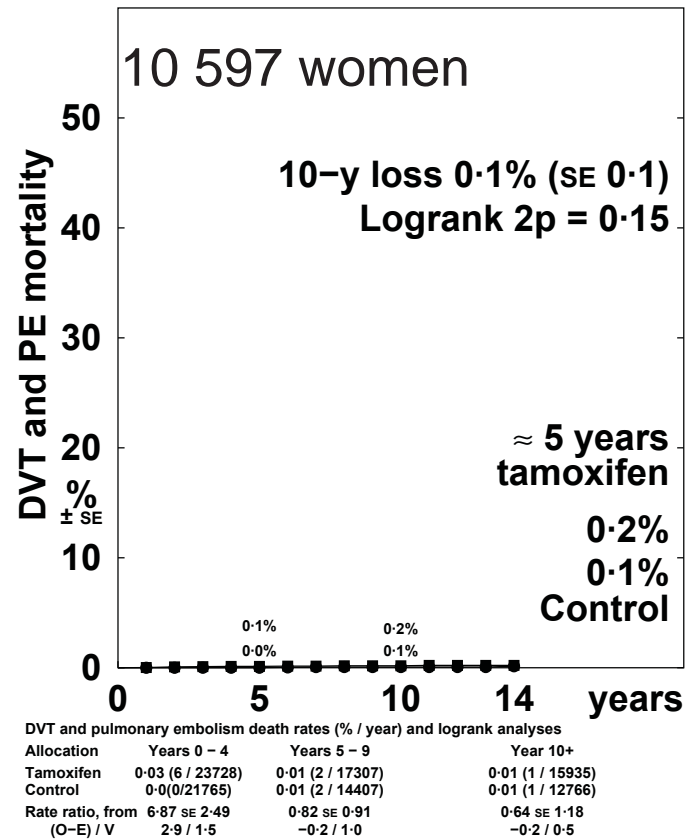


p 14: 15-year stroke, PE & other/all vascular mortality, ER+ disease: ~5 years tam.

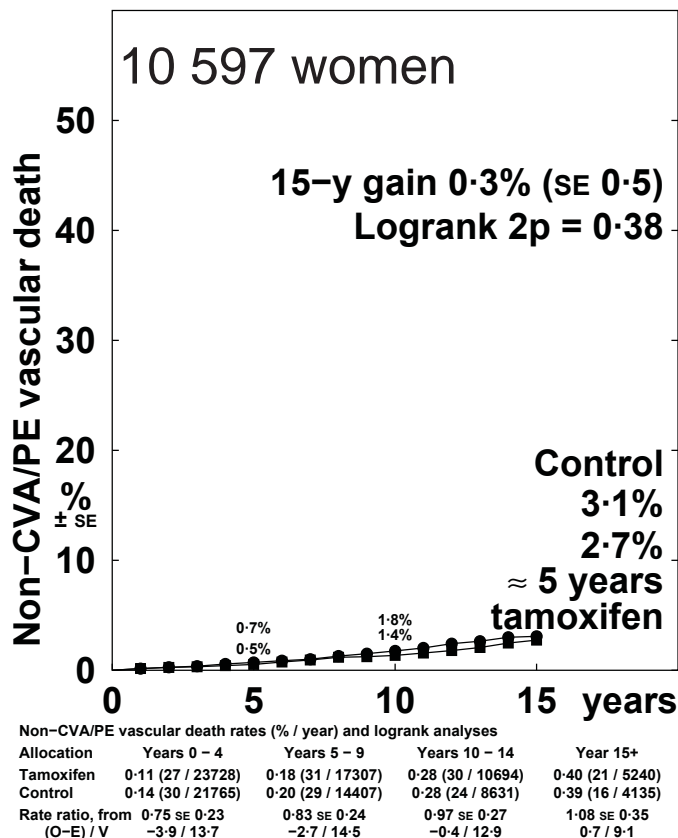
≈ 5 years tamoxifen vs. Not CEREBROVASCULAR MORTALITY ER+



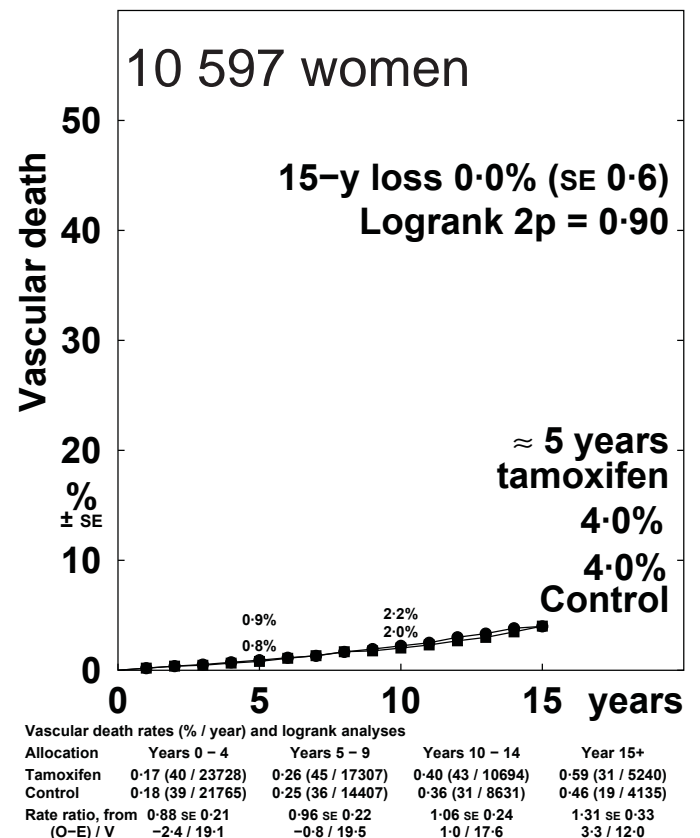
≈ 5 years tamoxifen vs. Not DVT AND PE MORTALITY ER+



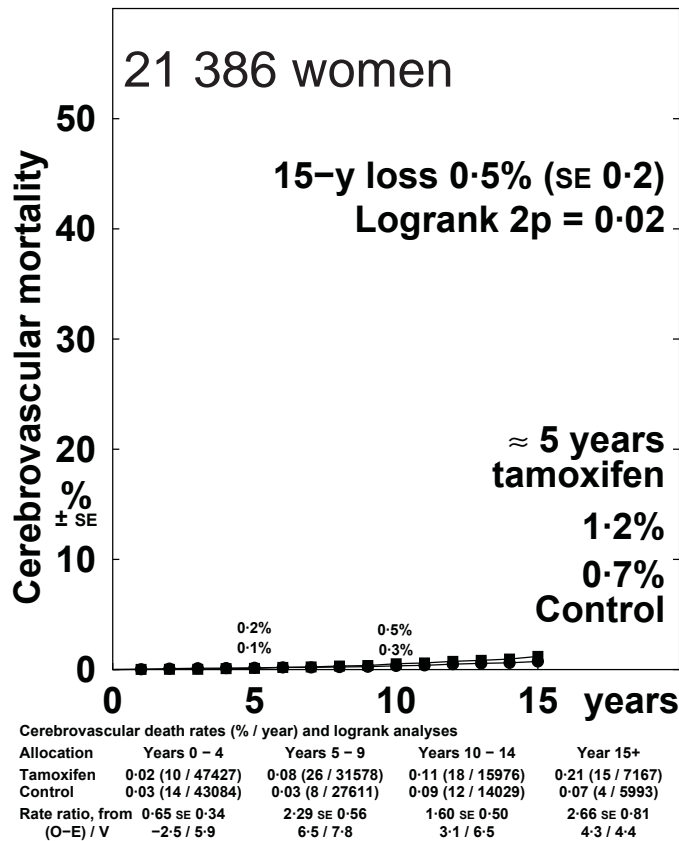
≈ 5 years tamoxifen vs. Not VASCULAR (excl. stroke & PE) DEATH ER+



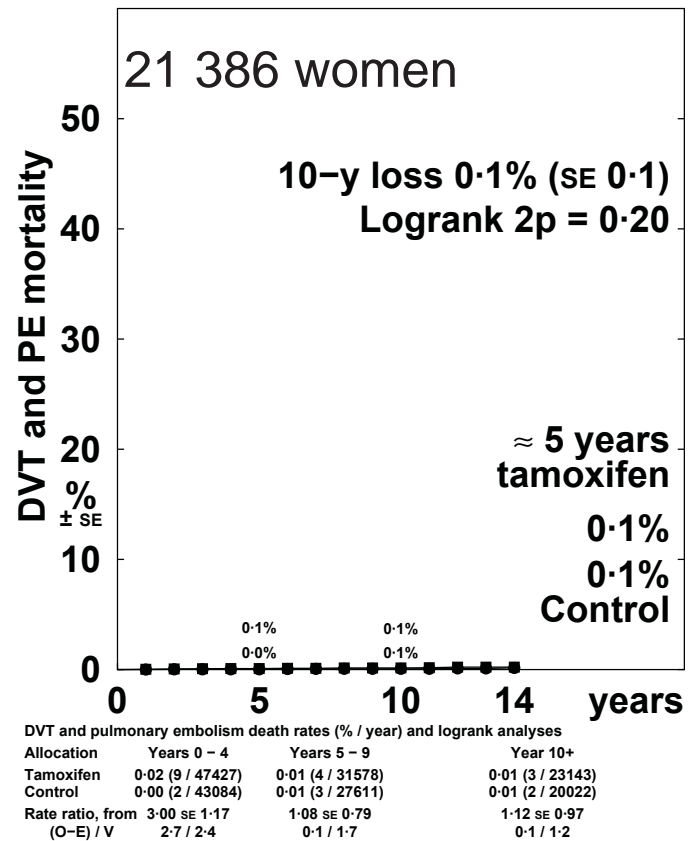
≈ 5 years tamoxifen vs. Not VASCULAR DEATH ER+



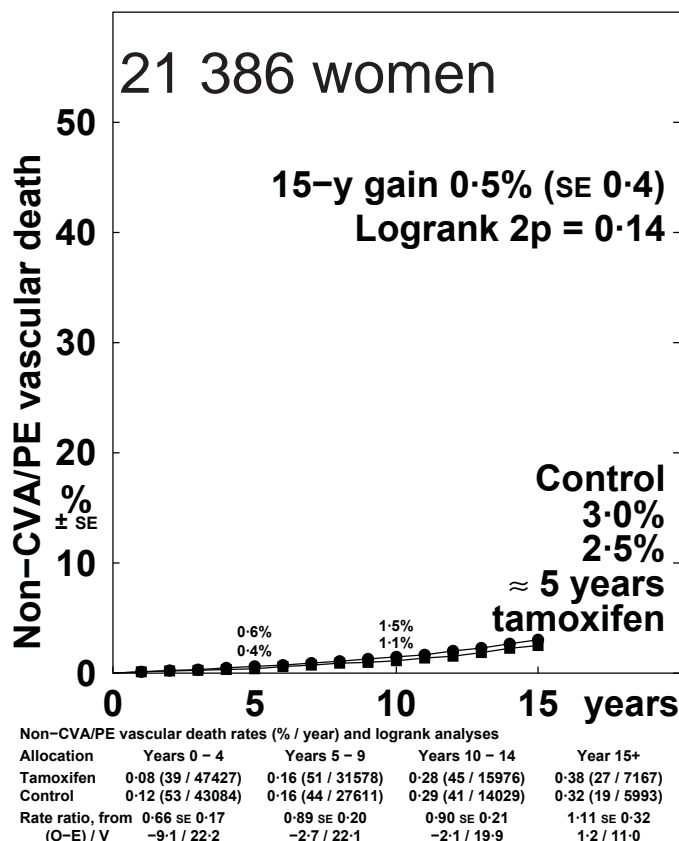
≈ 5 years tamoxifen vs. Not CEREBROVASCULAR MORTALITY



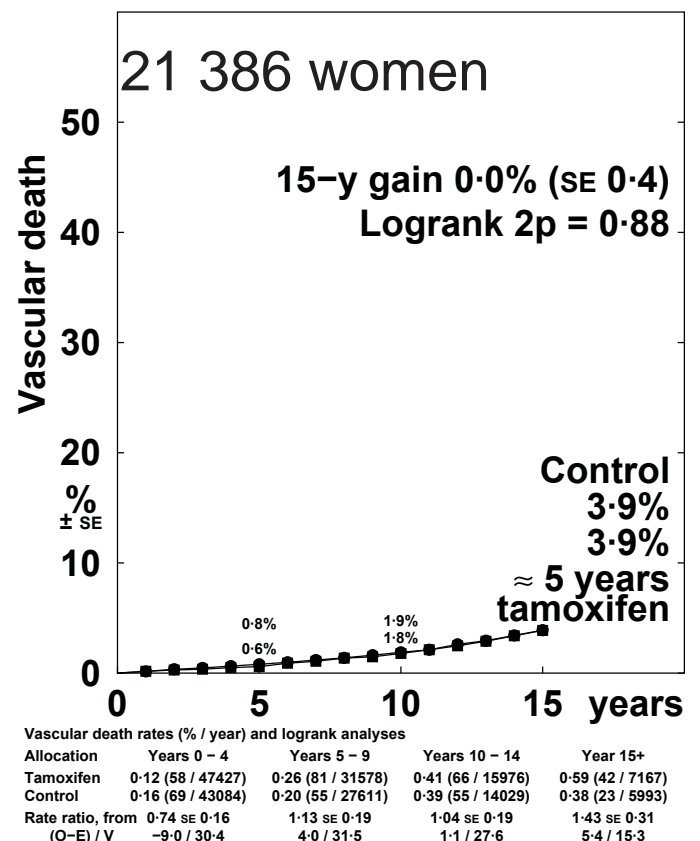
≈ 5 years tamoxifen vs. Not DVT AND PE MORTALITY



≈ 5 years tamoxifen vs. Not VASCULAR (excl. stroke & PE) DEATH



≈ 5 years tamoxifen vs. Not VASCULAR DEATH



p 16: Table 1: Mortality by cause and incidence of second cancers, ER+ disease. Outcome by allocated treatment in trials of about 5 years of adjuvant tamoxifen. (Webappendix p 17 gives results for all women, irrespective of ER status.)

	Events	(O-E)	Variance	Rate Ratio & SE		2p*
Death without recurrence	1117	4.9	258.6	1.02	0.06	0.79
Death with recurrence	2694	-224.5	620.2	0.70	0.03	< 0.00001
Any death	3811	-219.6	878.8	0.78	0.03	< 0.00001
Death without recurrence (selected groups of causes)						
Vascular disease:						
Stroke	64	4.8	15.2	1.37	0.30	0.27
Pulmonary embolus†	12	2.5	3.0	2.30	0.90	0.25
Heart & other vascular	212	-6.1	50.1	0.89	0.13	0.43
Neoplastic disease:						
Uterus excluding cervix‡	10	3.2	2.2	4.28	1.52	0.07
Other non-breast	187	-0.1	44.2	1.00	0.15	1.00
Other specified cause	312	4.6	71.0	1.07	0.12	0.63
Unknown cause (but definitely not-breast cancer**)	320	-4.0	72.9	0.95	0.11	0.68
Second cancer incidence without previous recurrence (selected sites)						
Contralateral breast,						
by age at entry (years)						
< 45	110	-17.7	27.2	0.52	0.14	0.001
45 - 54	169	-18.8	41.5	0.64	0.12	0.004
55 - 69	268	-28.7	64.0	0.64	0.10	0.00001
≥70	17	0.1	4.1	-	-	-
All ages	564	-65.1	136.7	0.62	0.07	< 0.00001
Uterus excluding cervix,‡						
by age at entry (years)						
< 45	11	0.1	2.7	1.04	0.62	1.00
45 - 54	25	3.3	5.9	1.75	0.55	0.25
55 - 69	71	18.0	16.6	2.96	0.44	0.00002
≥70	1	0.8	0.2	-	-	-
All ages	108	22.2	25.4	2.40	0.32	0.00002
Other or unknown site	606	2.6	143.6	1.02	0.08	0.86

* 2p, with continuity correction

† 6 vs 0 deaths from pulmonary embolus during years 0-4 (all with entry age 55-69 years) and 3 vs 3 later (all with entry age 55+ years).

‡ 9 vs 1 deaths (age at entry: 45-54 years, 1 vs 0; 55-69 years, 7 vs 1; 70+ years, 1 vs 0) and 83 vs 25 incident cases of uterine cancer, excluding cervix

** Deaths from an unknown cause that might possibly have been breast cancer were taken to have been immediately preceded by recurrence.

p 17: Table 2: Mortality by cause and incidence of second cancers, all ER. Outcome by allocated treatment in trials of about 5 years of adjuvant tamoxifen.

	Events	(O-E)	Variance	Rate Ratio & SE		2p*
Death without recurrence	1805	25.0	410.0	1.06	0.05	0.23
Death with recurrence	4789	-265.6	1074.5	0.78	0.03	< 0.00001
Any death	6594	-240.5	1484.5	0.85	0.02	< 0.00001
Death without recurrence (selected groups of causes)						
Vascular disease:						
Stroke	107	11.3	24.5	1.59	0.26	0.03
Pulmonary embolus†	23	3.0	5.4	1.74	0.58	0.28
Heart & other vascular	319	-12.8	74.8	0.84	0.11	0.16
Neoplastic disease:						
Uterus excluding cervix‡	19	7.3	4.3	5.46	1.27	0.001
Other non-breast	324	2.4	76.5	1.03	0.11	0.41
Other specified cause	470	5.6	103.6	1.06	0.10	0.62
Unknown cause (but definitely not-breast cancer**)	543	8.2	120.9	1.07	0.09	0.60
Second cancer incidence without previous recurrence (selected sites)						
Contralateral breast, All ages	940	-77.2	223.6	0.71	0.06	< 0.00001
Uterus excluding cervix,‡ by age at entry (years)						
< 45	21	-0.8	5.2	0.86	0.41	0.90
45 - 54	45	3.3	5.9	1.75	0.55	0.02
55 - 69	110	30.2	25.9	3.21	0.37	< 0.00001
≥70	6	1.6	1.1	-	-	-
All ages	182	39.3	42.9	2.50	0.25	< 0.00001
Other or unknown site	1026	-0.8	241.7	1.00	0.06	0.98

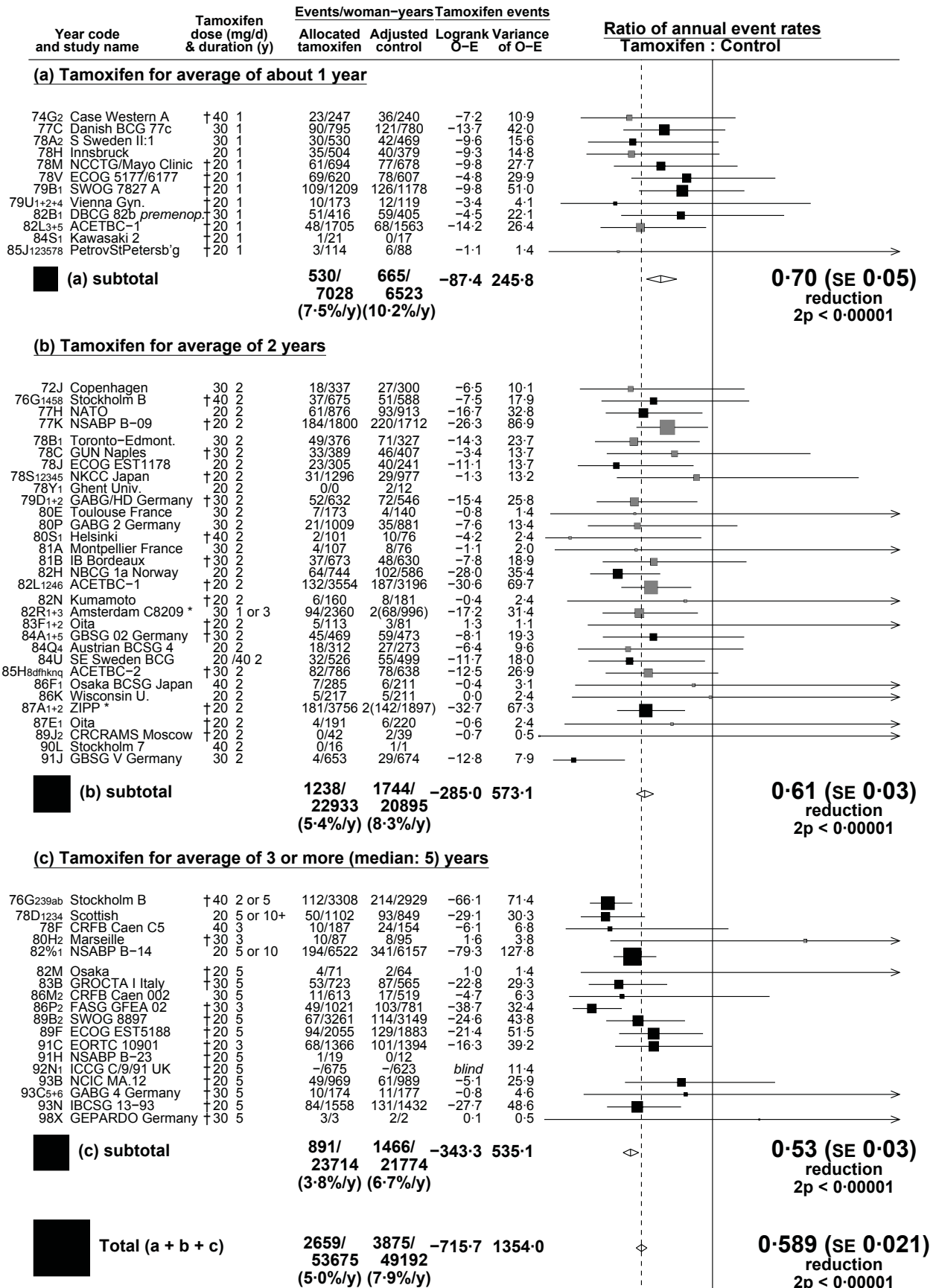
* 2p, with continuity correction

† 9 vs 2 deaths from pulmonary embolus during years 0-4 (age at entry: < 45 years 0 vs 1, 45-54 years 1 vs 0, 55-69 years 8 vs 1) and 7 vs 5 later (age at entry: < 45 1 vs 0, 55-69 5 vs 4, 70+ 1 vs 1).

‡ 18 vs 1 deaths (age at entry: 45-54 years, 4 vs 0; 55-69 years, 13 vs 1; 70+ years, 1 vs 0) and 137 vs 45 incident cases of uterine cancer, excluding cervix

** Deaths from an unknown cause that might possibly have been breast cancer were taken to have been immediately preceded by recurrence.

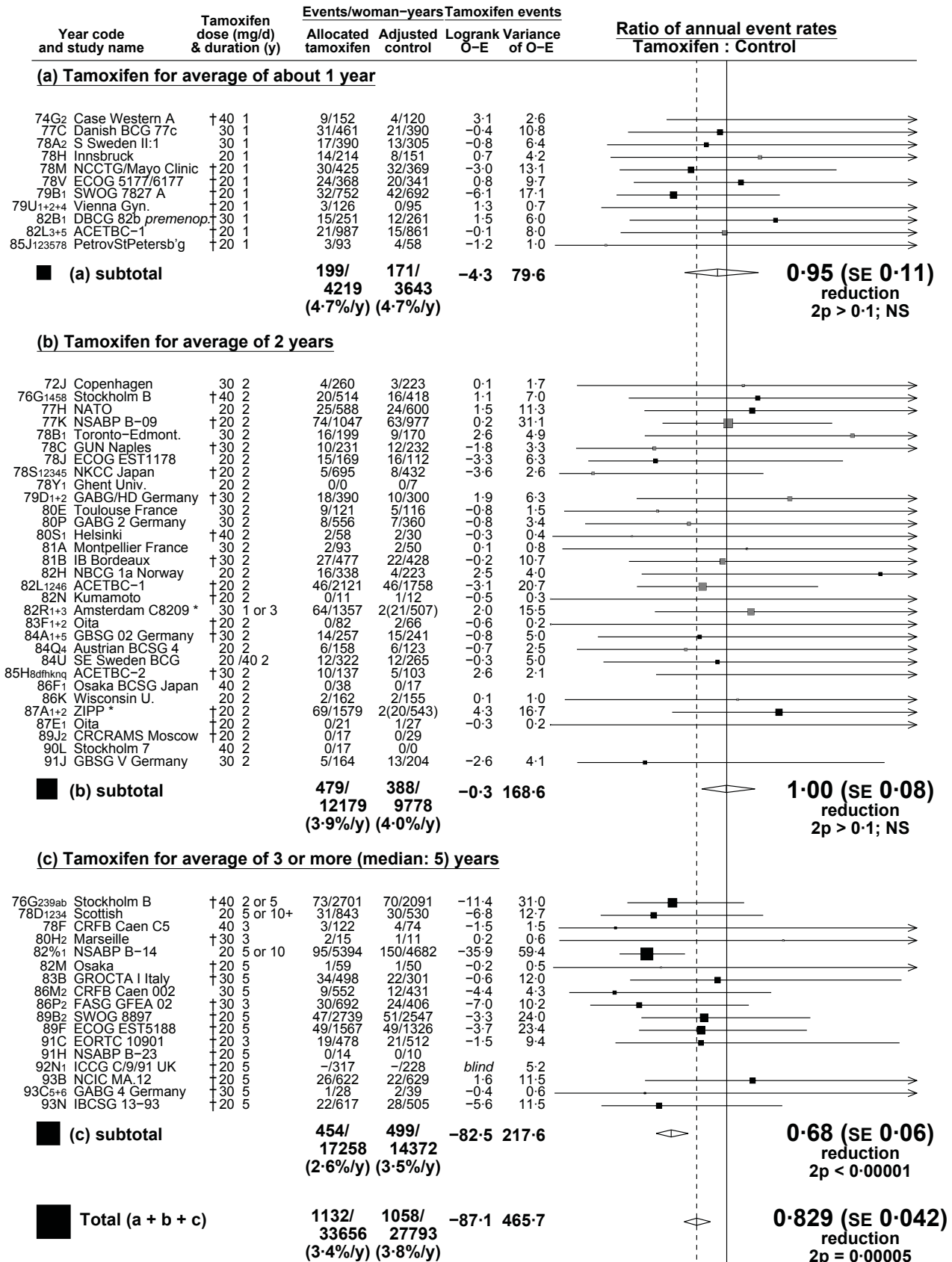
p 18: RRs for recurrence in years 0-4, one line / trial, ER+ disease: by tam. duration



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

† Tamoxifen plus chemotherapy versus same chemotherapy alone

p 19: RRs for recurrence in years 5-9, one line / trial, ER+ disease: by tam. duration



■ 99% or ◊ 95% confidence intervals

Heterogeneity between 3 subtotals: $\chi^2 = 15.2$; $p = 0.0005$

Heterogeneity within subtotals: $\chi^2_{51} = 47.5$; $p > 0.1$; NS

Heterogeneity between 54 trials: $\chi^2_{53} = 62.8$; $p > 0.1$; NS

0 0.5 1.0 1.5 2.0
Tamoxifen better | Tamoxifen worse

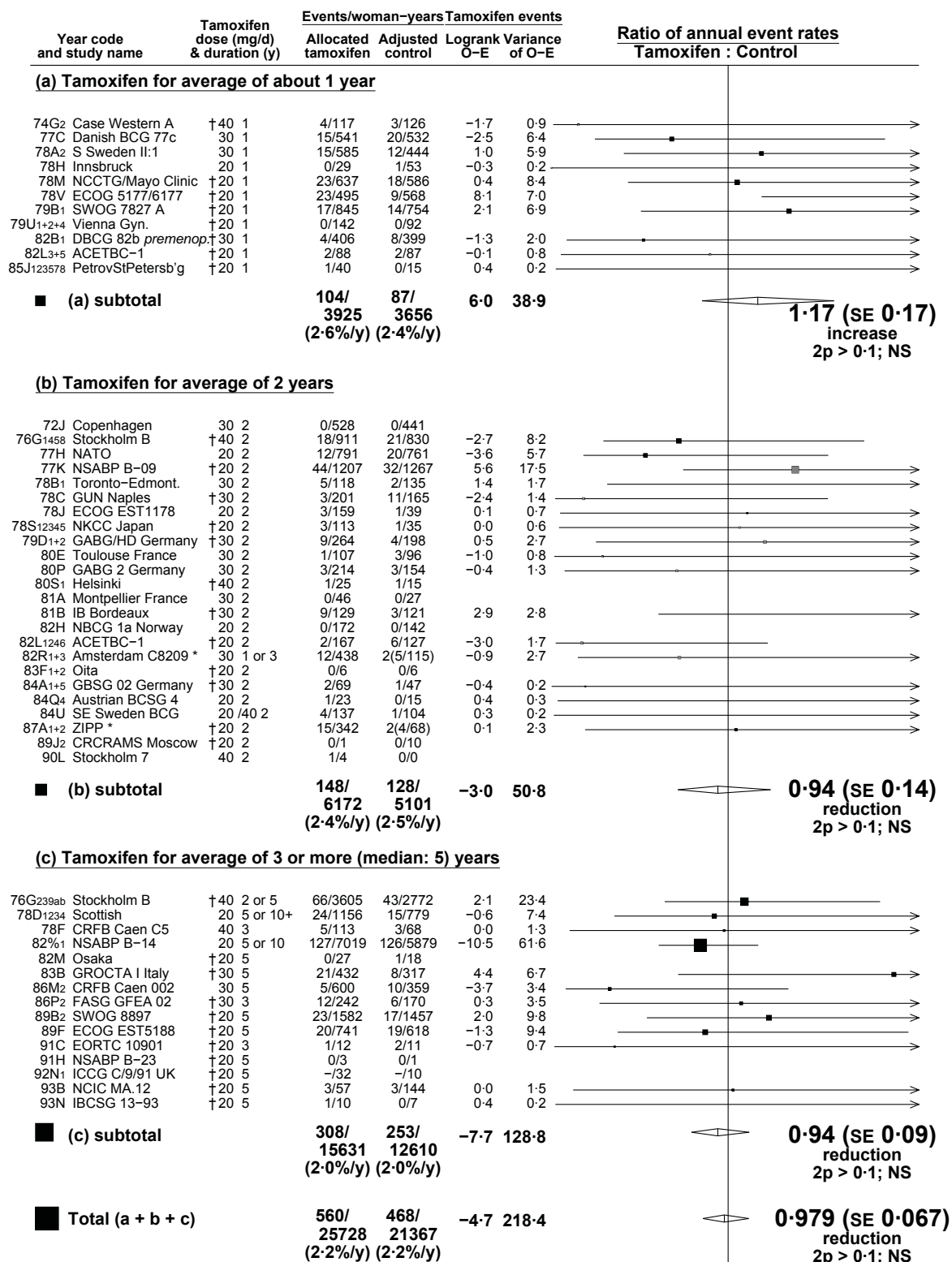
Treatment effect $2p = 0.00005$

Trend between 3 subtotals: $\chi^2_1 = 10.7$; $2p = 0.001$

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

† Tamoxifen plus chemotherapy versus same chemotherapy alone

p 20: RRs for recurrence in years 10+, one line / trial, ER+ disease: by tam. duration



■ 99% or ◁ 95% confidence intervals

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

Heterogeneity within subtotals: $\chi^2_{36} = 47.9$; $p = 0.09$

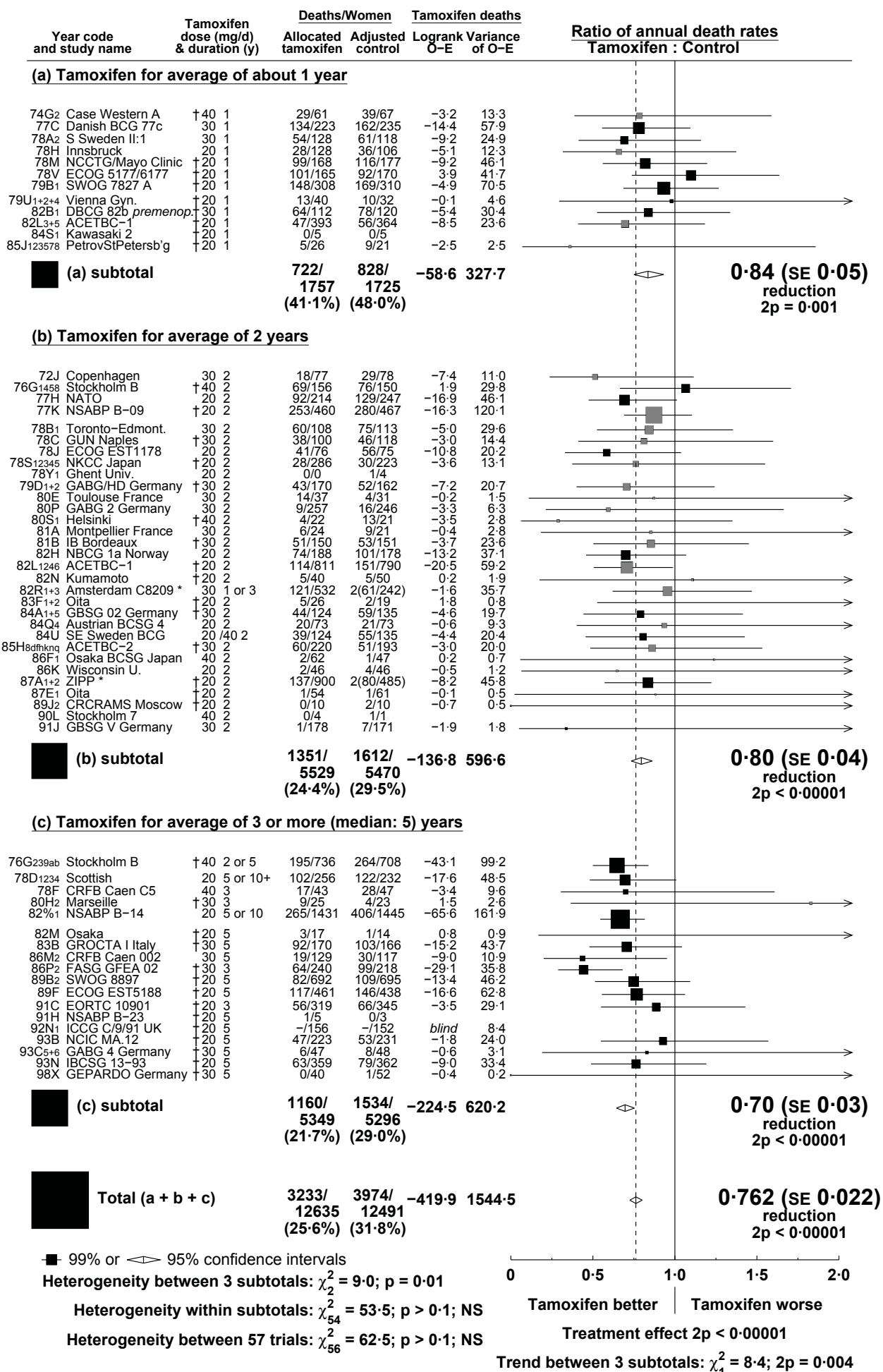
Heterogeneity between 39 trials: $\chi^2_{38} = 49.3$; $p > 0.1$; NS

Treatment effect $2p > 0.1$; NS
Trend between 3 subtotals: $\chi^2_1 = 1.1$; $2p > 0.1$; NS

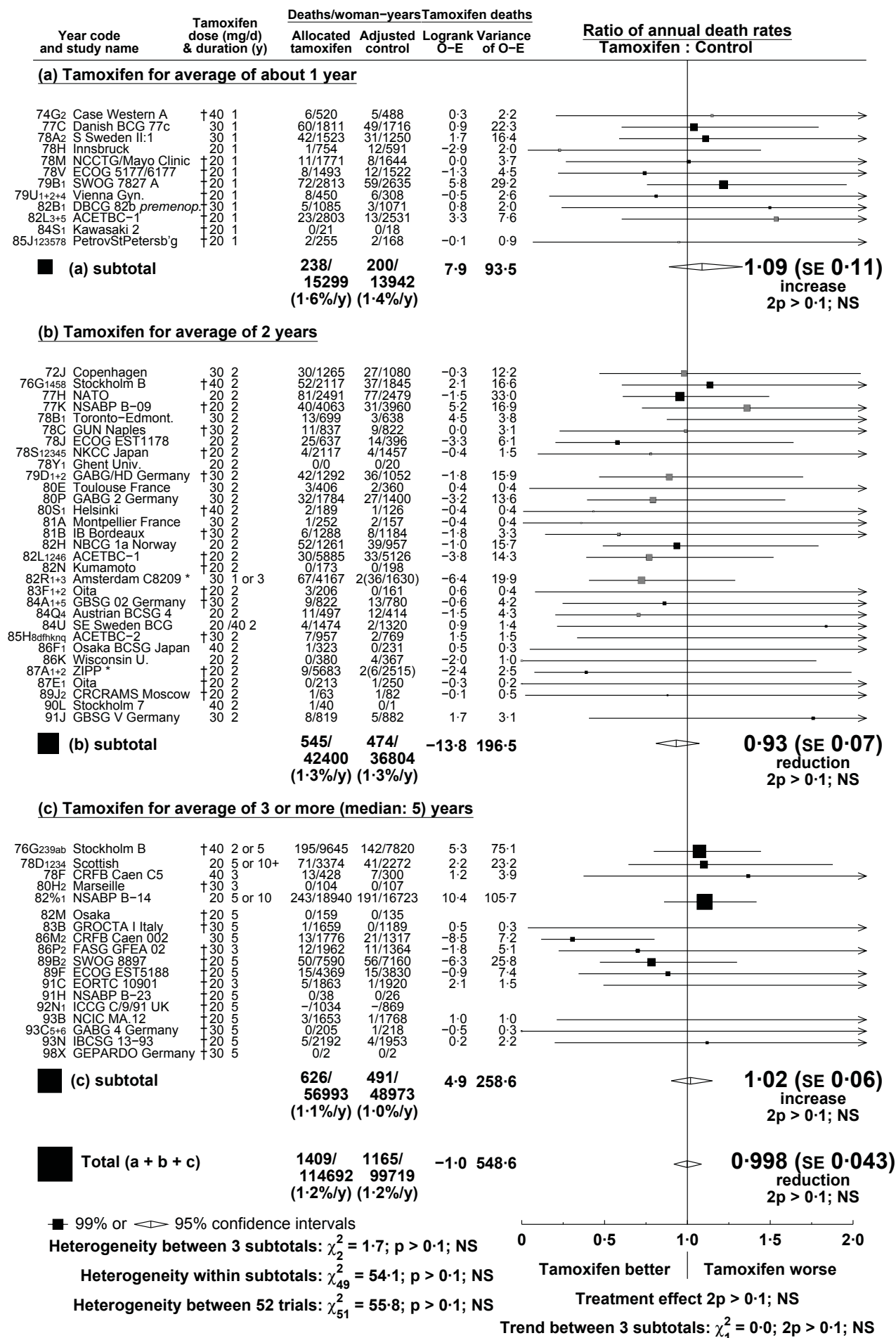
* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of events/woman-years.

† Tamoxifen plus chemotherapy versus same chemotherapy alone

p 21: RRs for death with recurrence, one line / trial, ER+ disease: by tam. duration



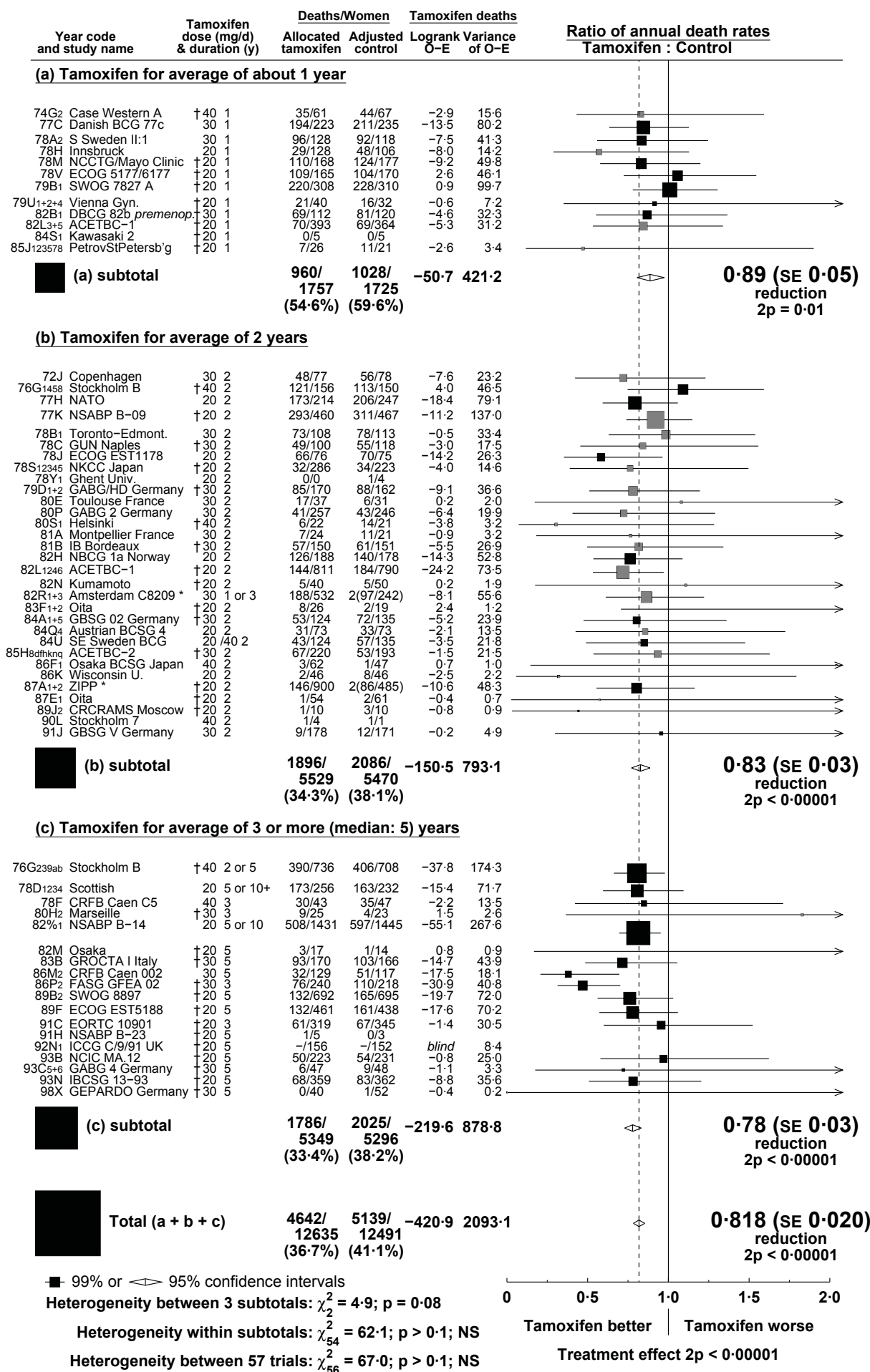
p 22: RRs for death without recurrence, one line / trial, ER+ disease: by tam. duration



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

† Tamoxifen plus chemotherapy versus same chemotherapy alone

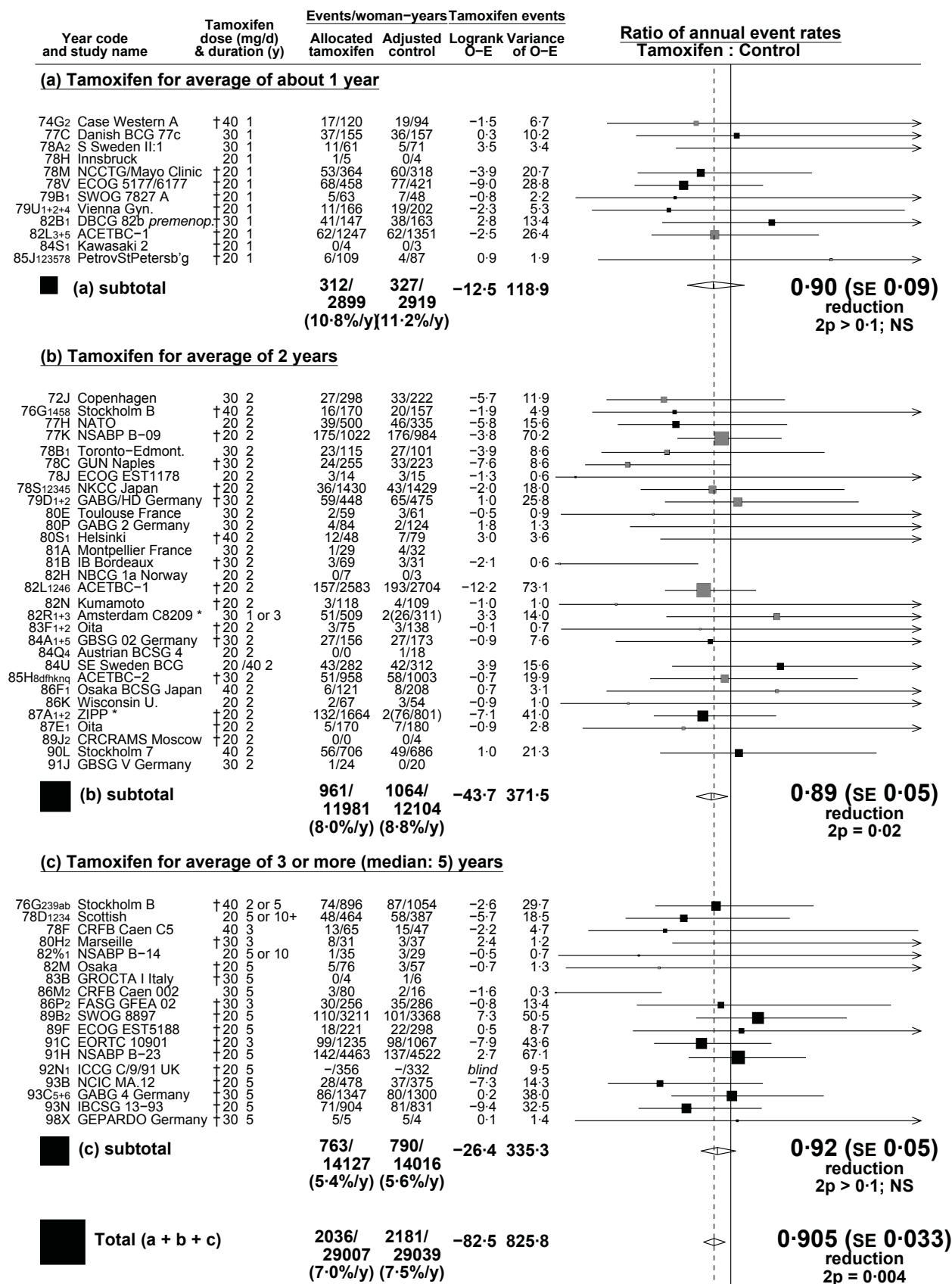
p 23: RRs for any death, one line / trial, ER+ disease: by tam. duration



* 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

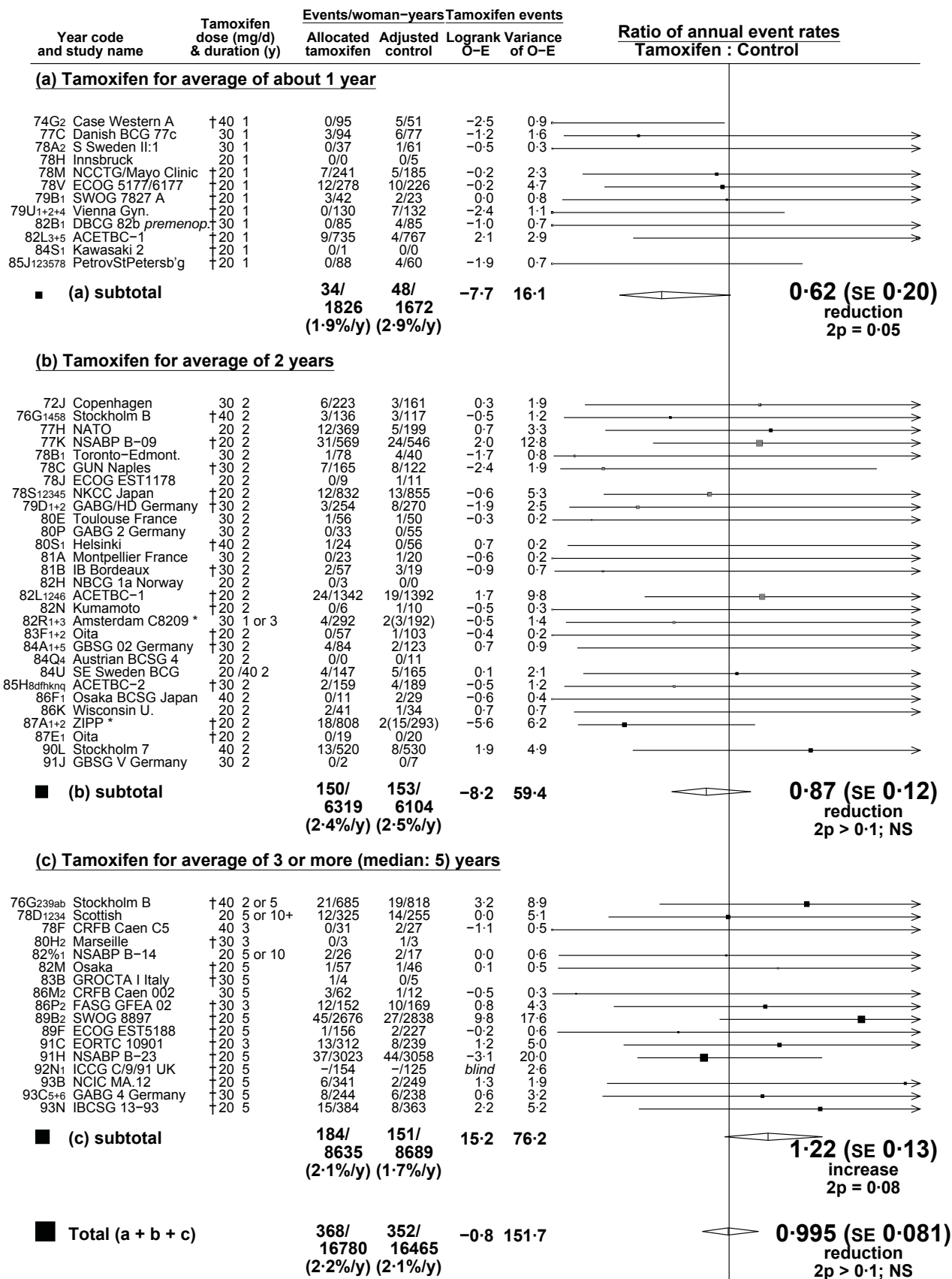
p 24: RRs for recurrence in years 0-4, one line / trial, ER-poor disease: by tam. duration



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

† Tamoxifen plus chemotherapy versus same chemotherapy alone

p 25: RRs for recurrence in years 5-9, one line / trial, ER-poor disease: by tam. duration



■ 99% or ◊ 95% confidence intervals

Heterogeneity between 3 subtotals: $\chi^2_2 = 7.9$; $p = 0.02$

Heterogeneity within subtotals: $\chi^2_{45} = 51.7$; $p > 0.1$; NS

Heterogeneity between 48 trials: $\chi^2_{47} = 59.6$; $p > 0.1$; NS

0 0.5 1.0 1.5 2.0
Tamoxifen better | Tamoxifen worse

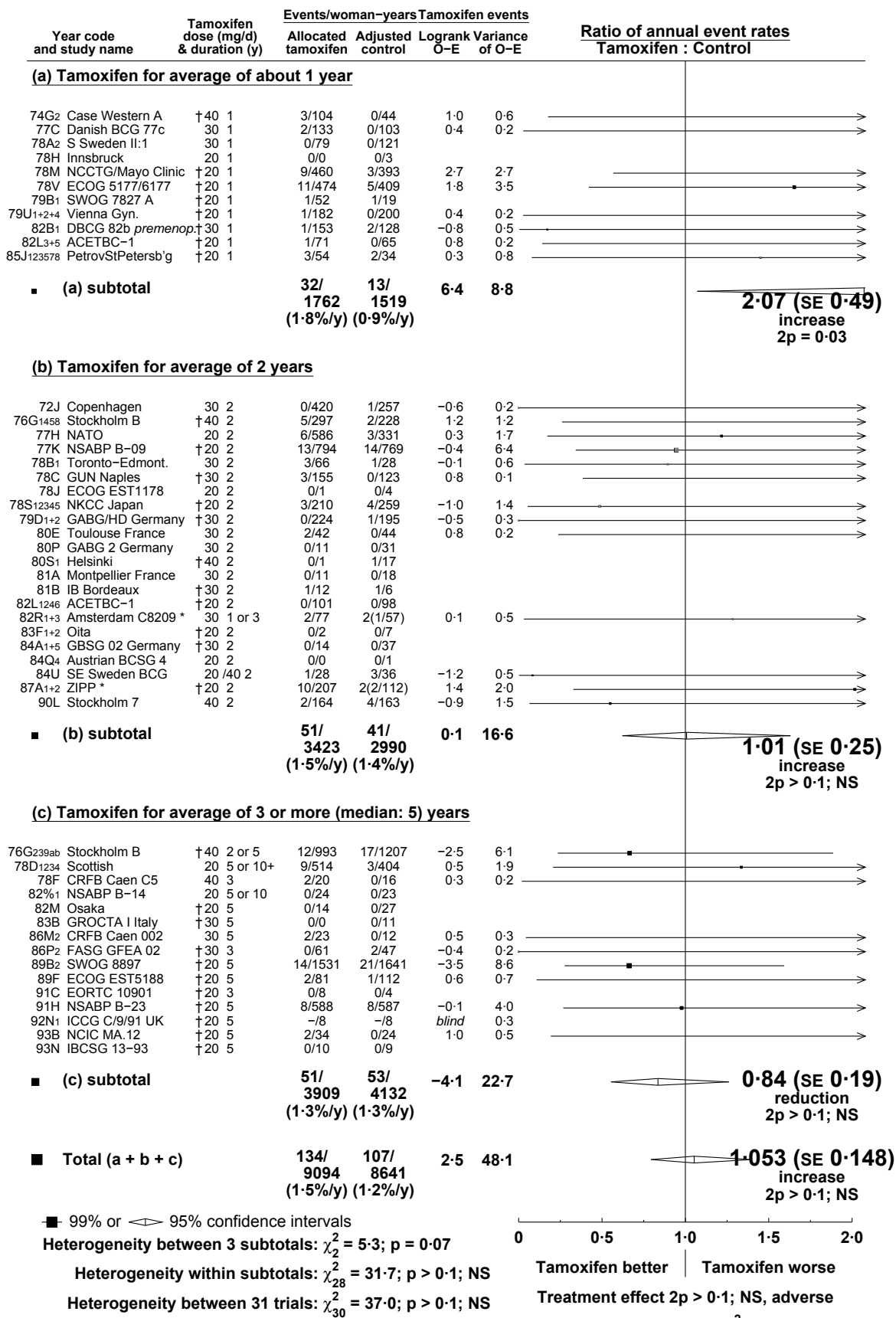
Treatment effect $2p > 0.1$; NS

Trend between 3 subtotals: $\chi^2_1 = 7.9$; $2p = 0.005$

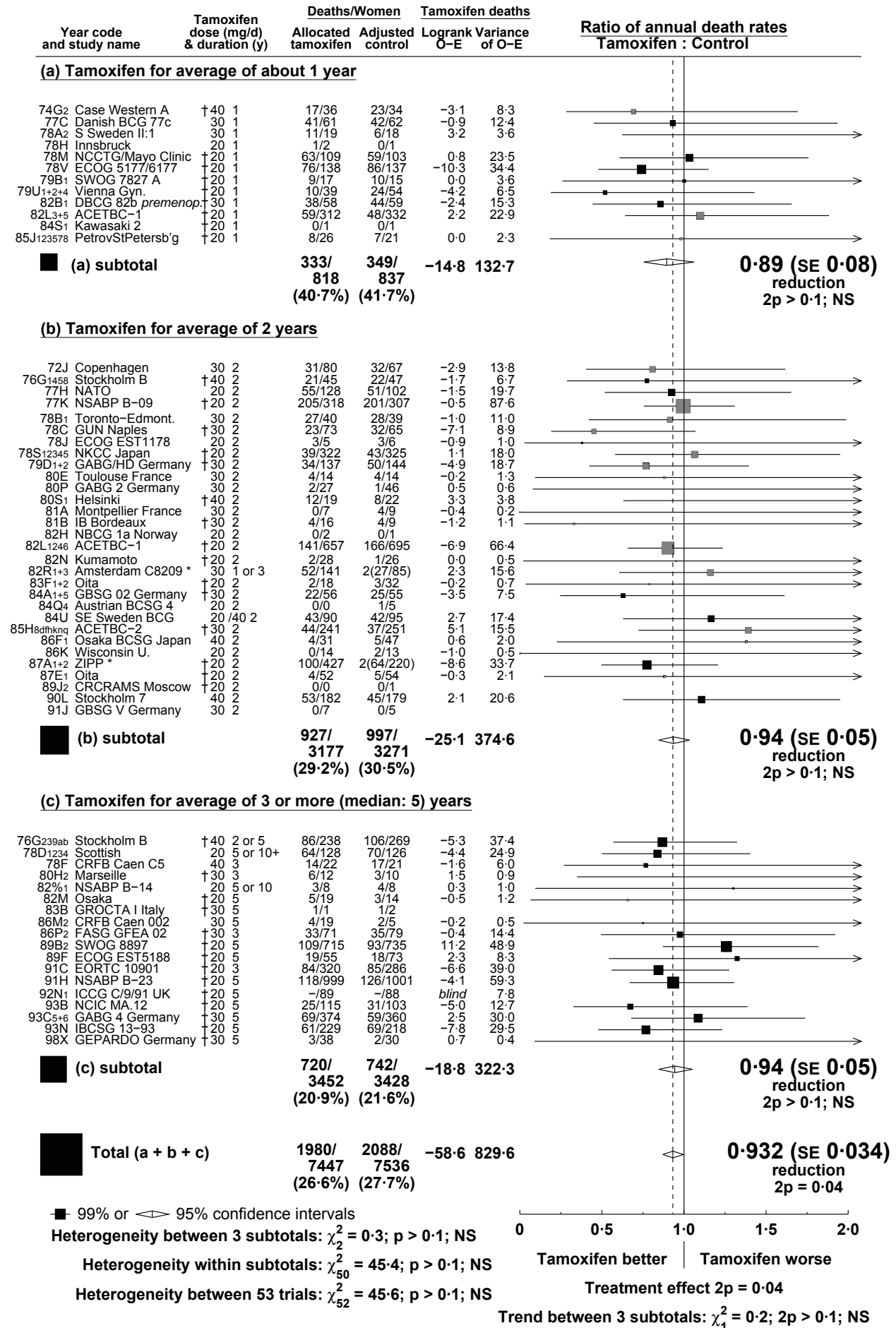
* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s)
and in final total of events/woman-years.

† Tamoxifen plus chemotherapy *versus* same chemotherapy alone

p 26: RRs for recurrence in years 10+, one line / trial, ER-poor disease: by tam. duration



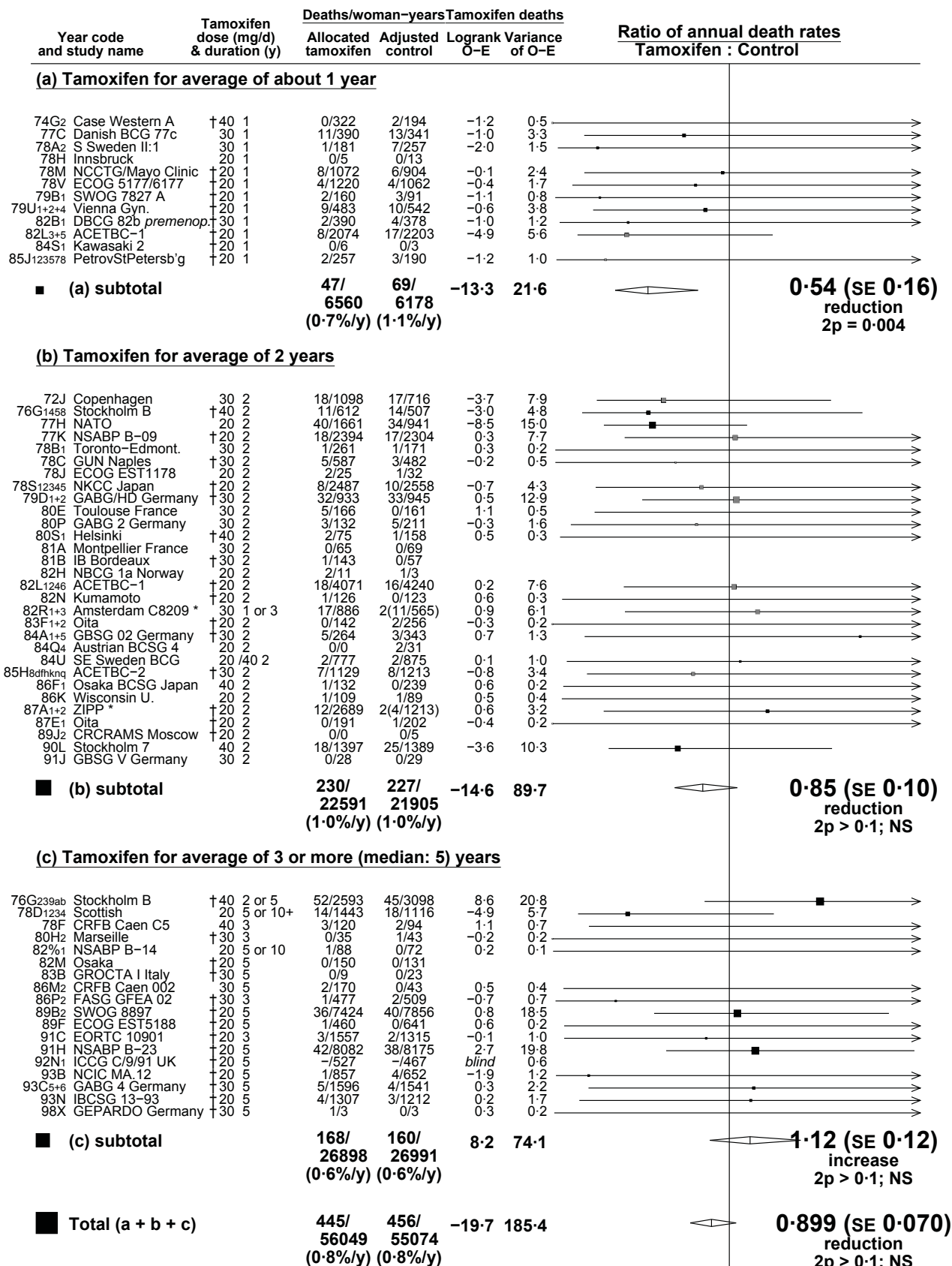
p 27: RRs for death with recurrence, one line / trial, ER-poor disease: by tam. duration



* 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

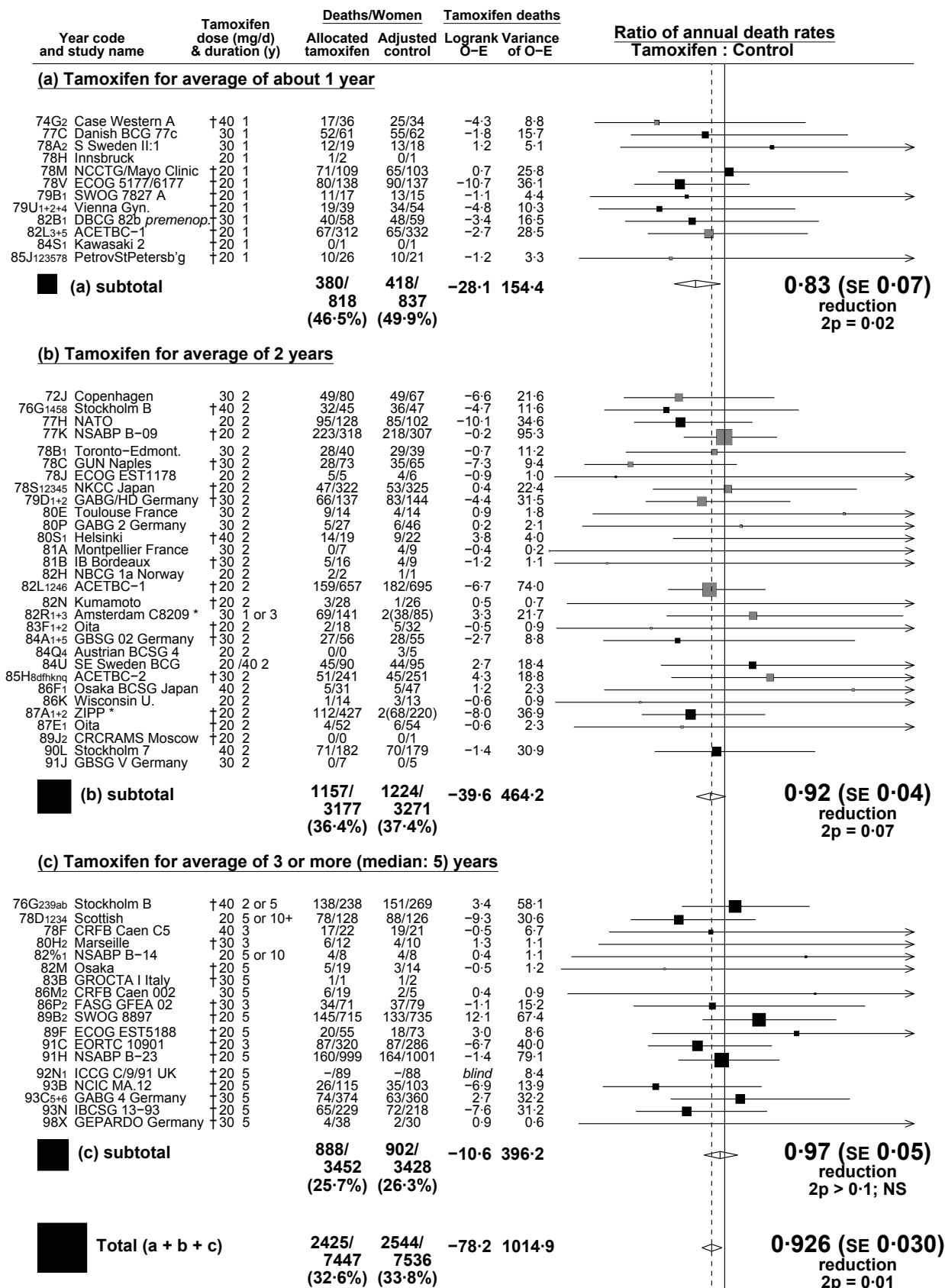
p 28: RRs for death without recurrence, one line / trial, ER-poor disease: by tam. duration



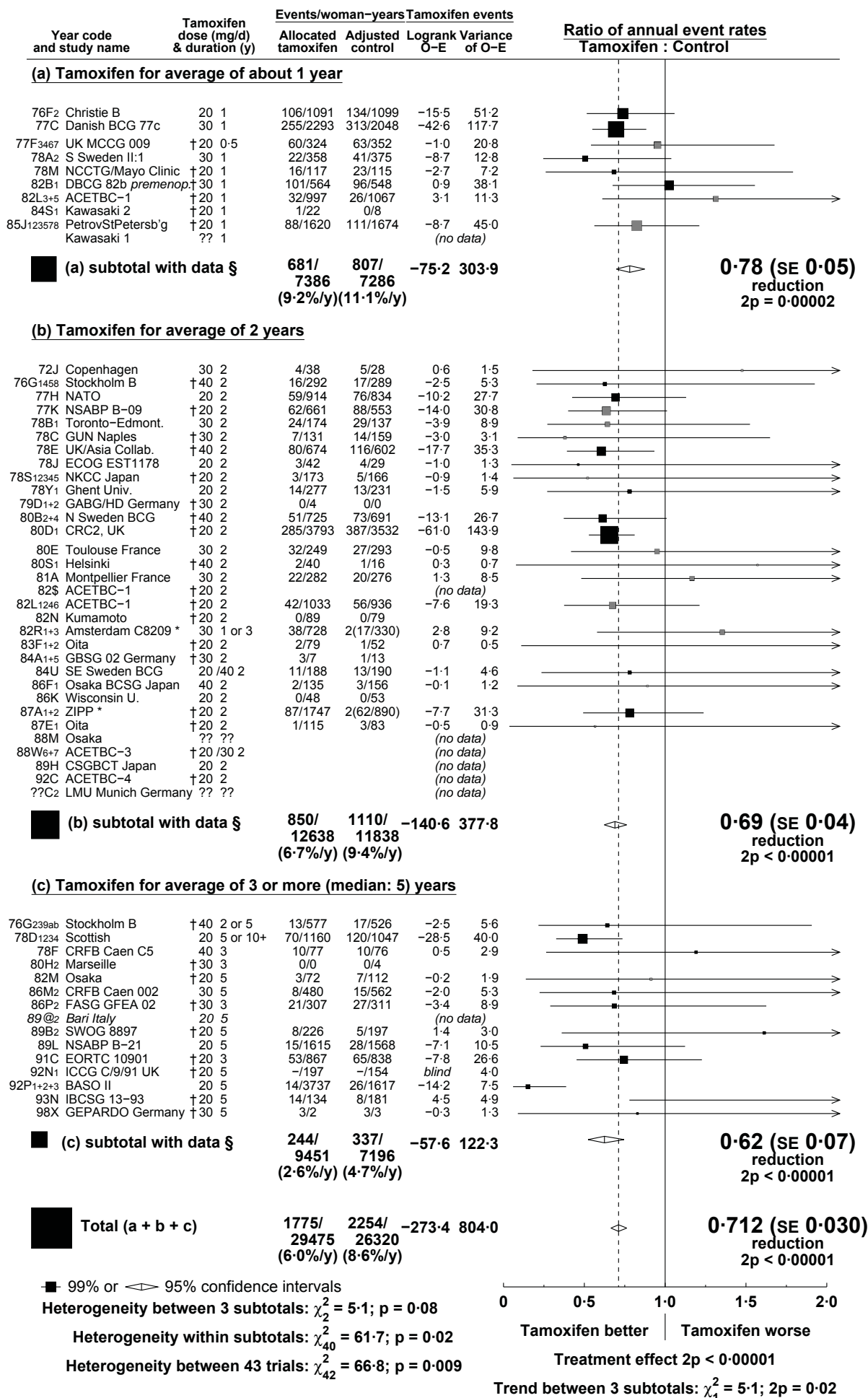
* For balance, control patients in 3-way trials or trial strata count half or twice in subtotal(s) and in final total of deaths/woman-years.

† Tamoxifen plus chemotherapy versus same chemotherapy alone

p 29: RRs for any death, one line / trial, ER-poor disease: by tam. duration



p 30: RRs for recurrence in years 0-4, one line / trial, ER-unknown disease: by tam. duration

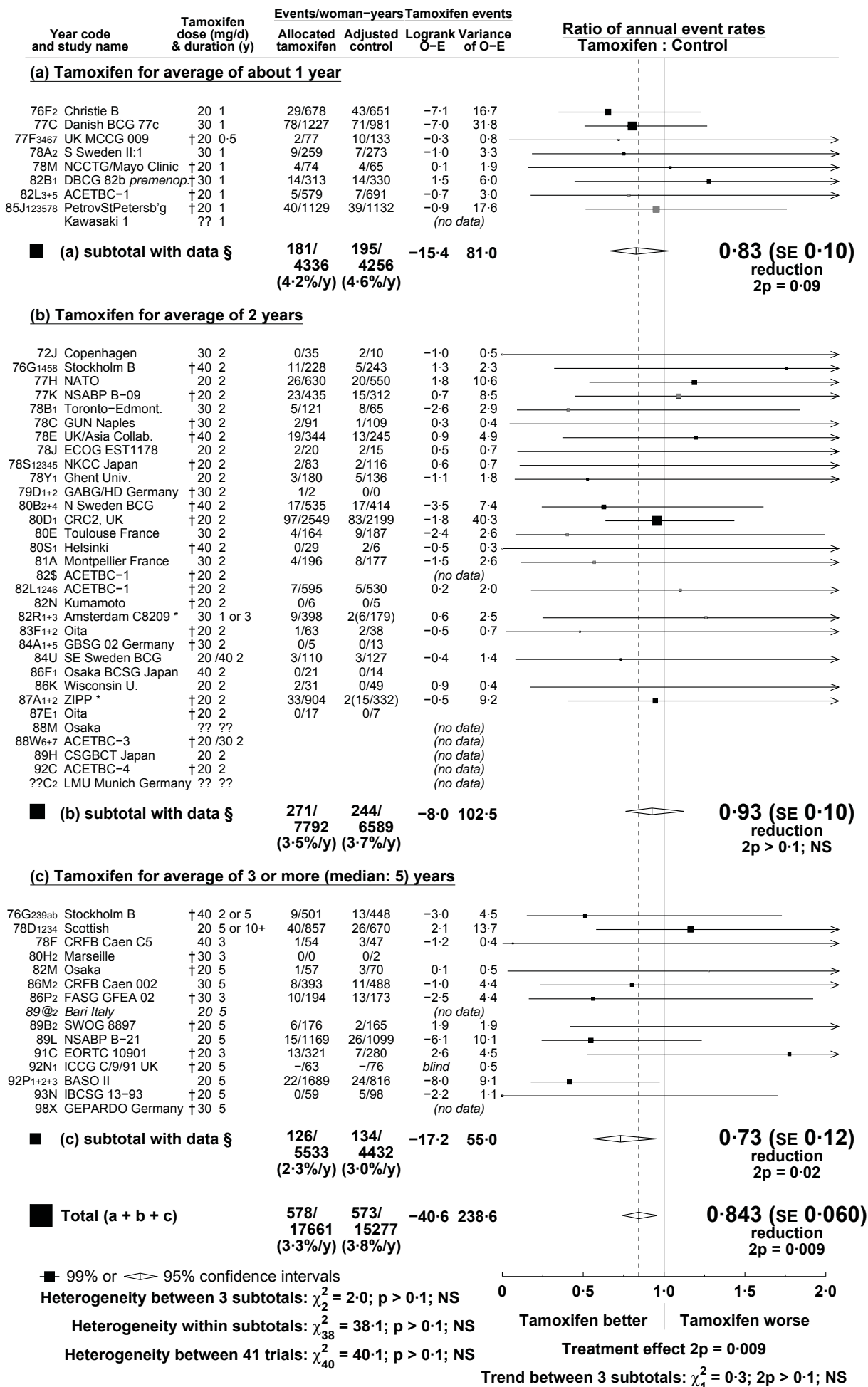


§ 1 trial with no data does not contribute to subtotals or to the overall total.

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

† Tamoxifen plus chemotherapy versus same chemotherapy alone

p 31: RRs for recurrence in years 5-9, one line / trial, ER-unknown disease: by tam. duration

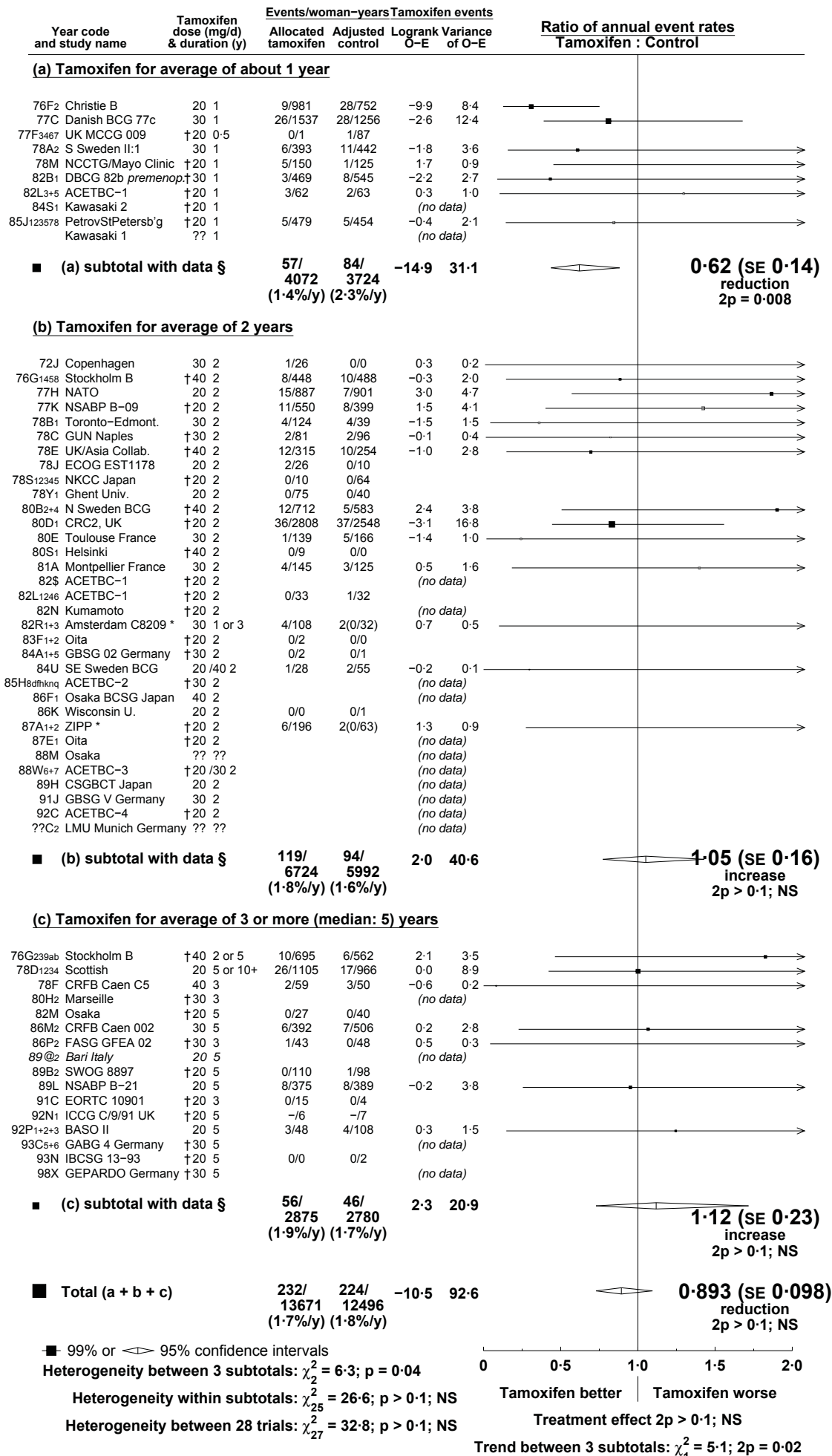


§ 1 trial with no data does not contribute to subtotals or to the overall total.

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

† Tamoxifen plus chemotherapy *versus* same chemotherapy alone

p 32: RRs for recurrence in years 10+, one line / trial, ER-unknown disease: by tam. duration

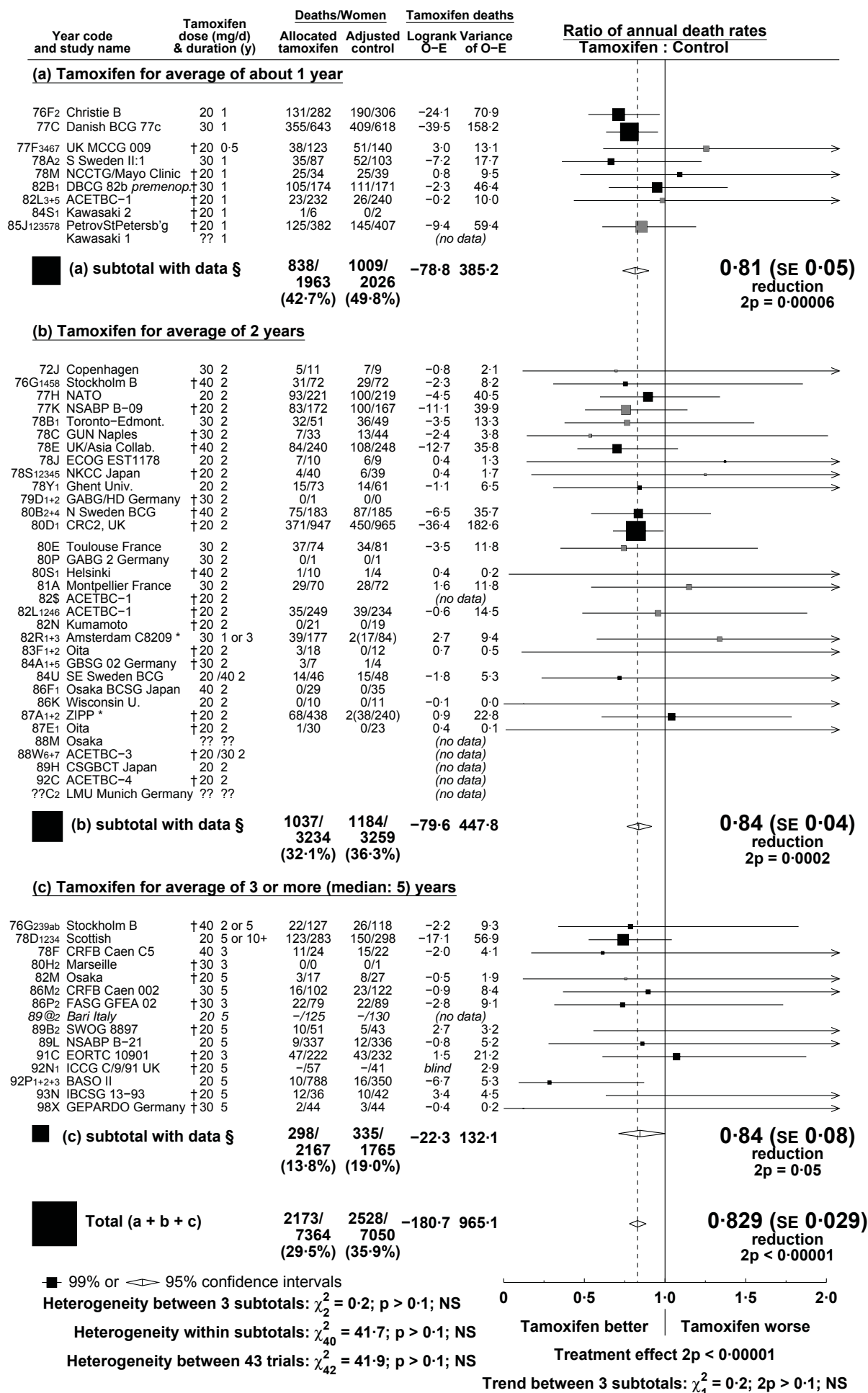


§ 1 trial with no data does not contribute to subtotals or to the overall total.

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

† Tamoxifen plus chemotherapy versus same chemotherapy alone

p 33: RRs for death with recurrence, one line / trial, ER-unknown disease: by tam. duration

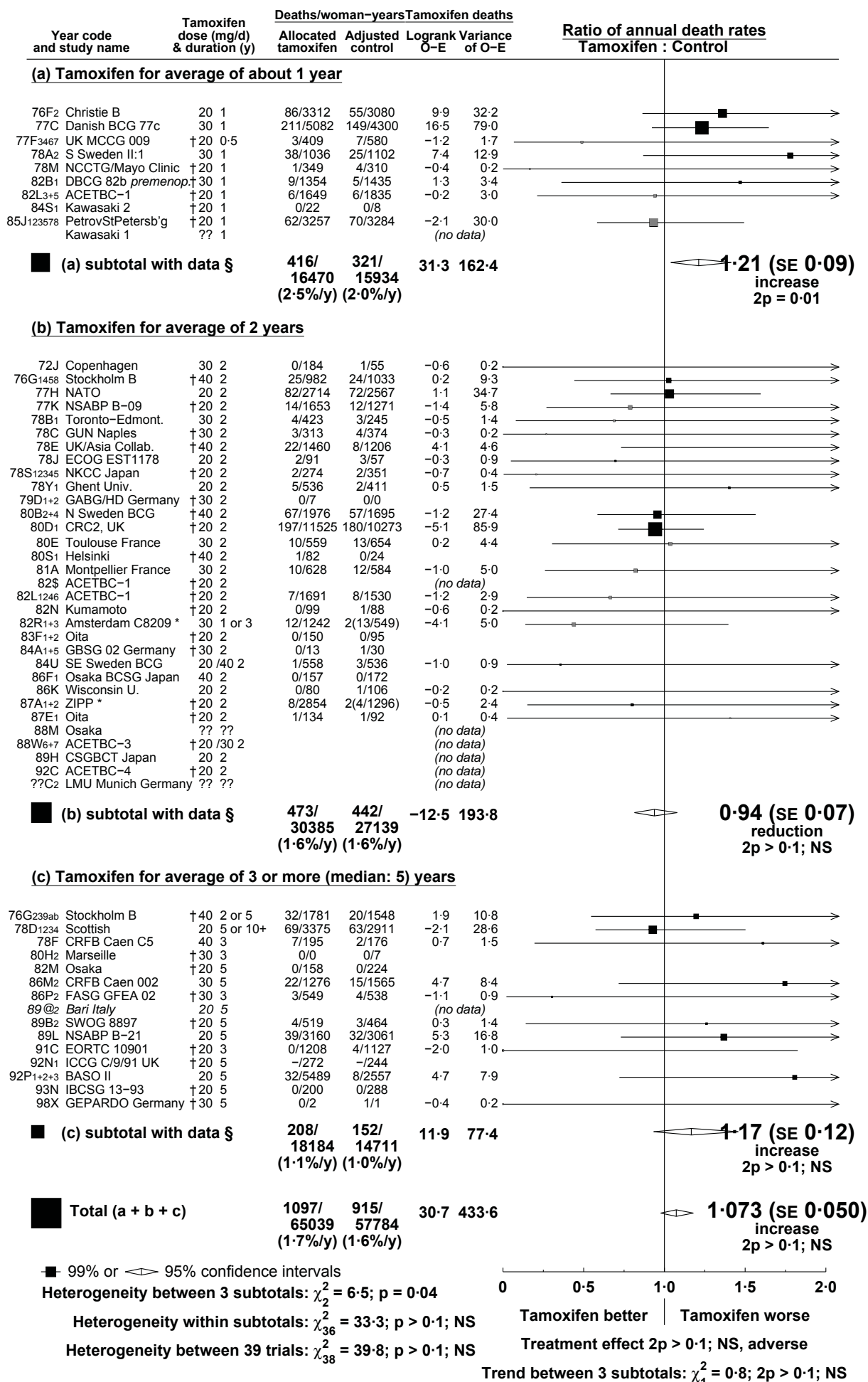


§ 1 trial with no data does not contribute to subtotals or to the overall total (allocated tamoxifen: 125; allocated control: 130)

* 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

p 34: RRs for death without recurrence, one line / trial, ER-unknown disease: by tam. duration

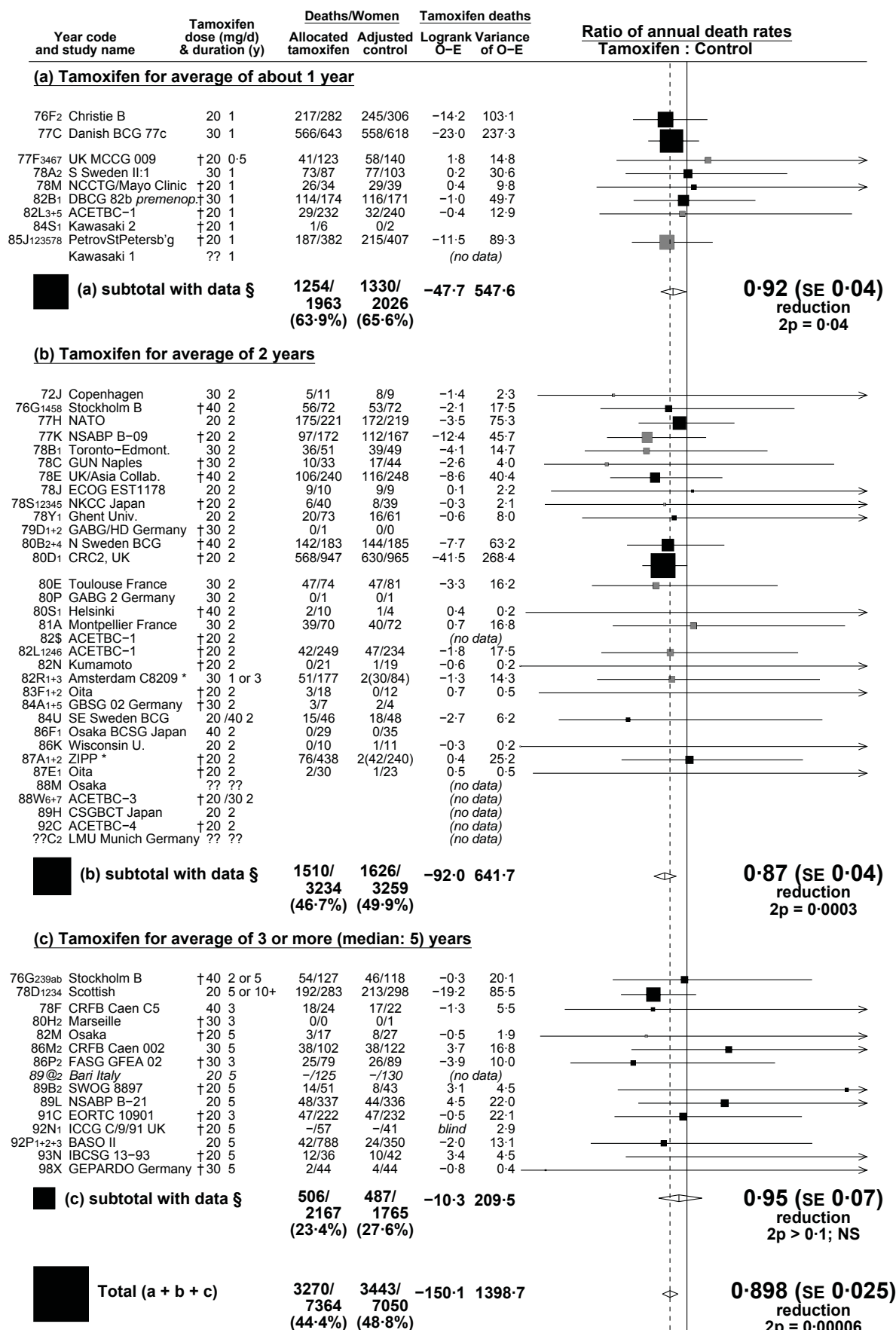


§ 1 trial with no data does not contribute to subtotals or to the overall total.

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

† Tamoxifen plus chemotherapy versus same chemotherapy alone

p 35: RRs for any death, one line / trial, ER-unknown disease: by tam. duration



■ 99% or ◊ 95% confidence intervals

Heterogeneity between 3 subtotals: $\chi^2_2 = 1.8$; $p > 0.1$; NS

Heterogeneity within subtotals: $\chi^2_{41} = 30.3$; $p > 0.1$; NS

Heterogeneity between 44 trials: $\chi^2_{43} = 32.0$; $p > 0.1$; NS

Treatment effect $2p = 0.00006$

Trend between 3 subtotals: $\chi^2_1 = 0.0$; $2p > 0.1$; NS

§ 1 trial with no data does not contribute to subtotals or to the overall total (allocated tamoxifen: 125; allocated control: 130)

* 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

Page 36: List of trials included in the EBCTCG meta-analysis of ~5 years of tamoxifen versus not: selected publications listed in chronological order of year starting

Year code	Text ref.	Trial name	Publication(s)
76G	22	Stockholm Adjuvant Tamoxifen Trial	Rutqvist LE, Johansson H, for the Stockholm Breast Cancer Study Group. Long-term follow-up of the randomized Stockholm trial on adjuvant tamoxifen among postmenopausal patients with early stage breast cancer. <i>Acta Oncol</i> 2007; 46 : 133–45.
78D	23,24	Scottish	Breast Cancer Trials Committee, Scottish Cancer Trials Office. Adjuvant tamoxifen in the management of operable breast cancer: the Scottish trial. <i>Lancet</i> 1987; 2 : 171–5. Stewart HJ, Prescott RJ, Forrest APM. Scottish Adjuvant Tamoxifen Trial: a randomized study updated to 15 years. <i>J Natl Cancer Inst</i> 2001; 93 : 456–62.
78F	17	CRFB Caen C5	Delozier T, Julien JP, Juret P, et al. Adjuvant tamoxifen in postmenopausal breast cancer: Preliminary results of a randomized trial. <i>Breast Cancer Res Treat</i> 1986; 7 : 105–09.
80H	18,19	Marseille	Ayme Y, Spitalier JM, Amalric R, et al. Preliminary results of a three-arm randomized trial of adjuvant chemo- and/or hormone-therapy for high-risk breast cancer. Fourth EORTC breast cancer working conference 1987 C2A.1; 30 June-3 July 1987; Imperial College, London, UK. Martin PM, Romain S, Spyrtas F, et al. Re-evaluation of the indications of adjuvant hormonotherapy in high risk primary breast cancer patients. <i>Bull Cancer</i> 1991; 78 : 709–723.
82%	25,26	NSABP B-14	Fisher B, Dignam J, Bryant J, et al. Five versus more than five years of tamoxifen therapy for breast cancer patients with negative lymph nodes and estrogen receptor-positive tumors [see comments]. <i>J Natl Cancer Inst</i> 1996; 88 : 1529–42. Fisher B, Dignam J, Bryant J, Wolmark N. Five versus more than five years of tamoxifen for lymph node-negative breast cancer: updated findings from the National Surgical Adjuvant Breast and Bowel Project B-14 randomized trial. <i>J Natl Cancer Inst</i> 2001; 93 : 684–90.
82M		Osaka	Personal communication
83B	15	GROCTA I	Boccardo F, Rubagotti A, Bruzzi P, et al. Chemotherapy versus tamoxifen versus chemotherapy plus tamoxifen in node-positive, estrogen receptor-positive breast cancer patients: Results of a multicentric Italian study. <i>J Clin Oncol</i> 1990; 8 : 1310–20.
89@	6	Bari, Italy	Paradiso A, De Lena M, Sambiasi M, et al. Adjuvant hormonotherapy for slow-proliferating node-negative breast cancer patients. Results of the phase III trial of NCI-Bari. <i>Breast</i> 2003; 12 : S40, P90.
89L	4	NSABP B-21	Fisher B, Bryant J, Dignam JJ, Wickerham DL, et al. Tamoxifen, radiation therapy, or both for prevention of ipsilateral breast tumor recurrence after lumpectomy in women with invasive breast cancers of one centimeter or less. <i>J Clin Oncol</i> 2002; 20 : 4141–49.
86M	16	CRFB Caen 002	Delozier T, Switers O, Genot JY et al. Late delayed adjuvant tamoxifen in breast cancer, a multicenter randomized trial. <i>Fourth International Congress on Anti-cancer Chemotherapy 1993 p.58; February 2-5, 1993; Paris, France.</i>
86P	20	FASG GFEA 02	Namer M, Fargeot P, Roche H, et al. Improved disease-free survival with epirubicin-based chemoendocrine adjuvant therapy compared with tamoxifen alone in one to three node-positive, estrogen-receptor-positive, postmenopausal breast cancer patients: results of French Adjuvant Study Group 02 and 07 trials. <i>Ann Oncol</i> 2006; 17 : 65–73.
89B	7	SWOG 8897 / INT 0102	Hutchins LF, Green SJ, Ravdin PM, et al. Randomized, controlled trial of cyclophosphamide, methotrexate, and fluorouracil versus cyclophosphamide, doxorubicin, and fluorouracil with and without tamoxifen for high-risk, node-negative breast cancer: treatment results of Intergroup protocol INT-0102. <i>J Clin Oncol</i> 2005; 23 : 8313–21.
89F	8	ECOG EST 5188 / INT 0101	Davidson NE, O'Neill AM, Vukov AM, et al. Chemoendocrine therapy for premenopausal women with axillary lymph node-positive, steroid hormone receptor-positive breast cancer: results from INT 0101 (E5188). <i>J Clin Oncol</i> 2005; 23 : 5973–82.
91C	21	EORTC 10901	Morales L, Canney P, Dyczka J, et al. Postoperative adjuvant chemotherapy followed by adjuvant tamoxifen versus nil for patients with operable breast cancer: a randomised phase III trial of the European Organisation for Research and Treatment of Cancer Breast Group. <i>Eur J Cancer</i> 2007; 43 : 331–40.
91H	9	NSABP B-23	Fisher B, Anderson S, Tan Chiu E, et al. Tamoxifen and chemotherapy for axillary node-negative, estrogen receptor-negative breast cancer: findings from National Surgical Adjuvant Breast and Bowel Project B-23. <i>J Clin Oncol</i> 2001; 19 : 931–42.
92N1	10	ICCG C/9/91 UK	Bliss JM, Wils J, Marty M et al. Evaluation of the tolerability of FE ₅₀ C versus FE ₇₅ C in a prospective randomised trial in adjuvant breast cancer patients. <i>Proc Ann Meet Am Soc Clin Oncol</i> 2002; 21 : 51b, A2017.
92P	5	BASO II	Blamey RW, Chetty U, Bates T, et al. Radiotherapy and/or Tamoxifen after conserving surgery for breast cancers of excellent prognosis: BASO II trial. <i>Eur J Cancer Suppl</i> 2008; 6 : 55, A17.
93B	11	NCIC MA.12	Bramwell VHC, Pritchard KI, Tu D, et al. A randomized placebo-controlled study of tamoxifen after adjuvant chemotherapy in premenopausal women with early breast cancer (National Cancer Institute of Canada Clinical Trials Group Trial, MA.12). <i>Ann Oncol</i> 2010; 21 : 283-90.
93C	12	GABG-4-D-93	Kaufmann M, Graf E, Jonat W, et al. Tamoxifen versus control after adjuvant, risk-adapted chemotherapy in postmenopausal, receptor-negative patients with breast cancer: a randomized trial (GABG-IV D-93) - the German Adjuvant Breast Cancer Group. <i>J Clin Oncol</i> 2005; 23 : 7842–48.
93N	13	IBCSG 13-93	Colleoni M, Gelber S, Goldhirsch A, et al. Tamoxifen after adjuvant chemotherapy for premenopausal women with lymph node-positive breast cancer: International Breast Cancer Study Group Trial 13–93. <i>J Clin Oncol</i> 2006; 24 : 1332–41.
98X	14	GEPARDO Germany	von Minckwitz G, Costa SD, Raab G, et al. Dose-dense doxorubicin, docetaxel, and granulocyte colony-stimulating factor support with or without tamoxifen as preoperative therapy in patients with operable carcinoma of the breast: a randomized, controlled, open phase IIb study. <i>J Clin Oncol</i> 2001; 19 : 3506–15.