Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials

Early Breast Cancer Trialists' Collaborative Group (EBCTCG)

Webappendix (click on page number to jump directly to it)

Webtable 1: Randomised trials comparing radiotherapy following breast-conserving surgery versus the same management without radiotherapy that began before the year 2000 — treatment details

Year, code and study name	Breast conserving surgery*	Axillary treatment	Breast irradiation	Boost irradiation	Regional nodal irradiation	Systemic chemoendocrine therapy common to both trial arms
A. Trials evaluating the benefit of radiotherapy after lumpectomy						
76B NSABP B-06	Lumpectomy	Levels I & II	50 Gy (2 Gy/f) c or m	None	None	pN+: FMel
82Y St George's	Lumpectomy	Levels I +/- AF RT†	54 Gy d (2 Gy/f) m	10 Gy (2 Gy/f) o or e	0-50 Gy (2 Gy/f) m (IMC and SC/AF)†	ER+: 2 yr tam; ER-: CMF
84P Ontario COG	Lumpectomy	Levels I & II	40 Gy (2.5 Gy/f) c	12.5 Gy (2.5 Gy/f) c	None	None
85B Scottish	Lumpectomy‡	Sample+ AF RT† or Levels I, II & III	50 Gy (2-2.5 Gy/f) m	10-30 Gy (2-3 Gy/f) o,e or i	50 Gy (2-2.5 Gy/f) m (IMC), 0-45 (2.3 Gy/f) m (SC/AF)†	ER+: 5 yr tam; ER-: CMF
85D West Midlands	Lumpectomy§	AF RT†	40 Gy (2.7 Gy/f) or 50 Gy (2 Gy/f) d c	15 Gy (3 Gy/f) e/c	40 Gy (2 .7 Gy/f) or 50 Gy (2 Gy/f) c (SC/AF)†	2 yr tam
86C CRC UK	Lumpectomy§	Various	Various	Various	Various	Various
B. Trials evaluating the benefit of radiotherapy after sector resection or quadrantectomy						
81L Uppsala-Örebro	Sector resection	Levels I & II	54 Gy (2 Gy/f) c or m	None	None	None
87R INT Milan III	Quadrantectomy	Levels I, II & III	50 Gy (2 Gy/f) c or m	10 Gy (2 Gy/f) o or e	None	pN+: CMF or tam
90M Tampere	Sector resection	Levels I & II	50 Gy (2 Gy/f) m	None	None	None
91P SweBCG 91-RT	Sector resection	Levels I & II	48-54 Gy (1.9-2.2 Gy/f) m	None	None	Tam, CMF, or none**
C. Trials evaulating the need for radiotherapy after lumpectomy in low risk women						
89L NSABP B-21	Lumpectomy	Levels I & II	50 Gy (2 Gy/f) c or m	10 Gy (2 Gy/f) o¶	None	5 yr tam
91J GBSG V Germany	Lumpectomy	Levels I & II	50 Gy (2 Gy/f) m	10-12 Gy (2.0 Gy/f) e	None	2 yr tam (in 2 of 4 trial arms)
92A PMH Toronto	Lumpectomy	Levels I & II	40 Gy (2.5 Gy/f) or 50 Gy (2 Gy/f) c or m	12.5 Gy (2.5 Gy/f) o or e¶	None	5yr tam
92P BASO II	Lumpectomy§	Sample	45-50Gy (2-2.3 Gy/f) m	10-15 Gy (2-3 Gy/f) e	None	5 yr tam (in 2 of 4 trial arms)
94C CALGB 9343††	Lumpectomy	None or Levels I & II ‡‡	45 Gy (1.8 Gy/f) c or m	14 Gy (2 Gy/f) e	None	5 yr tam
96Y ABCSG 8a††	Lumpectomy	SLN or Levels I & II	50 Gy (2 Gy/f) c or m	10 Gy (0-2 Gy/f) e or I ¶	None	5 yr tam or 2 yr tam then 3 yr anastrozole
99W PRIME 1††	Lumpectomy	Sample or Levels I, II & III or SLN‡‡	45-50Gy (2-2.3 Gy/f) m	0-15 Gy (0-2 Gy/f) e	None	5 yr tam

AF=axillary fossa, c=cobalt-60, C=cyclophosphamide, d=maximum tissue dose, e=electron, ER=oestrogen receptor, F=5-fluorouracil, f=fraction, Gy=Gray (intended dose), i =iridium-192, IMC=internal mammary chain, m=megavoltage (linear accelerator), M=methotrexate, Mel=melphalan, o=orthovoltage, pN+=pathologically node-positive, Quad=quadrentectomy, sample=sampling, RT=radiotherapy, SC=supraclavicular fossa, SLN=sentinel lymph node procedure, tam=tamoxifen.

* Negative surgical margins required, unless otherwise specified.

† Among those randomised to radiotherapy: IMC RT for medial tumours (19% of women, St.George's), and supraclavicular/axillary radiotherapy for all (West Midlands), for pN+ (28%, St. George's), or after axillary sampling surgery (60%, Scottish).

‡ Negative surgical margins not required.

§ Margin status not specified.

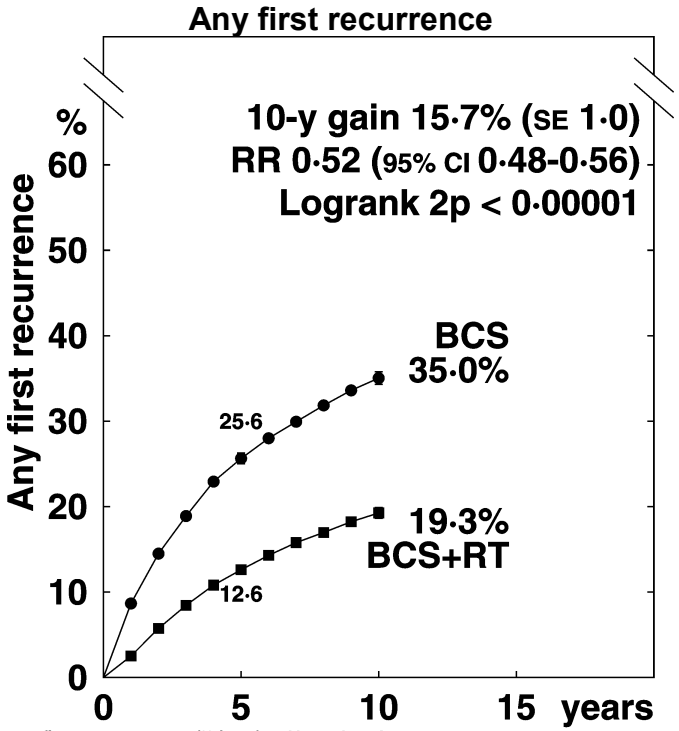
¶ Among those randomized to radiotherapy: boost in 25% (NSABP B-21), 97% (PMH Toronto), or 65% (ABCSG 8a).

** Tamoxifen in 7%, and CMF in 2% (all with tumours > 2 cm in size).

†† Trials with low-risk patients, i.e. all patients with pT1-2, c or pN-, negative surgical margins and either older age (≥ 65), post-menopausal status, and/or ER+ tumours.

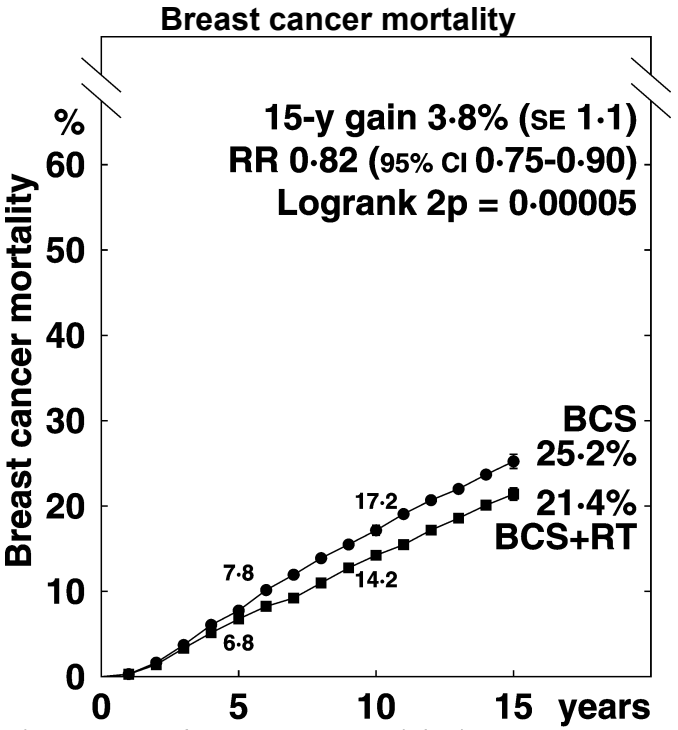
‡‡ No axillary surgery (64%) or level I & II dissection (36%) in CALGB 9343. Axillary sampling (73%), or level I, II & III dissection (26%), or sentinel lymph node procedure (1%) in PRIME 1.

Webfigure 1a. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on 10-year risk of any (locoregional or distant) first recurrence and on 15-year risks of breast cancer mortality and all-cause mortality. Data from 10,801 women (67% pathologically node-negative) in 17 trials.
Vertical lines indicate 1 SE above or below the 5, 10 and 15 year percentages.



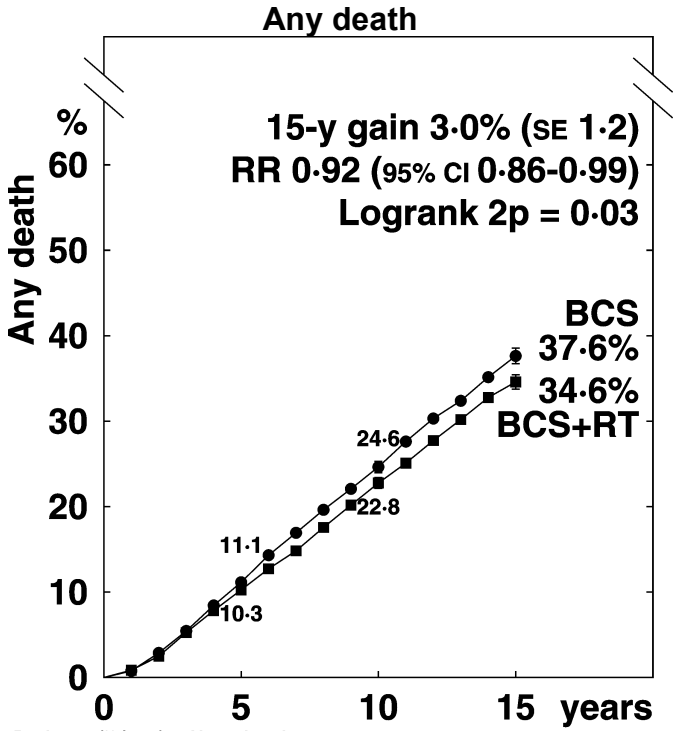
any first recurrence rates (% / year) and logrank analyses

	Years 0 - 4	Years 5 - 9	Year 10+
BCS+RT	2·98 (705 / 23657)	1·74 (265 / 15239)	1·20 (125 / 10414)
BCS	5·97 (1274 / 21324)	2·74 (338 / 12339)	0·96 (76 / 7915)
Rate ratio, from	0·46 SE 0·03	0·59 SE 0·07	1·17 SE 0·16
(O-E) / V	-339·0 / 435·1	-73·6 / 140·0	7·1 / 45·0



After-recurrence or possible-breast-cancer death rates (% / year) and logrank analyses

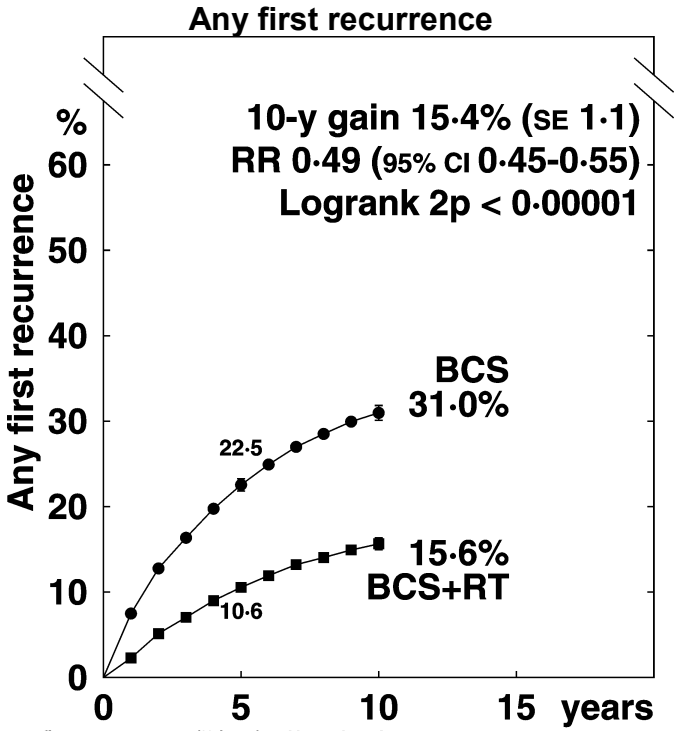
	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
BCS+RT	1·36 SE 0·07	1·59 SE 0·10	1·62 SE 0·14	2·22 SE 0·23
BCS	1·61 SE 0·08	2·25 SE 0·12	2·21 SE 0·16	2·62 SE 0·27
Rate ratio, from	0·87 SE 0·07	0·75 SE 0·07	0·84 SE 0·11	0·89 SE 0·14
(O-E) / V	-24·0 / 170·0	-42·6 / 151·1	-13·6 / 75·9	-5·1 / 43·3



Death rates (% / year) and logrank analyses

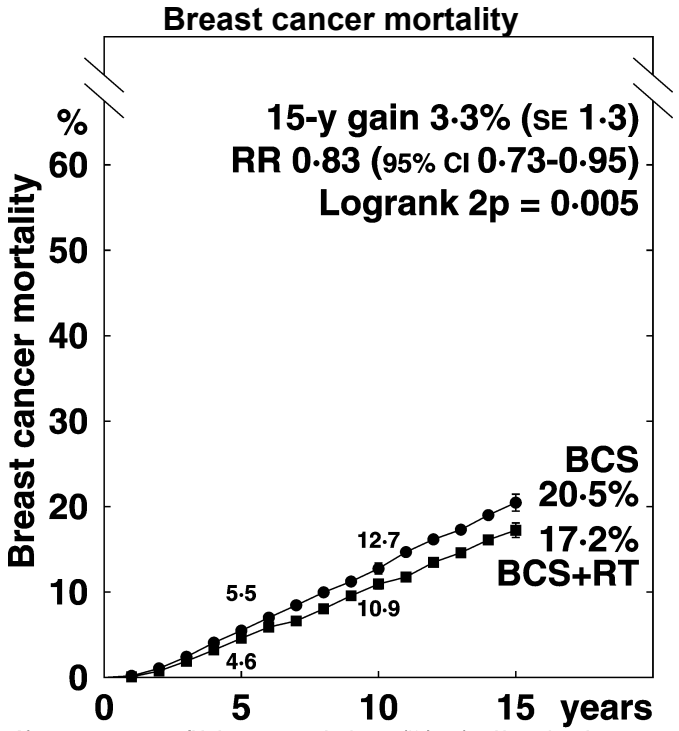
	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
BCS+RT	2·12 (532 / 25074)	2·96 (515 / 17410)	3·31 (293 / 8848)	4·83 (196 / 4062)
BCS	2·33 (573 / 24608)	3·32 (553 / 16642)	3·82 (317 / 8292)	4·39 (164 / 3735)
Rate ratio, from	0·92 SE 0·06	0·89 SE 0·06	0·88 SE 0·08	1·12 SE 0·12
(O-E) / V	-22·7 / 259·7	-27·8 / 250·5	-18·2 / 141·1	8·7 / 80·1

Webfigure 1b. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on 10-year risk of any (locoregional or distant) first recurrence and on 15-year risks of breast cancer mortality and all-cause mortality. Data from 7,287 women with pathologically node-negative disease. Vertical lines indicate 1 SE above or below the 5, 10 and 15 year percentages.



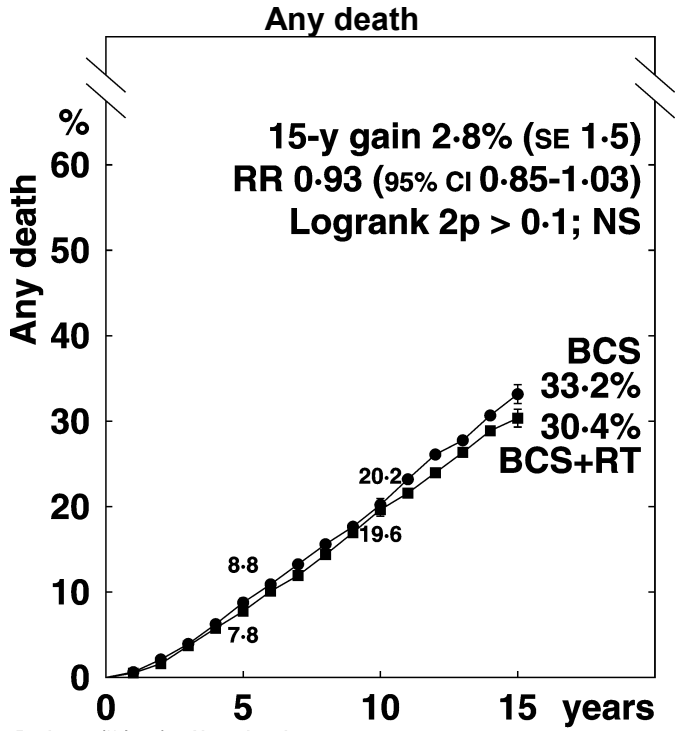
any first recurrence rates (% / year) and logrank analyses

	Years 0 - 4	Years 5 - 9	Year 10+
BCS+RT	2·45 (396 / 16180)	1·31 (135 / 10341)	0·94 (63 / 6676)
BCS	5·17 (763 / 14771)	2·41 (205 / 8507)	0·77 (40 / 5212)
Rate ratio, from	0·45 SE 0·04	0·52 SE 0·08	1·25 SE 0·23
(O-E) / V	-212·2 / 263·0	-53·8 / 81·4	5·4 / 24·4



After-recurrence or possible-breast-cancer death rates (% / year) and logrank analyses

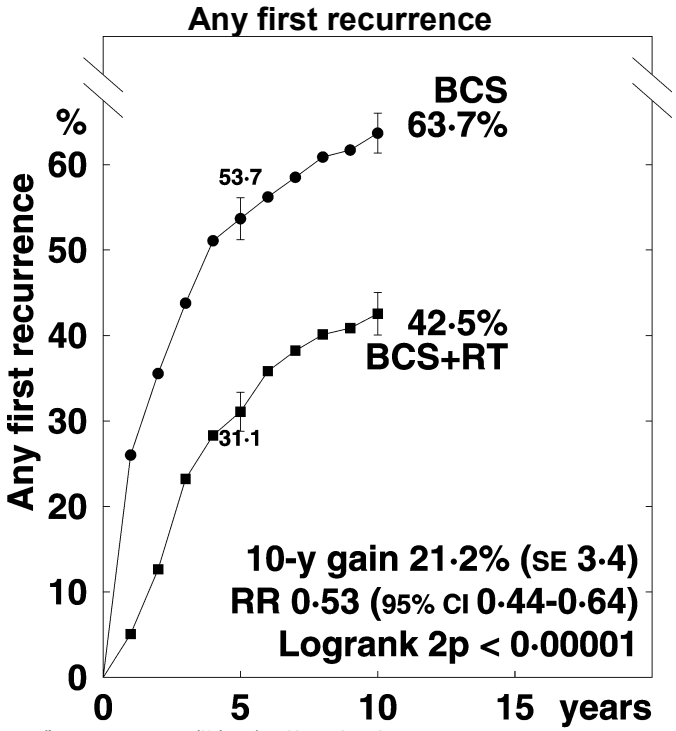
	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
BCS+RT	0·90 SE 0·07	1·28 SE 0·10	1·30 SE 0·15	2·13 SE 0·28
BCS	1·12 SE 0·08	1·68 SE 0·12	2·02 SE 0·19	2·61 SE 0·33
Rate ratio, from	0·83 SE 0·10	0·85 SE 0·10	0·76 SE 0·13	0·95 SE 0·18
(O-E) / V	-15·7 / 82·7	-13·7 / 82·8	-12·3 / 44·9	-1·5 / 27·7



Death rates (% / year) and logrank analyses

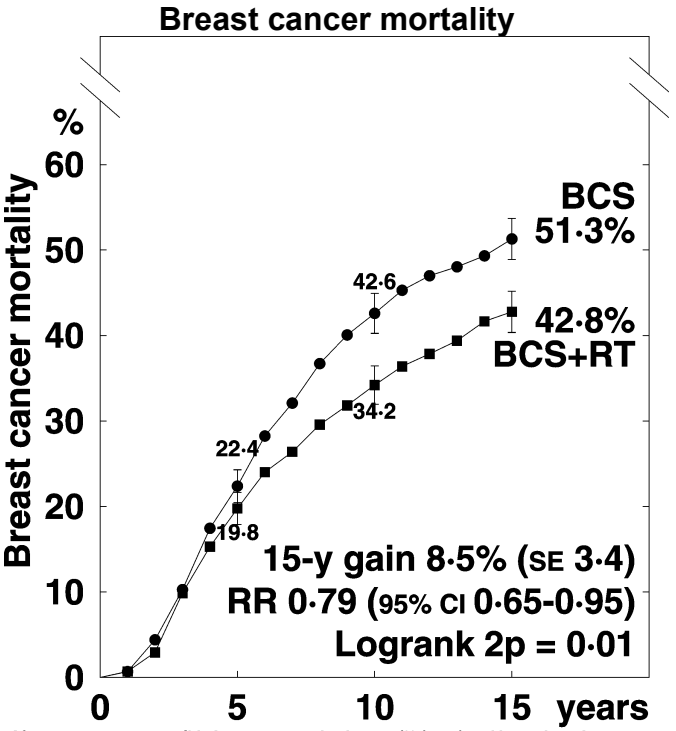
	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
BCS+RT	1·58 (271 / 17127)	2·70 (319 / 11816)	2·85 (164 / 5762)	4·75 (125 / 2630)
BCS	1·80 (303 / 16842)	2·66 (306 / 11499)	3·58 (200 / 5584)	4·61 (113 / 2449)
Rate ratio, from	0·88 SE 0·08	1·02 SE 0·08	0·80 SE 0·10	1·06 SE 0·14
(O-E) / V	-17·8 / 139·5	3·4 / 151·2	-19·0 / 87·3	3·4 / 54·5

Webfigure 1c. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on 10-year risk of any (locoregional or distant) first recurrence and on 15-year risks of breast cancer mortality and all-cause mortality. Data from 1,050 women with pathologically node-positive disease. Vertical lines indicate 1 SE above or below the 5, 10 and 15 year percentages.



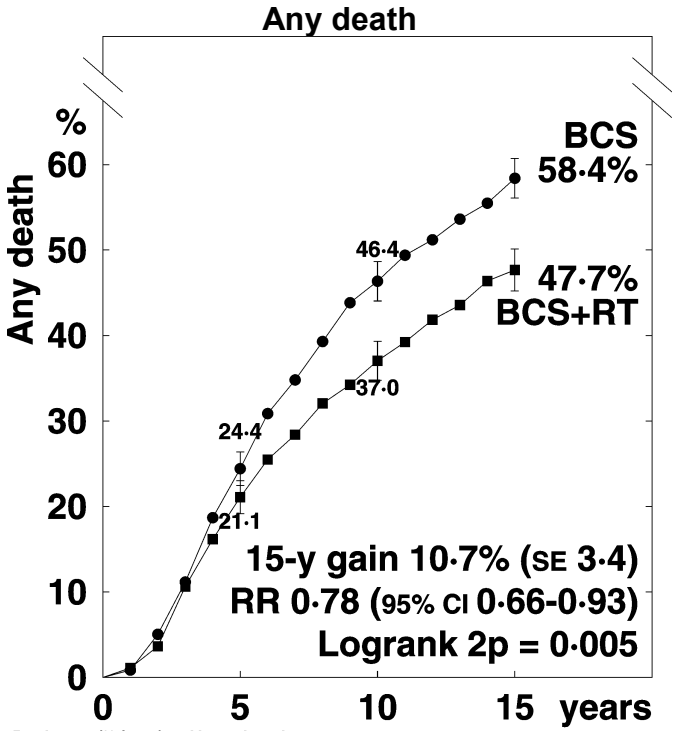
any first recurrence rates (% / year) and logrank analyses

	Years 0 - 4	Years 5 - 9	Year 10+
BCS+RT	8·04 (162 / 2014)	4·14 (55 / 1329)	1·90 (30 / 1578)
BCS	16·77 (263 / 1568)	4·67 (43 / 921)	1·39 (15 / 1083)
Rate ratio, from	0·44 SE 0·07	0·76 SE 0·20	1·18 SE 0·35
(O-E) / V	-68·8 / 84·9	-5·5 / 20·1	1·6 / 9·4



After-recurrence or possible-breast-cancer death rates (% / year) and logrank analyses

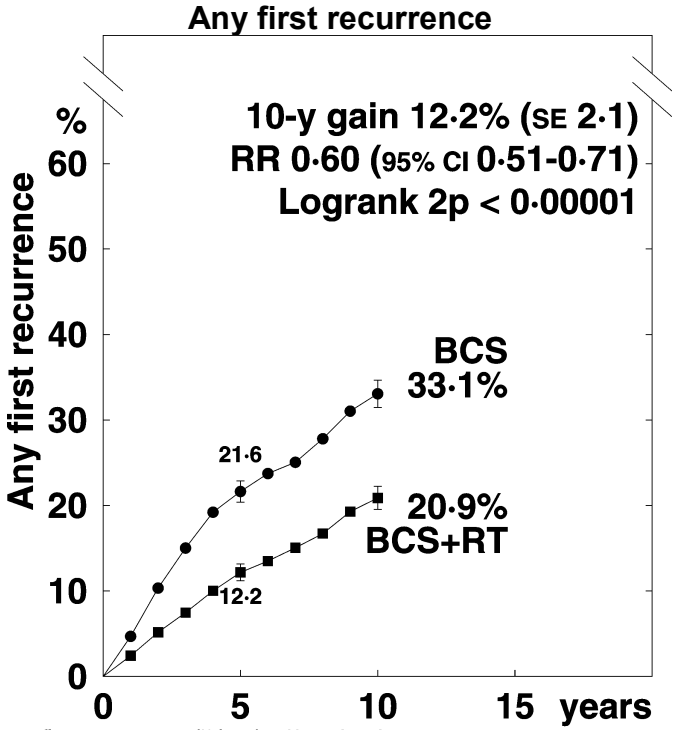
	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
BCS+RT	4·33 SE 0·43	3·97 SE 0·48	2·91 SE 0·50	2·78 SE 0·56
BCS	4·83 SE 0·46	6·27 SE 0·64	3·24 SE 0·56	3·02 SE 0·62
Rate ratio, from	0·87 SE 0·14	0·65 SE 0·13	0·84 SE 0·24	0·93 SE 0·29
(O-E) / V	-6·5 / 45·1	-15·8 / 36·7	-2·6 / 15·3	-0·8 / 10·7



Death rates (% / year) and logrank analyses

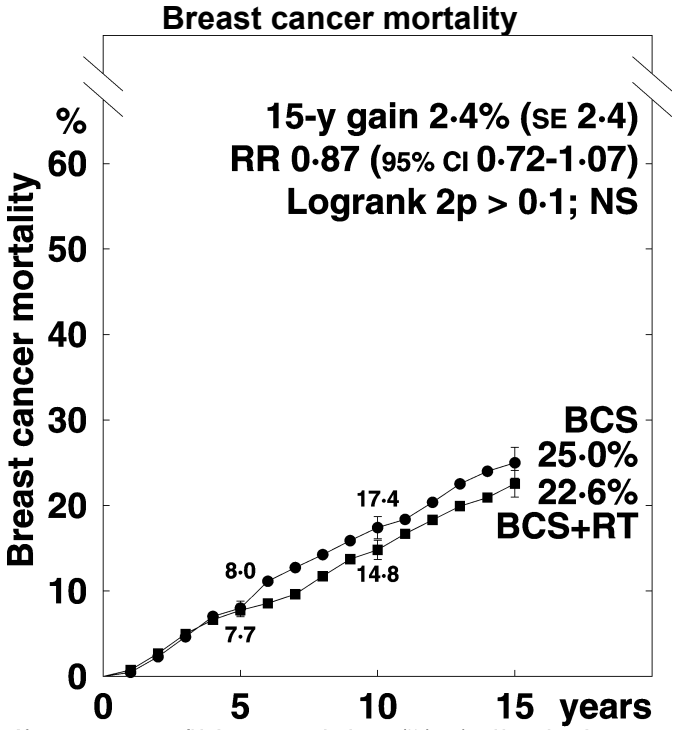
	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
BCS+RT	4·72 (108 / 2289)	4·62 (78 / 1689)	4·02 (47 / 1168)	4·68 (42 / 898)
BCS	5·27 (120 / 2279)	6·98 (108 / 1547)	4·77 (50 / 1048)	4·02 (32 / 796)
Rate ratio, from	0·84 SE 0·13	0·65 SE 0·13	0·74 SE 0·19	1·06 SE 0·26
(O-E) / V	-8·4 / 49·4	-18·0 / 41·7	-6·5 / 21·7	0·9 / 16·2

Webfigure 1d. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on 10-year risk of any (locoregional or distant) first recurrence and on 15-year risks of breast cancer mortality and all-cause mortality. Data from 2464 women with pathological nodal status unknown. Vertical lines indicate 1 SE above or below the 5, 10 and 15 year percentages.



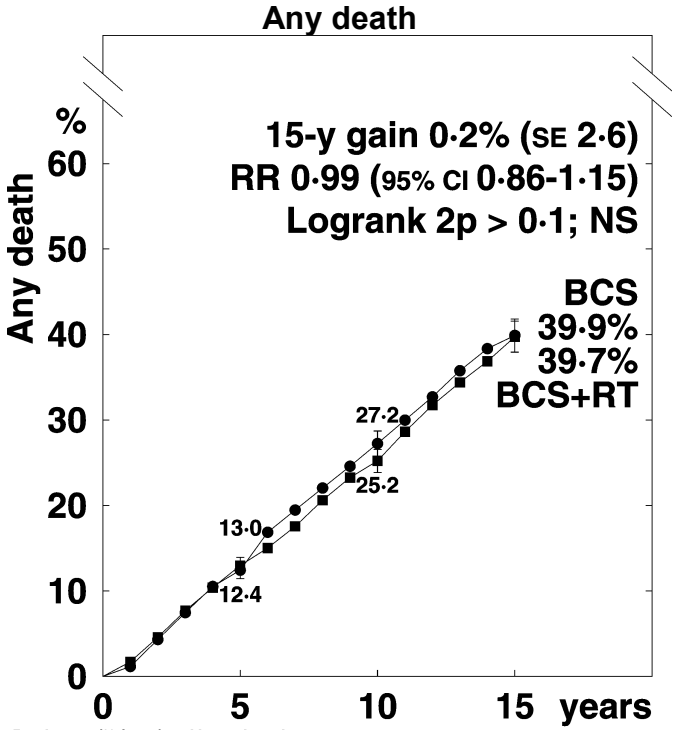
any first recurrence rates (% / year) and logrank analyses

	Years 0 - 4	Years 5 - 9	Year 10+
BCS+RT	2·67 (147 / 5496)	2·09 (75 / 3593)	1·45 (32 / 2210)
BCS	4·95 (248 / 5010)	3·07 (90 / 2936)	1·26 (21 / 1668)
Rate ratio, from	0·53 SE 0·08	0·66 SE 0·13	1·13 SE 0·30
(O-E) / V	-57·3 / 90·6	-16·1 / 39·1	1·5 / 12·6



After-recurrence or possible-breast-cancer death rates (% / year) and logrank analyses

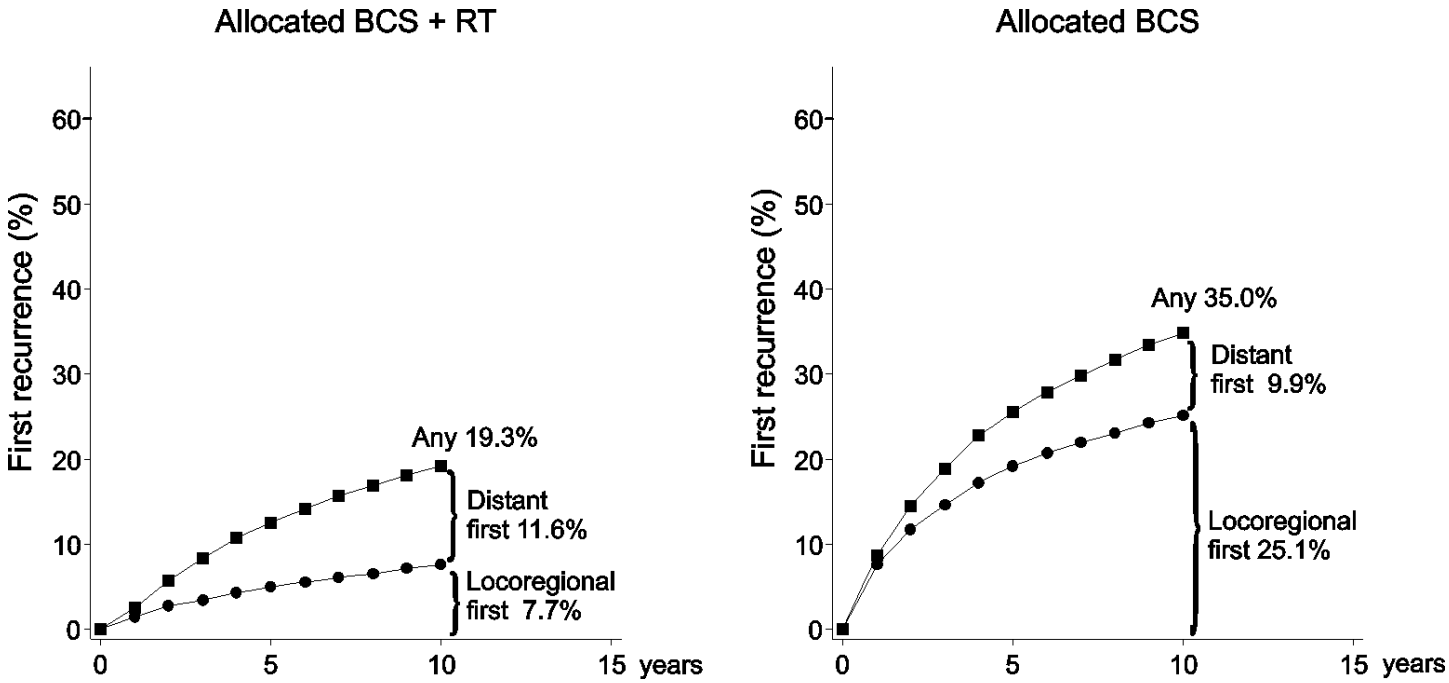
	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
BCS+RT	1·53 SE 0·16	1·47 SE 0·19	1·75 SE 0·30	1·59 SE 0·53
BCS	1·74 SE 0·18	2·34 SE 0·25	2·13 SE 0·36	1·94 SE 0·61
Rate ratio, from	0·98 SE 0·15	0·69 SE 0·15	1·00 SE 0·25	1·11 SE 0·49
(O-E) / V	-0·9 / 42·0	-12·4 / 33·0	0·0 / 16·4	0·5 / 4·6



Death rates (% / year) and logrank analyses

	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
BCS+RT	2·69 (153 / 5694)	3·00 (118 / 3937)	4·23 (82 / 1938)	5·12 (29 / 566)
BCS	2·72 (150 / 5514)	3·83 (139 / 3628)	3·97 (67 / 1689)	3·68 (19 / 516)
Rate ratio, from	1·05 SE 0·12	0·79 SE 0·11	1·12 SE 0·18	1·62 SE 0·38
(O-E) / V	3·4 / 71·2	-14·0 / 60·3	3·8 / 35·2	5·5 / 11·4

Webfigure 2a. 10-year risk of any first recurrence in trials of radiotherapy (RT) after breast-conserving surgery (BCS) by type of first recurrence and allocated treatment in 10,801 women. Women found to have both a locoregional and a distant recurrence at the time of their first recurrence are classified as having a distant recurrence. The contribution for a specific year is the estimated probability of not having either a locoregional or a distant recurrence in any previous year multiplied by the estimated probability of having a locoregional recurrence before any distant recurrence in that year. Note that although radiotherapy somewhat delays or prevents distant recurrence, as evidenced by the reduction in breast cancer mortality it produces, it greatly delays or prevents local recurrence thereby allowing some distant recurrences to be seen as first events that would otherwise have been preceded by a local recurrence.

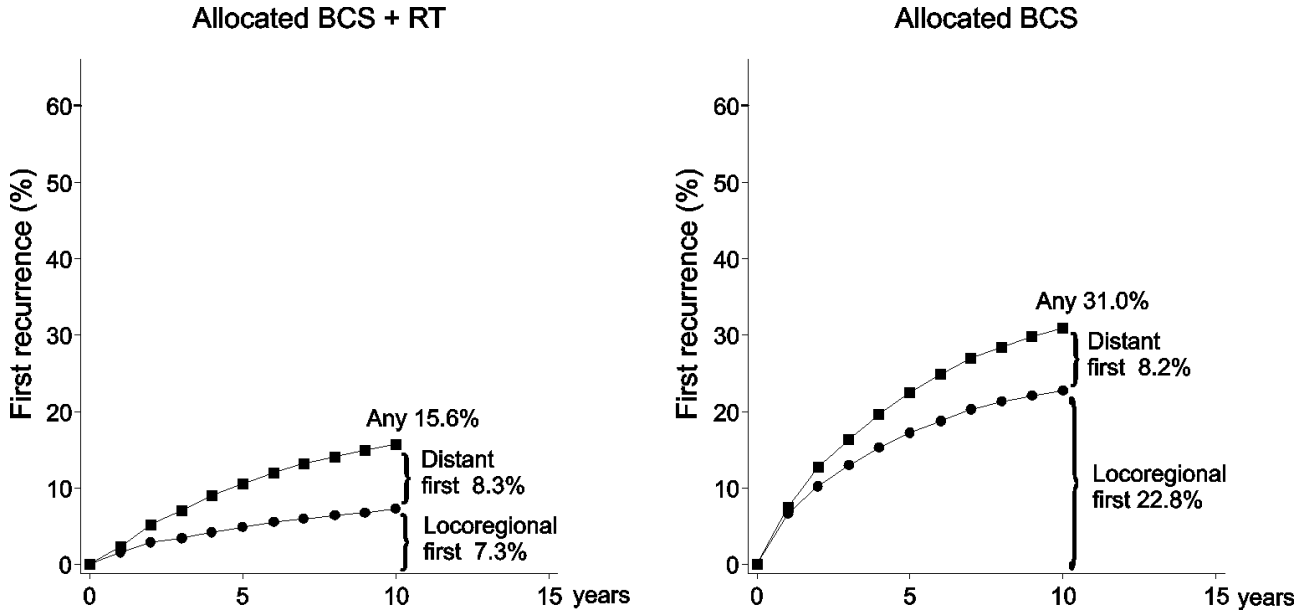


Numbers of women with first recurrence by 10 years according to type of first recurrence and allocated treatment (BCS+RT /BCS):

a. Ipsilateral breast	b. Ipsilateral axilla	c. Other locoregional site	d. Locoregional, site unknown	Any locoregional (ie a+b+c+d)	Distant	Any recurrence
235/713	6/16	49/60	123/389	413/1178	557/434	970/1612

Webfigure 2b. 10-year risk of any first recurrence in trials of radiotherapy (RT) after breast-conserving surgery (BCS) by pathological nodal status, type of first recurrence and allocated treatment. Women found to have both a locoregional and a distant recurrence at the time of their first recurrence are classified as having a distant recurrence. This figure does not provide evidence that radiotherapy increases the risk of distant recurrence, see legend on webappendix p9.

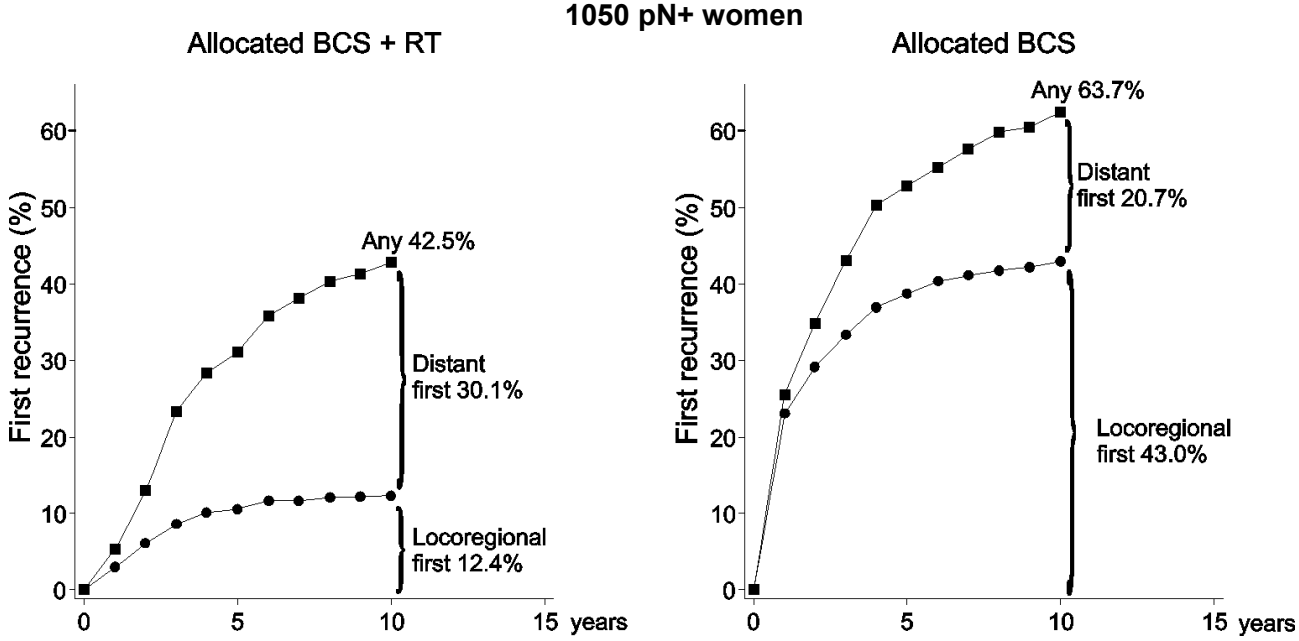
7287 pN0 women



Numbers of women with first recurrence by 10 years according to type of first recurrence and allocated treatment (BCS+RT /BCS):

a. Ipsilateral breast	b. Ipsilateral axilla	c. Other locoregional site	d. Locoregional, site unknown	Any locoregional (ie a+b+c+d)	Distant	Any recurrence
164/451	6/15	23/25	64/229	257/720	274/248	531/968

1050 pN+ women

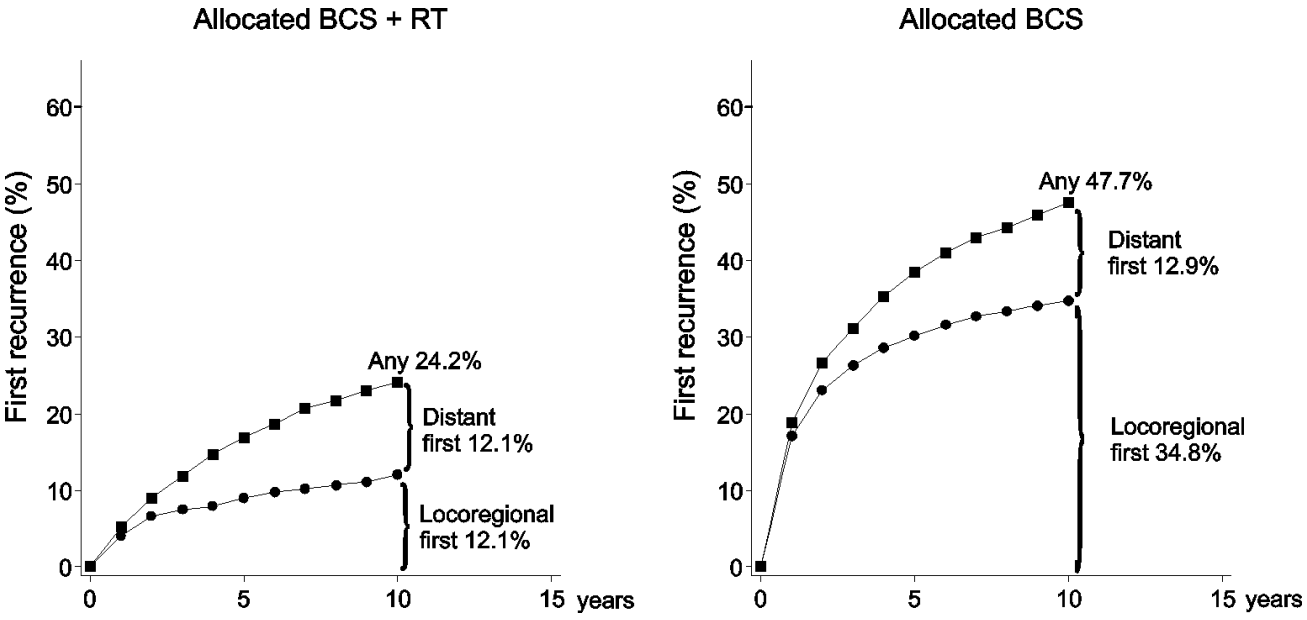


Numbers of women with first recurrence by 10 years according to type of first recurrence and allocated treatment (BCS+RT /BCS):

a. Ipsilateral breast	b. Ipsilateral axilla	c. Other locoregional site	d. Locoregional, site unknown	Any locoregional (ie a+b+c+d)	Distant	Any recurrence
18/110	0/0	19/19	33/81	70/210	147/96	217/306

Webfigure 2c. 10-year risk of any first recurrence in trials of radiotherapy (RT) after breast-conserving surgery (BCS) by surgery, oestrogen receptor status and whether tamoxifen was given to both trial arms or not at all, type of first recurrence and allocated treatment. Women found to have both a locoregional and a distant recurrence at the time of their first recurrence are classified as having a distant recurrence. This figure does not provide evidence that radiotherapy increases the risk of distant recurrence, see legend on webappendix p9.

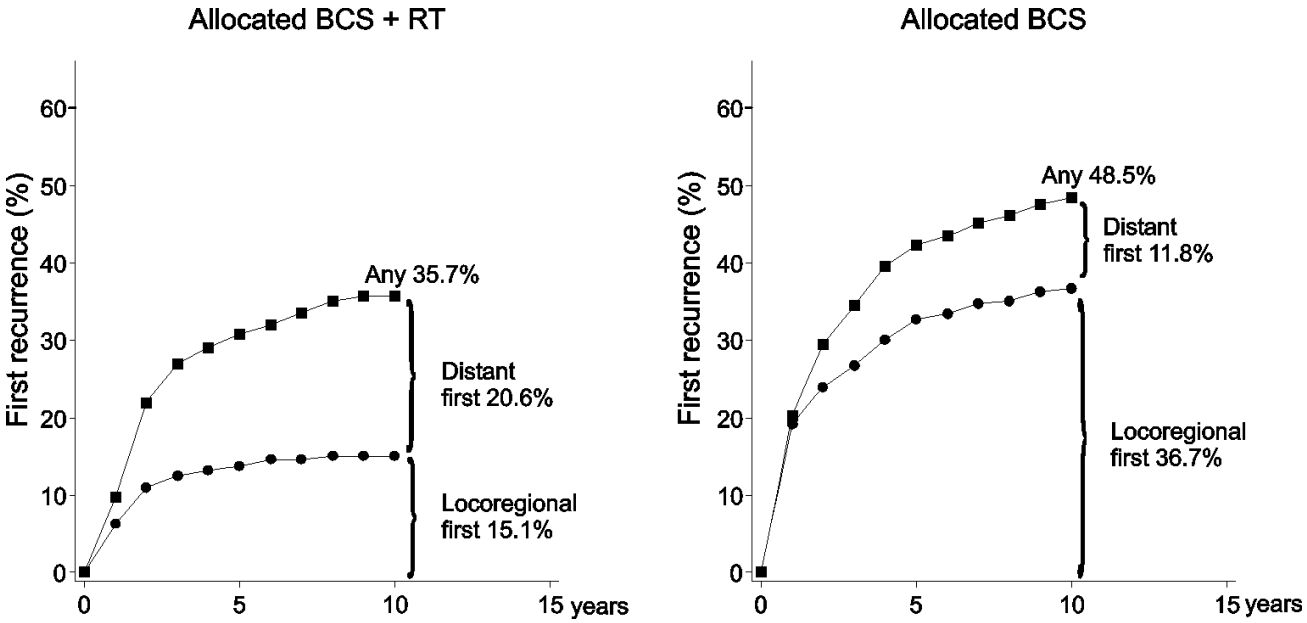
1656 pN0 women: Lumpectomy, ER+tam-



Numbers of women with first recurrence by 10 years according to type of first recurrence and allocated treatment (BCS+RT /BCS):

a. Ipsilateral breast	b. Ipsilateral axilla	c. Other locoregional site	d. Locoregional, site unknown	Any locoregional (ie a+b+c+d)	Distant	Any recurrence
89/223	0/0	12/15	6/26	107/264	95/94	202/358

575 pN0 women: Lumpectomy, ER-poor

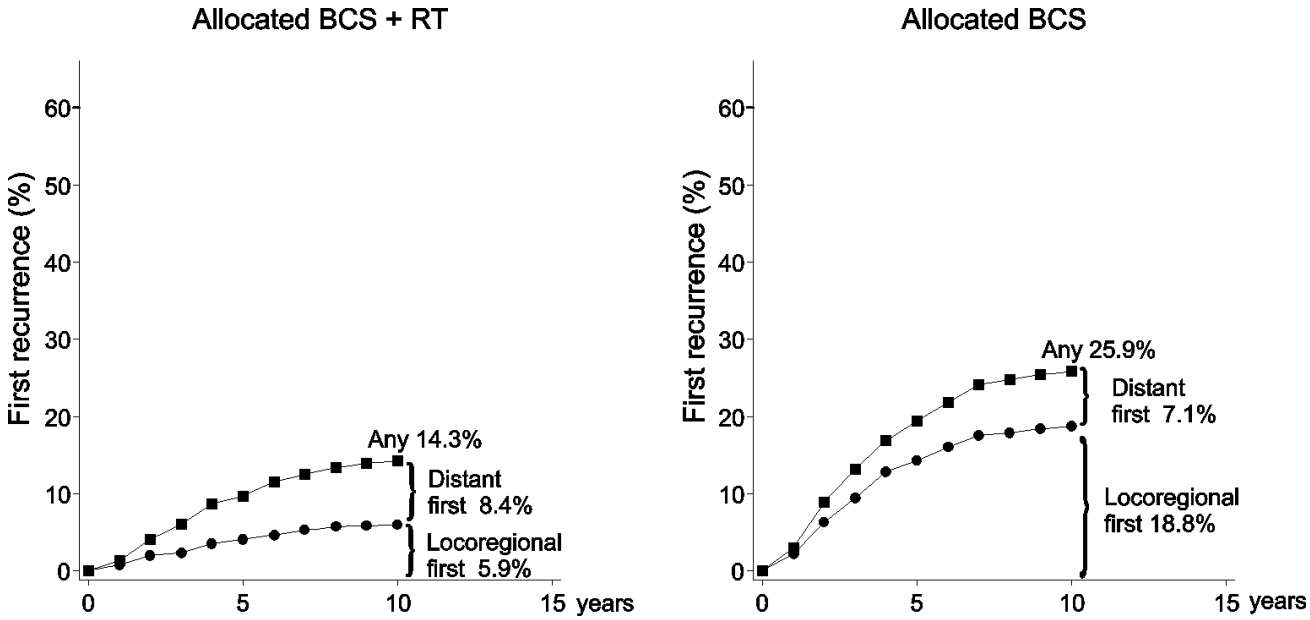


Numbers of women with first recurrence by 10 years according to type of first recurrence and allocated treatment (BCS+RT /BCS):

a. Ipsilateral breast	b. Ipsilateral axilla	c. Other locoregional site	d. Locoregional, site unknown	Any locoregional (ie a+b+c+d)	Distant	Any recurrence
26/66	0/0	9/10	9/23	44/99	56/36	100/135

Webfigure 2d. 10-year risk of any first recurrence in trials of radiotherapy (RT) after breast-conserving surgery (BCS) by surgery, oestrogen receptor status and whether tamoxifen was given to both trial arms or not at all, type of first recurrence and allocated treatment. Women found to have both a locoregional and a distant recurrence at the time of their first recurrence are classified as having a distant recurrence. This figure does not provide evidence that radiotherapy increases the risk of distant recurrence, see legend on webappendix p9.

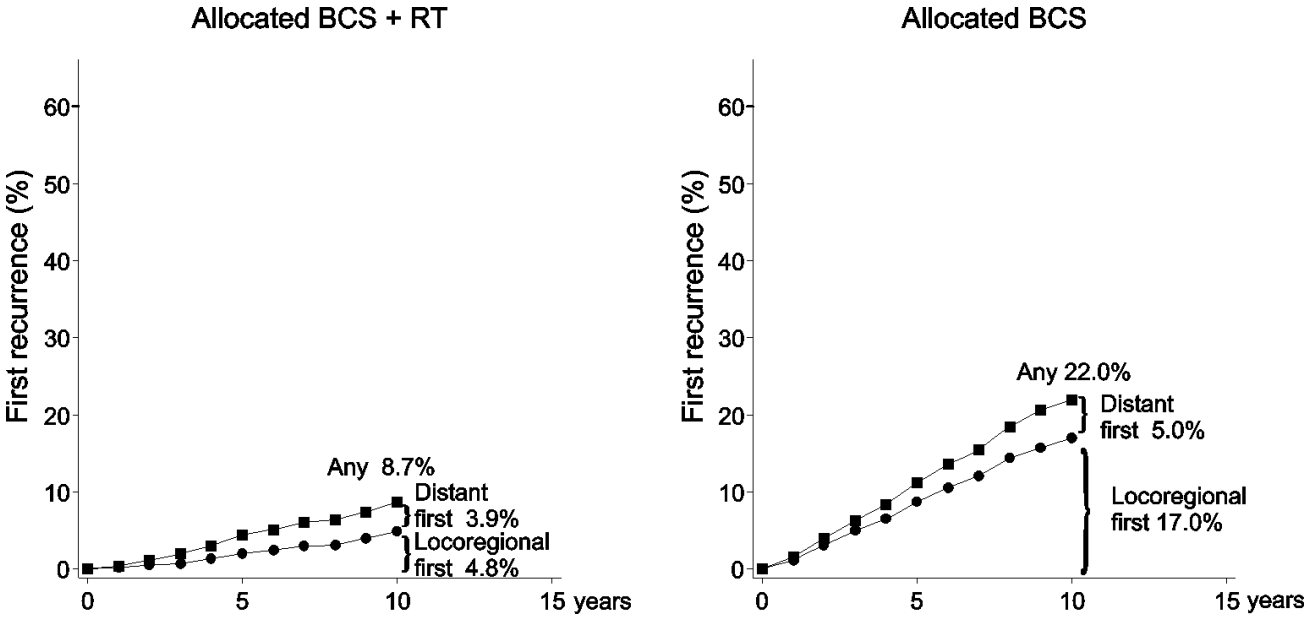
1956 pN0 women: >Lumpectomy, ER+tam- or ER-poor



Numbers of women with first recurrence by 10 years according to type of first recurrence and allocated treatment (BCS+RT /BCS):

a. Ipsilateral breast	b. Ipsilateral axilla	c. Other locoregional site	d. Locoregional, site unknown	Any locoregional (ie a+b+c+d)	Distant	Any recurrence
32/88	6/14	2/0	18/73	58/175	79/65	137/240

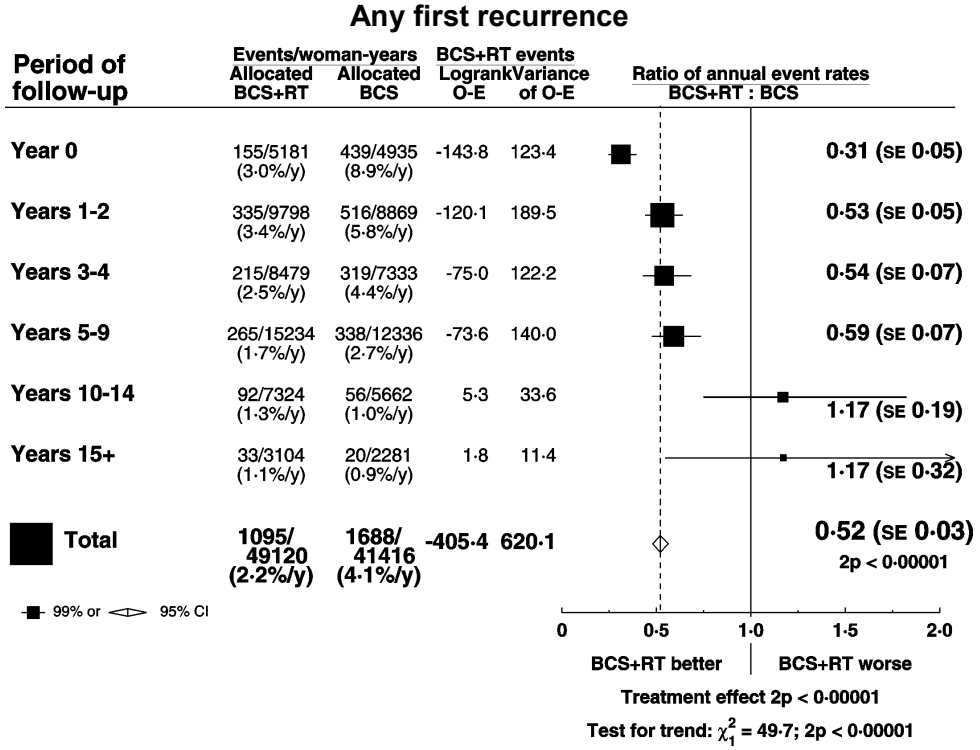
3100 pN0 women: Lumpectomy, ER+tam+



Numbers of women with first recurrence by 10 years according to type of first recurrence and allocated treatment (BCS+RT /BCS):

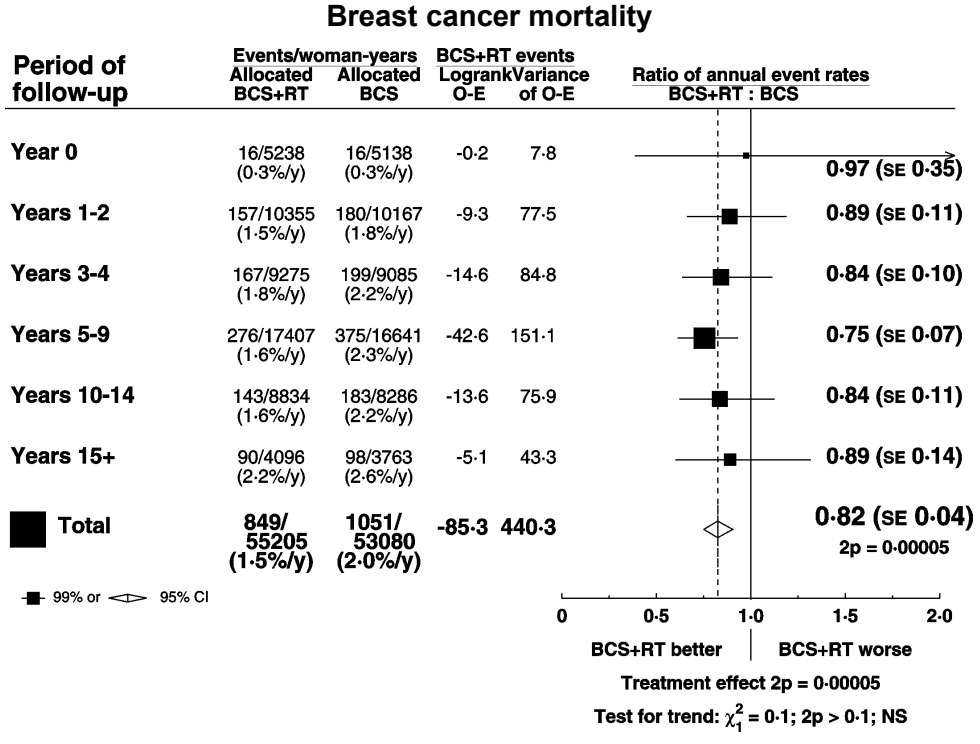
a. Ipsilateral breast	b. Ipsilateral axilla	c. Other locoregional site	d. Locoregional, site unknown	Any locoregional (ie a+b+c+d)	Distant	Any recurrence
17/74	0/1	0/0	31/107	48/182	44/53	92/235

Webfigure 3. Proportional effect of radiotherapy (RT) after breast-conserving surgery (BCS) on time to first recurrence of any type (locoregional or distant) and on breast-cancer mortality in 10,801 women. Event rate ratios by period of follow-up.

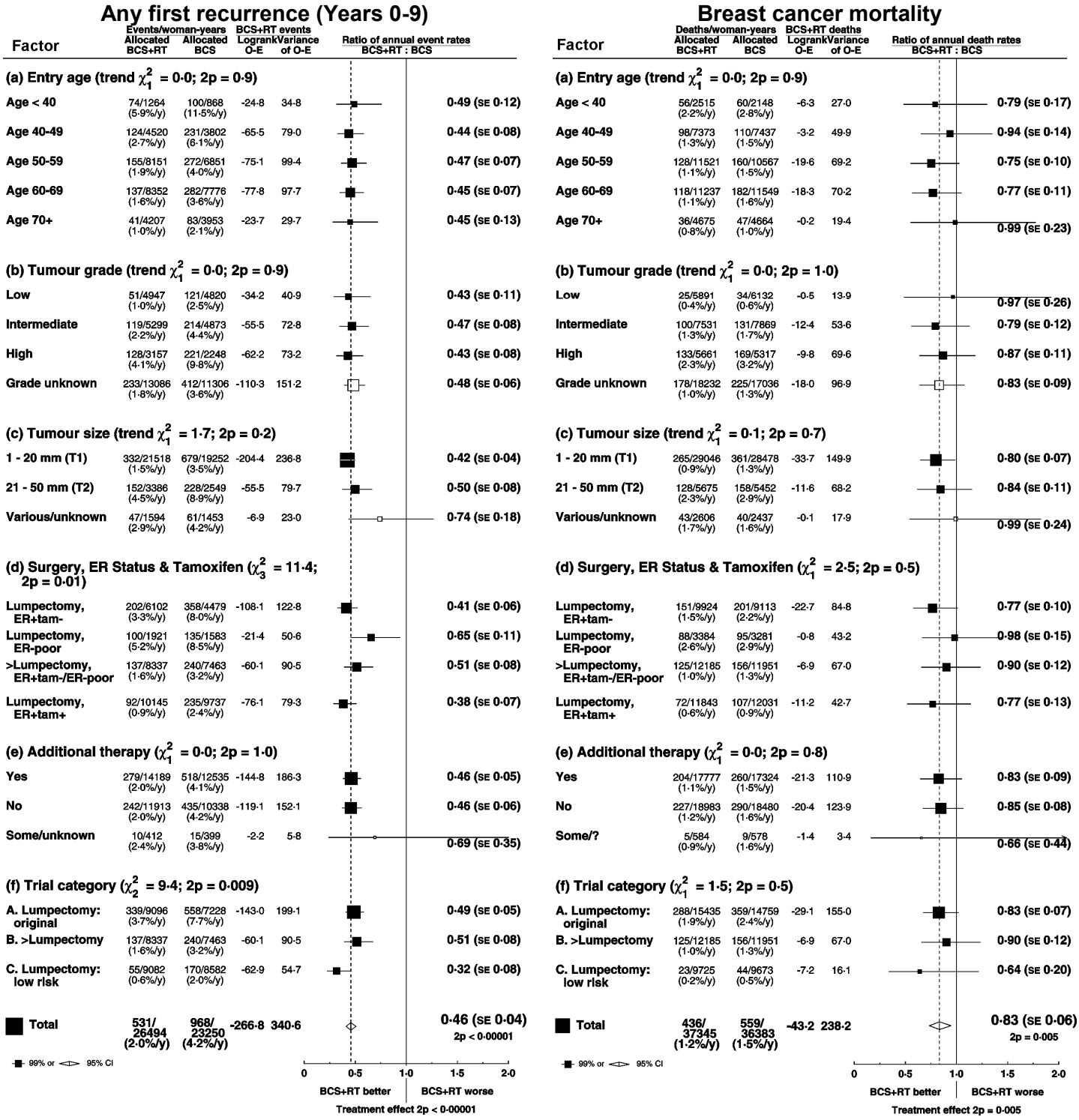


Numbers of women with first recurrence by type of first recurrence, period of follow-up and allocated treatment (BCS+RT/BCS):

Period of follow-up (years)	a. Ipsilateral breast	b. Ipsilateral axilla	c. Other locoregional site	d. Locoregional, site unknown	Any locoregional (ie a+b+c+d)	Distant	Any recurrence
0	78/312	1/3	5/14	15/54	99/383	58/57	157/440
1-2	59/181	2/5	27/27	34/143	122/356	212/159	334/515
3-4	43/109	3/3	7/10	32/95	85/217	131/102	216/319
5-9	55/111	0/5	10/9	42/97	107/222	156/116	263/338
10-14	11/9	0/1	3/1	3/1	16/13	62/32	92/56
15+	1/0	0/0	0/0	4/4	5/4	28/16	33/20
Total	247/722	6/17	52/61	143/406	448/1206	647/482	1095/1688



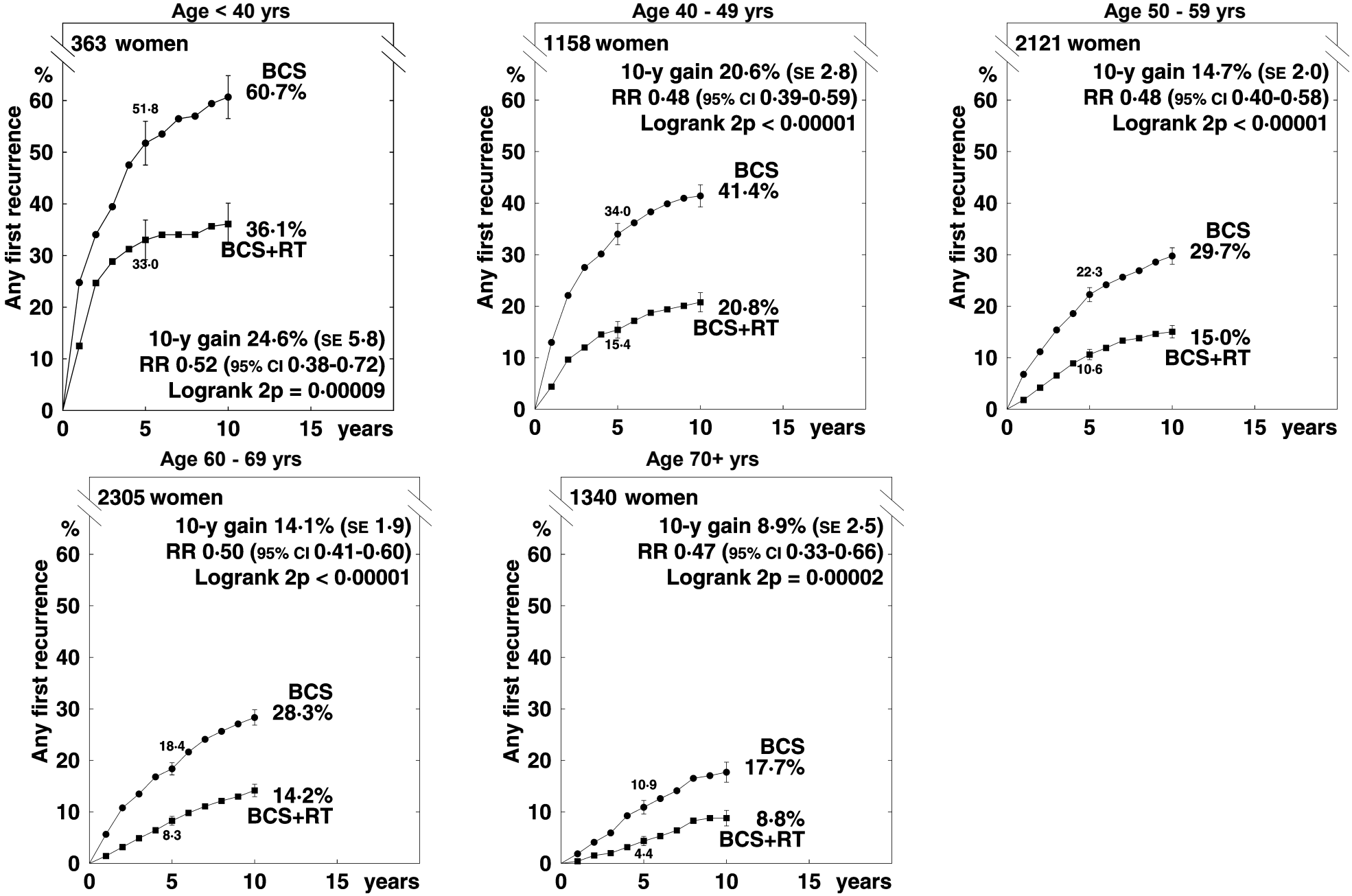
Webfigure 4. Proportional effect of radiotherapy (RT) after breast-conserving surgery (BCS). Event rate ratios for any (locoregional or distant) first recurrence, during years 0-9, and for breast cancer mortality in women with pathologically node-negative disease by prognostic and other factors.



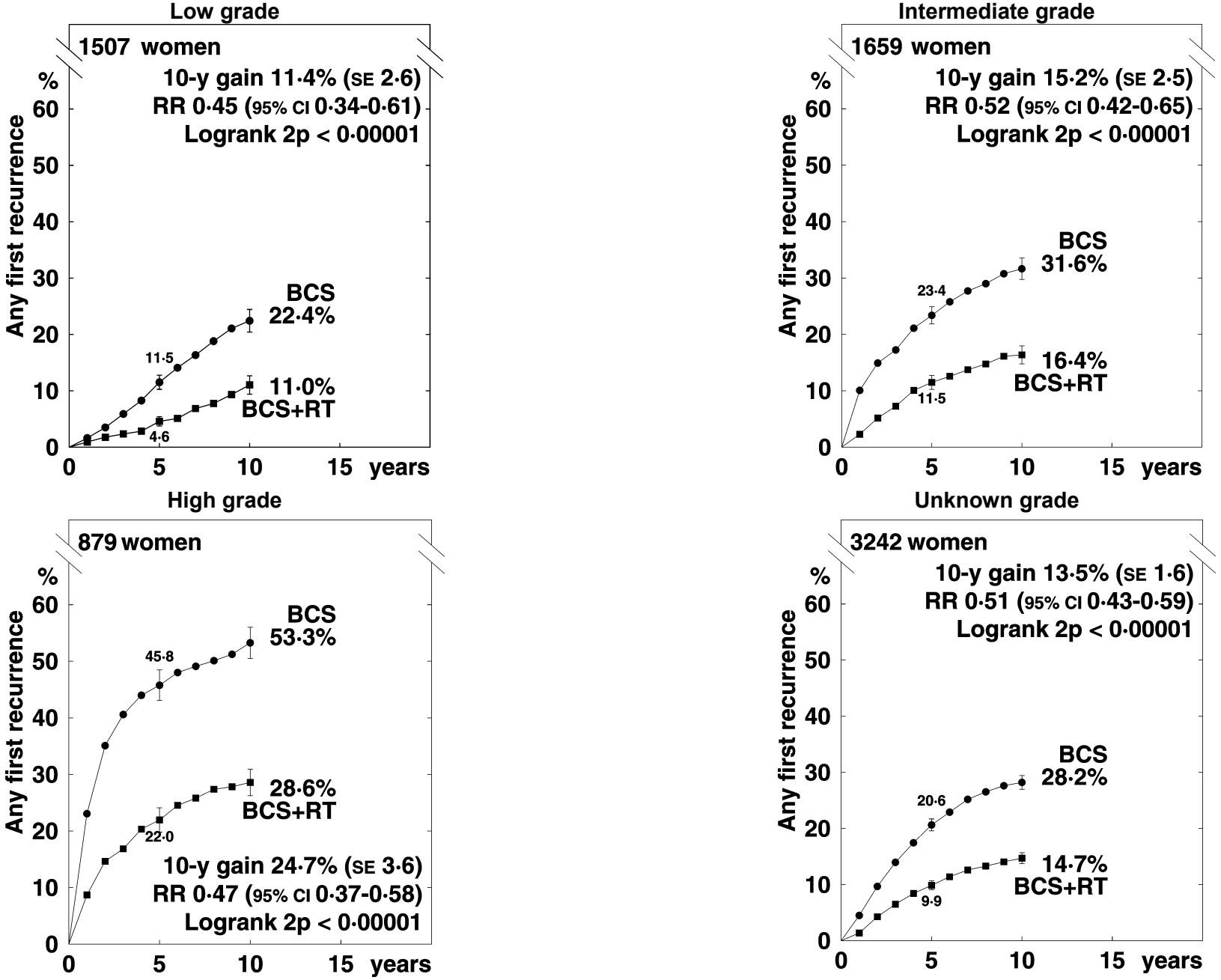
Categories including unknowns excluded from tests for trend and heterogeneity.

See Table 1 in main paper for definitions of trial categories. For years 0-4 only test of heterogeneity between different trial categories in women with pN0 disease has χ^2 =3.85 on 2 df, p=0.15.

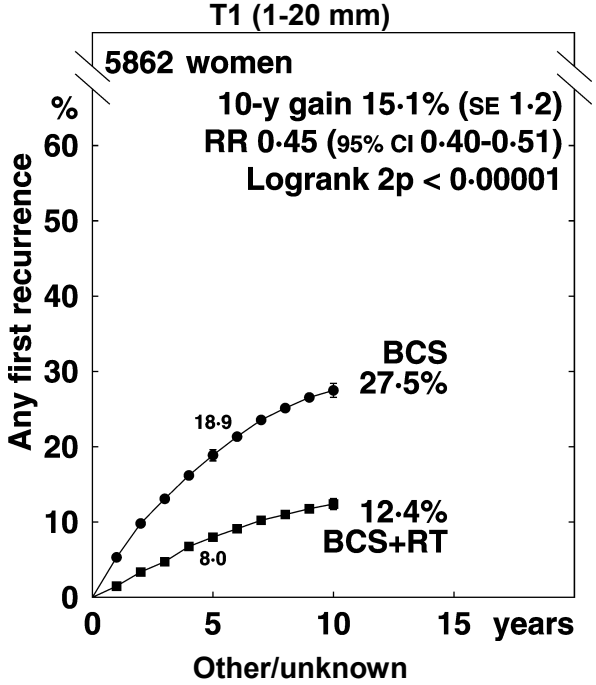
Webfigure 5a. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on any (locoregional or distant) first recurrence in pathologically node-negative women — 10-year risks by age at entry. Vertical lines indicate 1 SE above or below the 5 and 10 year percentages.

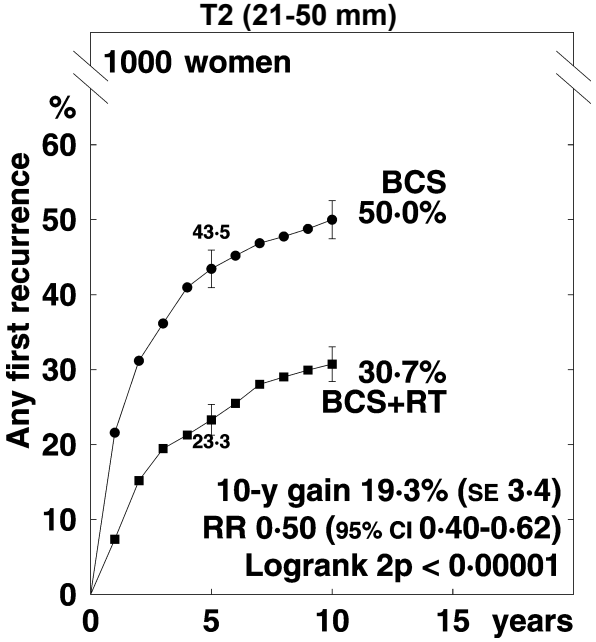


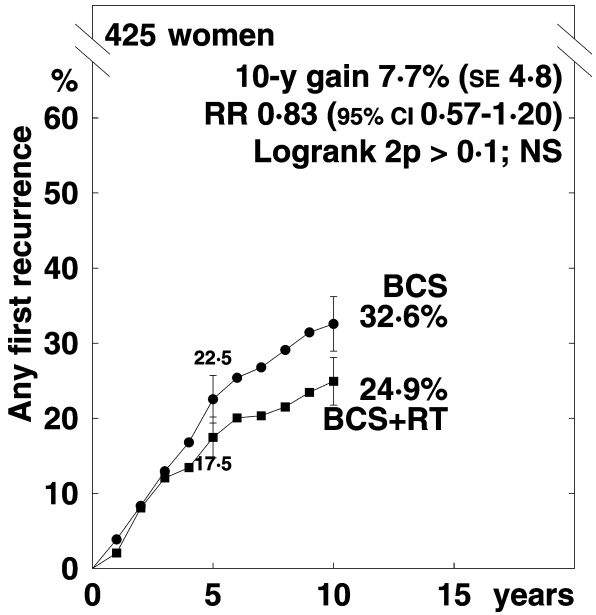
Webfigure 5b. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on any (locoregional or distant) first recurrence in pathologically node-negative women — 10-year risks according to tumour grade. Vertical lines indicate 1 SE above or below the 5 and 10 year percentages.



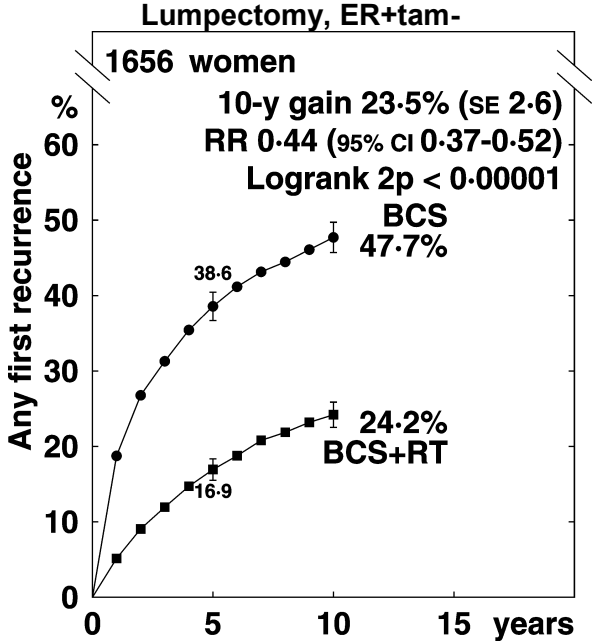
Webfigure 5c. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on any (locoregional or distant) first recurrence in pathologically node-negative women — 10-year risks according to tumour size. Vertical lines indicate 1 SE above or below the 5 and 10 year percentages.

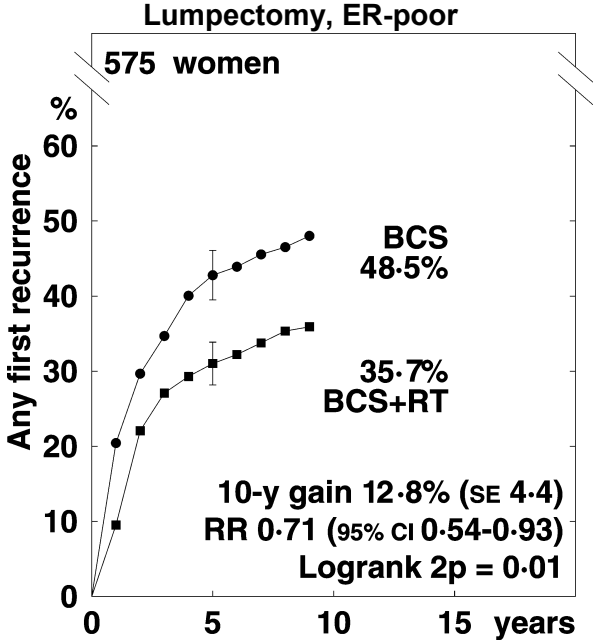


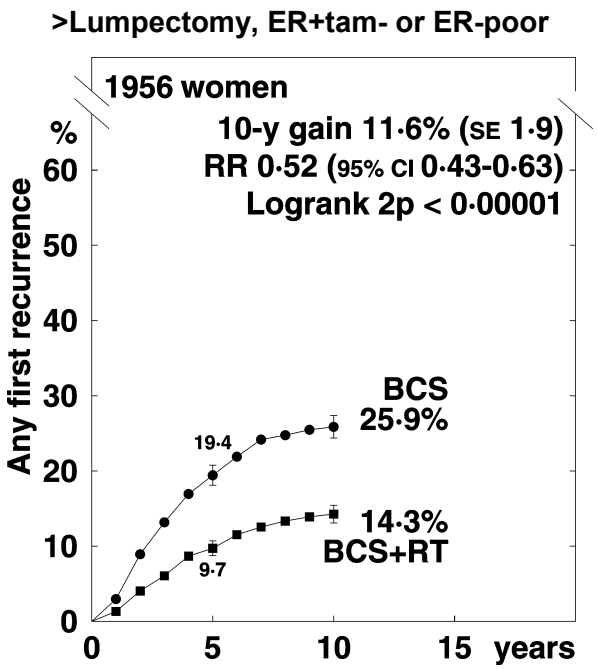


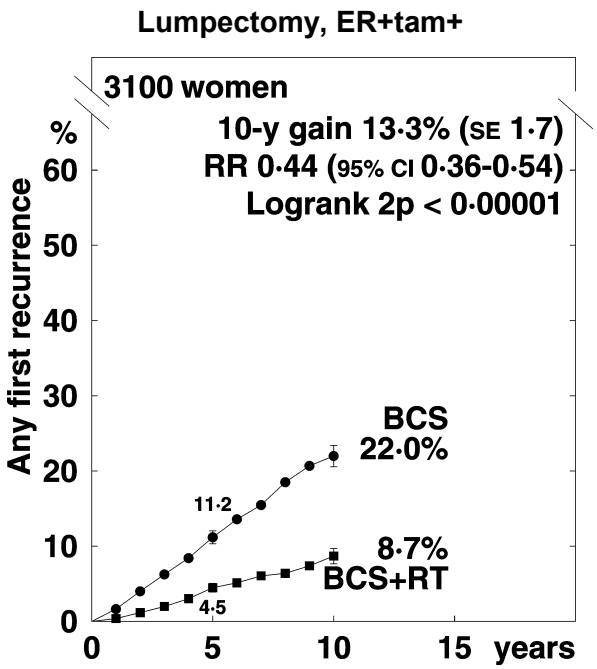


Webfigure 5d. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on any (locoregional or distant) first recurrence in pathologically node-negative women — 10-year risks according to extent of surgery and ER-status & trial policy of tamoxifen use. Vertical lines indicate 1 SE above or below the 5 and 10 year percentages.

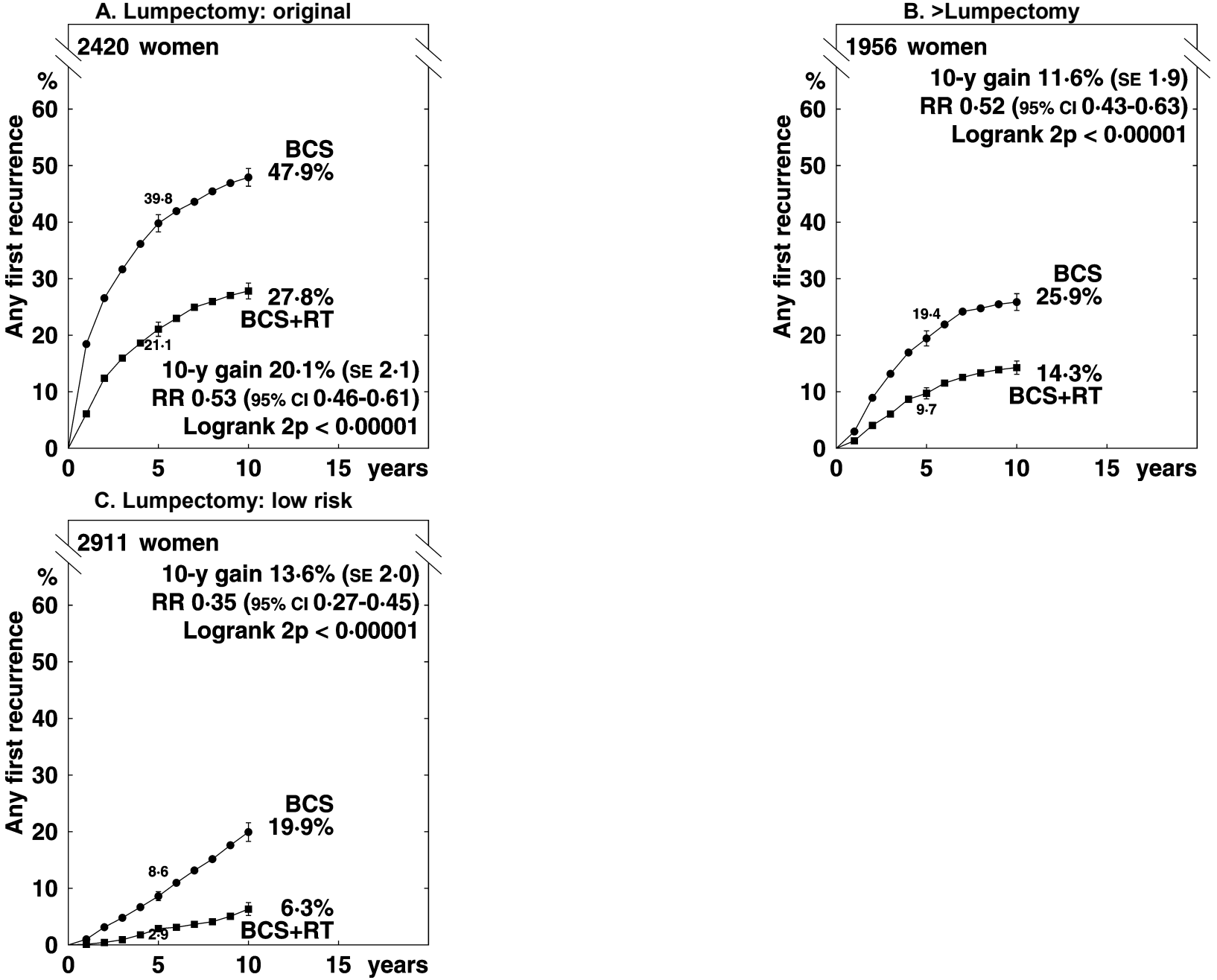








Webfigure 5e. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on any (locoregional or distant) first recurrence in pathologically node-negative women — 10-year risks according to trial category. Vertical lines indicate 1 SE above or below the 5 and 10 year percentages.



Webfigure 6a. Statistical method for modelling the absolute risk of any (locoregional or distant) first recurrence in women allocated to radiotherapy (RT) and the reduction in absolute risk of any (locoregional or distant) first recurrence at 10 years.

Introduction

The statistical methodology used in previous EBCTCG reports did not readily extend to estimating the dependence of the absolute risk of recurrence, or the absolute reduction in risk from radiotherapy, on several factors simultaneously. Therefore, estimates of these quantities (shown in table 2 and figure 4 of the main paper and in webappendix p21-29), are based on an alternative method. The first step in this method was to tabulate the numbers of events and woman-years at risk by all the following factors simultaneously: trial, treatment allocated (RT, No RT), age (<40, 40-, 50-, 60-, 70+ years), tumour grade (Low, Intermediate, High, Unknown), tumour size (T1 [1-20 mm], T2 [21-50 mm], other/unknown), ER-status & trial policy of tamoxifen use (ER+Tam+, ER+Tam-, ER-poor) and, for pN+ women, number of positive nodes (pN1-3, pN4+). Two different types of Poisson regression models, described in sections (ii) and (iii) below, were fitted to the tabulated data by the method of maximum likelihood using the computer program Epiwin v1.81. Inspection of the crude recurrence rates by year of follow-up suggested that the rates in the first few years were larger than those in subsequent years and so weights, (4,4,3,3,2,2,2,1,1,1 in pN0 women and 4,3,3,3,1,1,1,1,1,1 in pN+ women) were used in the models to take account of this variation. Significance tests were carried out using the likelihood ratio and were two-sided.

(ii) Identification of form of model for women allocated to RT

To identify an appropriate form for a model characterising the recurrence rate in women allocated to breast-conserving surgery (BCS) + RT in the main modelling process in section (iii) below, initial model-fitting considered only women allocated to RT. In this initial stage, the Poisson mean took the form $LL(0)=\exp(V_1+V_2+ \ldots + V_k)$, where V_1, V_2 etc are categorical terms representing the factors by which the data had been subdivided. This initial model-fitting suggested that the 10-year recurrence rate for women allocated to RT could be summarised by a model that included terms for : trial (30 categories — this is larger than the number of trials, as some trials were divided into 2 strata, eg where ER+women were given tamoxifen and ER- poor women given CMF), age (5 categories), tumour grade (4 categories), tumour size (3 categories), ER-status & trial policy of tamoxifen use (3 categories) and, for pN+ women, number of positive nodes (2 categories). Therefore, in the main modelling process all models included these terms in LL(0).

(iii) Modelling the absolute reduction in 10-year recurrence rate from radiotherapy

To identify and characterise the factors determining the absolute difference in recurrence rate between women allocated to BCS + RT and women allocated to BCS only, models were fitted to the data for both treatment groups with mean of form: LL(0) + LI(1).LL(1), where LL(0) has the form suggested by the initial modelling process (but during this second stage of the modelling process, the parameter values for the terms in LL(0) were re-estimated), LI(1) is a binary variable taking value 0 for irradiated women and 1 for unirradiated women (with coefficient constrained to be equal to 1), and LL(1) is a term with form $LL(1)=\exp(W_1+W_2+ \ldots + W_k)$, where W_1, W_2 etc are categorical terms representing the factors being considered as determinants of the absolute reduction in the recurrence rate. The factors considered were selected from the factors by which the data had already been subdivided. Two further factors [trial policy of additional therapy (yes/no/some), and trial category (A: B: and C, as defined in table 1 of the main paper)], which vary between trials but not within a trial were also considered, as well as pairwise interactions between all the factors. The results of this selection process are presented in table 2 of the main paper and in webappendix p26. In the final model for node-negative women, presented in figure 4 of the main paper and in the webappendix p27, LL(1) retained the terms that were statistically significant in table 2 when each factor had been adjusted for all others. Tumour size was also included, as it was independently prognostic of the absolute risk in irradiated women [ie, in LL(0)] and, when only the first 5 years after entry were considered of the absolute reduction in the recurrence rate. There were no significant two-way interactions between the factor representing these 4 rows and age, grade or tumour size. Therefore, the effects of grade, tumour size and age were assumed to be identical regardless of extent of surgery, and ER-status, & trial policy of tamoxifen use. For women aged <40, 40-49, 50-59, 60-69 and 70+ at entry, the logarithm of the estimated rate ratios was approximately linear across age-groups and so a log-linear trend was assumed. After concluding the modelling process, the coefficients of the parameters in LL(0) in the main modelling process were compared with those obtained during the initial model-fitting in which only data for women allocated to radiotherapy were considered, and were found to have changed by only a small amount. The parameter estimates, standard errors, and the correlation matrices for the final model are given in the webappendix p21-24.

(iv) Estimation of cumulative risk and absolute gain with radiotherapy

Estimates of the recurrence rate indicated by the terms in LL(0) in the final fitted models were used to calculate the cumulative 10-year risks of any (ie locoregional or distant) first recurrence in women allocated to BCS+RT, while estimates of the recurrence rate indicated by the terms in LL(0)+LI(1).LL(1) were used to calculate the cumulative 10-year risks of any (ie locoregional or distant) first recurrence in women allocated to BCS only. Estimates are presented with the factor representing trial set to median values when grouped by extent of surgery. The non-linear relationship between the recurrence rate and cumulative risk, which is non-linear, is illustrated in webappendix p25. Estimates of the reduction in absolute recurrence risk at 10 years were then taken to be the difference between these two estimates. Estimates of the reduction in absolute recurrence risk at 5 years were derived from the same models (see webappendix p31-34). Analyses of residuals and other statistical procedures confirmed that the estimates presented fitted the data well. Despite this, confidence intervals have not been presented for the estimates of absolute risk, as such estimates are subject to many sources of uncertainty over and above those that can be included in formal statistical confidence intervals. Displaying them might, therefore, give the impression that the estimates presented are more precise than is, in fact, the case.

Webfigure 6b. Model, using the method described in webappendix p20, for the dependence on prognostic and other factors of the absolute 10-year rate of any (locoregional or distant) first recurrence rate in women with pN0 disease allocated to radiotherapy.

Absolute 10-year local recurrence rate per 100 years at risk=

$$\exp(d_1.\beta_1 + d_2.\beta_2 + d_3.\beta_3 + d_4.\beta_4 + d_5.\beta_5 + d_6.\beta_6 + d_7.\beta_7 + d_8.\beta_8 + d_9.\beta_9 + d_{10}.\beta_{10} + d_{11}.\beta_{11} + d_{12}.\beta_{12} + d_{13}.\beta_{13} + d_{14}.\beta_{14})$$

where

d_1 =	1	Age <40	0	Otherwise	d_8 =	1	Unknown grade,	0	Otherwise
d_2 =	1	Age 40-49	0	Otherwise	d_9 =	1	T2 (21-50 mm),	0	Otherwise
d_3 =	1	Age 50-59	0	Otherwise	d_{10} =	1	Tumour size unknown,	0	Otherwise
d_4 =	1	Age 60-69	0	Otherwise	d_{11} =	1	ER+Tam-,	0	Otherwise
d_5 =	1	Age 70+	0	Otherwise	d_{12} =	1	ER+Tam+,	0	Otherwise
d_6 =	1	Intermediate grade,	0	Otherwise	d_{13} =	1	Lumpectomy*	0	Otherwise
d_7 =	1	High grade,	0	Otherwise	d_{14} =	1	>Lumpectomy*	0	Otherwise

* Note: The fitted model included a term for each trial stratum, this shorthand notation represents the median values of these estimated coefficients, one for those trials in which the surgery performed was lumpectomy and the other for those where the surgery was >lumpectomy.

and	β_1 =	0.13	(se 0.53)	β_8 =	0.06	(se 0.16)
	β_2 =	-0.40	(se 0.52)	β_9 =	0.49	(se 0.10)
	β_3 =	-0.65	(se 0.53)	β_{10} =	0.16	(se 0.25)
	β_4 =	-0.68	(se 0.54)	β_{11} =	-0.25	(se 0.10)
	β_5 =	-0.77	(se 0.55)	β_{12} =	-1.52	(se 0.38)
	β_6 =	0.43	(se 0.15)	β_{13} =	-0.78	-
	β_7 =	0.37	(se 0.16)	β_{14} =	-1.53	-

Webfigure 6c. Correlation matrix for estimates of parameters in model for dependence on prognostic and other factors of the absolute 10-year rate of any (locoregional or distant) first recurrence rate in women with pN0 disease allocated to radiotherapy.

	β_1	β_2	β_3	β_4	β_5	β_6	β_7	β_8	β_9	β_{10}	β_{11}	β_{12}	β_{13}	β_{14}
β_1	1.00													
β_2	0.76	1.00												
β_3	0.76	0.81	1.00											
β_4	0.74	0.80	0.83	1.00										
β_5	0.59	0.65	0.69	0.71	1.00									
β_6	-0.61	-0.63	-0.64	-0.64	-0.53	1.00								
β_7	-0.71	-0.71	-0.69	-0.68	-0.56	0.69	1.00							
β_8	-0.66	-0.71	-0.71	-0.71	-0.58	0.74	0.75	1.00						
β_9	-0.13	-0.16	-0.15	-0.14	-0.11	-0.09	-0.12	-0.04	1.00					
β_{10}	-0.16	-0.13	-0.09	-0.07	-0.02	-0.01	0.01	-0.15	0.16	1.00				
β_{11}	-0.41	-0.45	-0.50	-0.51	-0.42	0.04	0.14	0.05	0.07	0.17	1.00			
β_{12}	-0.33	-0.38	-0.44	-0.46	-0.46	0.04	0.19	0.16	0.13	-0.06	0.51	1.00		
β_{13}	-	-	-	-	-	-	-	-	-	-	-	-	1.00	
β_{14}	-	-	-	-	-	-	-	-	-	-	-	-	-	1.00

Webfigure 6d. Model for the dependence of the absolute reduction in 10-year rate of any (locoregional or distant) first recurrence rate in women with pN0 disease on prognostic and other factors derived using the method described in webappendix p20.

Absolute reduction in 10-year local recurrence rate per 100 years at risk= $\exp(d_1.\beta_1 + d_2.\beta_2 + d_3.\beta_3 + d_4.\beta_4 + d_5.\beta_5 + d_6.\beta_6 + d_7.\beta_7 + d_8.\beta_8 + d_9.\beta_9 + a.\ \beta_{10})$

where

d_1 =	1	Lump, ER+Tam-,	0	otherwise
d_2 =	1	Lump, ER-poor,	0	otherwise
d_3 =	1	Lump, ER+Tam+,	0	otherwise
d_4 =	1	>Lump, ER+Tam-/ERpoor,	0	otherwise
d_5 =	1	Intermediate grade,	0	otherwise
d_6 =	1	High grade,	0	otherwise
d_7 =	1	Unknown grade,	0	otherwise
d_8 =	1	T2 (21-50 mm),	0	otherwise
d_9 =	1	Tumour size unknown,	0	Otherwise

a =1,2,3,4,5 for ages <40, 40-49, 50-59, 60-69, & 70+

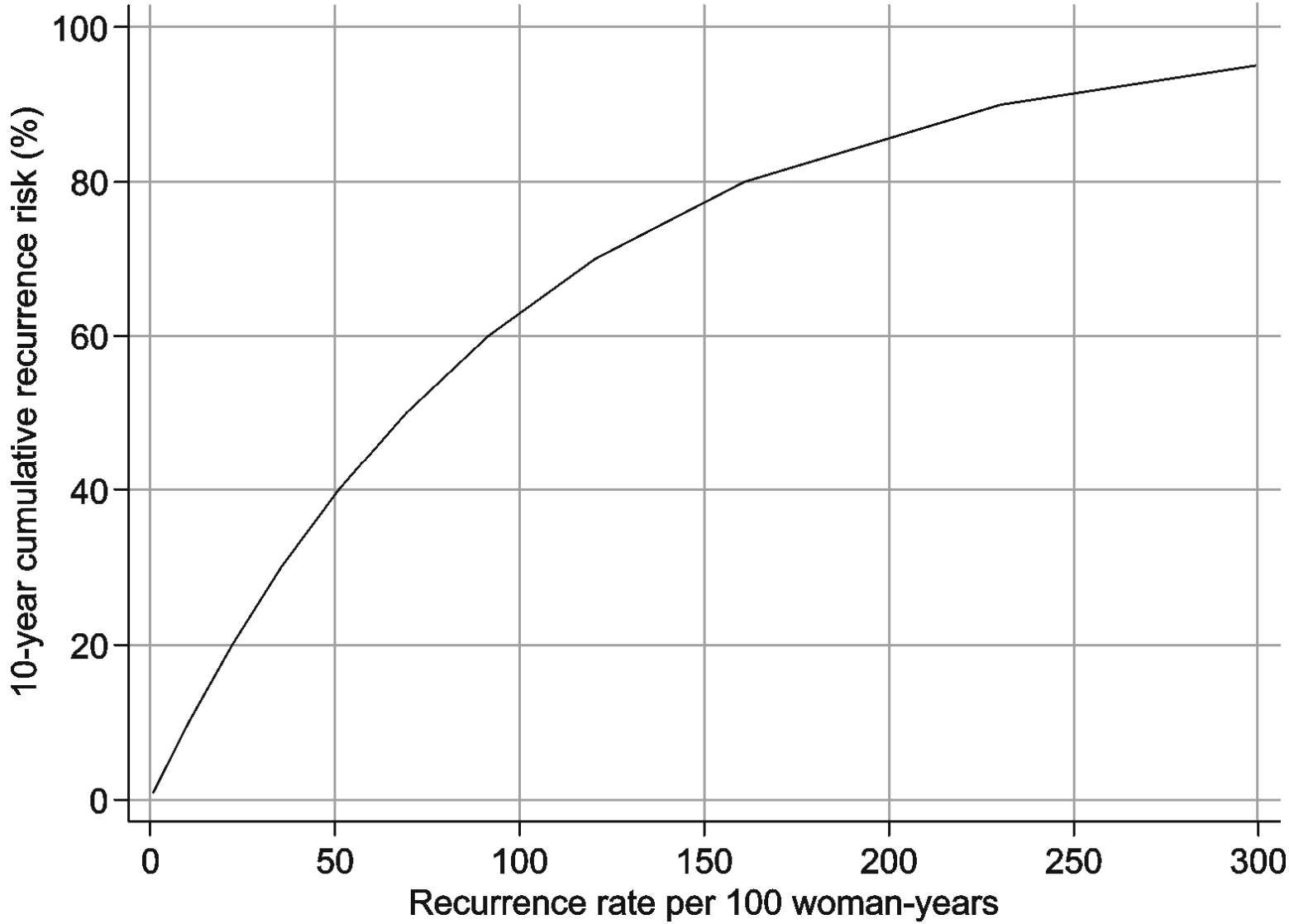
and

β_1 =	-0.95	(se 0.28)
β_2 =	-2.09	(se 0.44)
β_3 =	-1.92	(se 0.32)
β_4 =	-1.94	(se 0.33)
β_5 =	0.66	(se 0.25)
β_6 =	1.52	(se 0.24)
β_7 =	0.74	(se 0.24)
β_8 =	0.42	(se 0.17)
β_9 =	-0.30	(se 0.46)
β_{10} =	-0.25	(se 0.06)

Webfigure 6e. Correlation matrix for estimates of parameters in model for dependence of the absolute reduction in 10-year rate of any (locoregional or distant) first recurrence rate in women with pN0 disease on prognostic and other factors derived using the method described in webappendix p20.

	β_1	β_2	β_3	β_4	β_5	β_6	β_7	β_8	β_9	β_{10}
β_1	1.00									
β_2	0.60	1.00								
β_3	0.84	0.54	1.00							
β_4	0.81	0.52	0.78	1.00						
β_5	-0.51	-0.35	-0.51	-0.47	1.00					
β_6	-0.65	-0.49	-0.52	-0.60	0.65	1.00				
β_7	-0.57	-0.39	-0.49	-0.66	0.66	0.74	1.00			
β_8	-0.08	-0.11	0.03	0.04	-0.11	-0.16	-0.11	1.00		
β_9	-0.06	-0.09	-0.12	-0.01	0.00	-0.03	-0.10	0.07	1.00	
β_{10}	-0.66	-0.39	-0.72	-0.59	-0.01	0.07	-0.01	-0.02	0.11	1.00

Webfigure 6f. Relationship between recurrence rate per 100 woman-years and 10-year cumulative risk of recurrence.

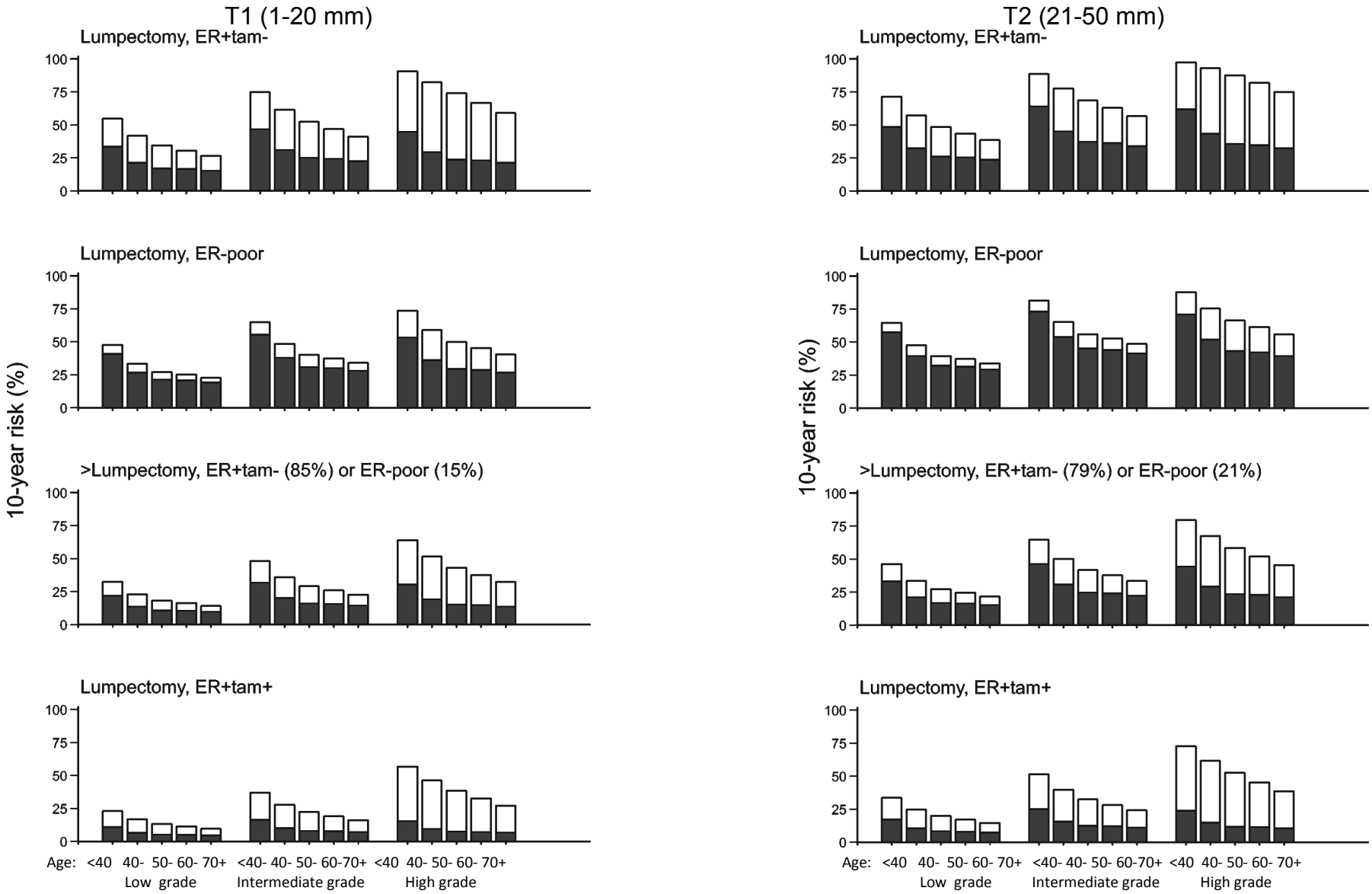


Webtable 2. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on 10-year risk (%) of first recurrence of any type (locoregional or distant) in 7287 pathologically node-negative women according to prognostic and other factors.

Factor*	Events/woman-year in years 0-9 (10-yr risk %)				Test for trend or heterogeneity‡	
	Allocated BCS+RT		Allocated BCS		Unadjusted§	Adjusted¶
Age at entry (years)						
< 40	74/1267	36.1	100/875	60.7	X^2_1=34.1,	X^2_1=13.5,
40 – 49	124/4528	20.8	231/3808	41.4	2p<0.001	2p <0.001
50 – 59	155/8157	15.0	272/6856	29.7		
60 – 69	137/8360	14.2	281/7785	28.3		
70+	41/4202	8.8	83/3956	17.7		
Tumour grade						
Low	51/4959	11.0	120/4831	22.4	X^2_1=43.3,	X^2_1=23.7,
Intermediate	119/5305	16.4	214/4879	31.6	2p<0.001	2p <0.001
High	128/3153	28.6	221/2254	53.3		
Unknown**	233/13098	14.7	412/11316	28.2		
Tumour size						
T1 (1-20 mm)	332/21519	12.4	678/19260	27.5	X^2_1=5.7,	X^2_1=3.7,
T2 (21-50 mm)	152/3392	30.7	228/2558	50.0	2p=0.02	2p=0.06
Other/unknown**	47/1604	24.9	61/1462	32.6		
ER status & trial policy of tamoxifen use††						
ER-poor	127/3223	28.9	183/2603	43.8		
ER+Tam-	312/13143	18.6	549/10936	36.0	2p<0.001	2p=0.003
ER+Tam+	92/10149	8.7	235/9740	22.0	X^2_2=24.6,	X^2_2=11.7,
Trial policy of additional therapy‡‡						
No	242/11904	15.8	434/10338	31.6	X^2_1=3.5,	X^2_1=0.6,
Yes	279/14198	16.1	518/12542	31.8	2p=0.06	2p=0.45
Some/Unknown**	10/413	-	15/400	-		
Trial category§§						
A. Lump: original	339/9101	27.8	558/7232	47.9	A vs C:	A vs C:
B. >Lump	137/8329	14.3	239/7464	25.9	X^2_1=45.8,	X^2_1=2.0,
C. Lump: low risk	55/9086	6.3	170/8585	19.9	2p<0.001	2p=0.16
					A+C vs B:	A+C vs B:
					X^2_1=0.0,	X^2_1=17.2,
					2p=0.90	2p<0.001

* Age at entry, tumour grade, tumour size, and ER status are characteristics of the individual women or their tumours; tamoxifen use, trial policy of additional therapy, and trial category are characteristics of the trials in which they were entered.
‡ Test for trend/heterogeneity in absolute reduction in recurrence rate.
§ Unadjusted: each factor alone.
¶ Adjusted: each factor adjusted for all others using regression modelling.
** Category excluded from test for trend/heterogeneity.
†† Tamoxifen use: tamoxifen given to both trial arms. ER unknown included with ER+.
‡‡ Chemotherapy (usually CMF) given to both trials arms and/or nodal RT or boost given to those allocated BCS+RT.
§§ See table 1 in main paper for explanation of trial categories.

Webfigure 7. Absolute reduction in 10-year risk (%) of any (locoregional or distant) first recurrence from radiotherapy (RT) after breast-conserving surgery (BCS) in pathologically node-negative women: dependence on prognostic and other factors suggested by modelling data from 7287 women. Black bars give 10-year risks in women allocated to BCS+RT, black+white bars give 10-year risks in women allocated to BCS only, and white bars give absolute reduction with RT.



Webtable 3a. 10-year risk (%) of any (locoregional or distant) first recurrence according to prognostic and other factors: Absolute reduction with radiotherapy (RT) after breast-conserving surgery (BCS) in pathologically node negative women. Reductions of 20% and above are shown in dark boxes, 10-19% in light boxes, and less than 10% in clear boxes.

	Absolute reduction in 10-year risk of recurrence with radiotherapy (%)																			
	Low grade					Intermediate grade					High grade					Unknown grade				
	Age (years)					Age (years)					Age (years)					Age (years)				
	<40	40	50	60	70+	<40	40	50	60	70+	<40	40	50	60	70+	<40	40	50	60	70+
T1 (1-20mm) tumours																				
Lumpectomy, ER+tam-	21	21	17	14	11	28	31	27	23	19	46	53	50	44	38	36	36	32	26	22
Lumpectomy, ER-poor	7	7	6	4	4	9	11	9	7	6	20	23	21	17	14	13	13	11	9	7
>Lumpectomy, ER+tam- or ER-poor*	10	9	7	6	5	17	16	13	10	8	34	33	28	23	19	20	18	15	12	9
Lumpectomy, ER+tam+	12	10	8	6	5	21	18	15	12	9	41	37	31	25	20	23	20	16	13	10
T2 (21-50mm) tumours																				
Lumpectomy, ER+tam-	23	25	22	18	15	25	32	31	27	23	36	50	52	47	43	35	41	38	33	28
Lumpectomy, ER-poor	7	8	7	6	5	8	11	11	9	7	17	24	23	19	16	13	16	14	11	9
>Lumpectomy, ER+tam- or ER-poor*	13	12	10	8	7	19	20	17	14	11	35	38	35	29	24	24	23	20	16	13
Lumpectomy, ER+tam+	17	14	12	9	7	26	24	20	16	13	49	47	41	34	28	31	27	23	18	15

Webtable 3b. 10-year risk (%) of any (locoregional or distant) first recurrence according to prognostic and other factors: Absolute risks in pathologically node negative women allocated to breast-conserving surgery (BCS) and BCS+ radiotherapy (RT).

	10-year risk of recurrence (%)																			
	Low grade					Intermediate grade					High grade					Unknown grade				
	Age (years)					Age (years)					Age (years)					Age (years)				
	<40	40	50	60	70+	<40	40	50	60	70+	<40	40	50	60	70+	<40	40	50	60	70+
T1 (1-20mm) tumours in women allocated to BCS																				
Lumpectomy, ER+tam-	55	42	34	30	27	75	62	52	47	41	91	82	74	67	59	71	59	50	44	38
Lumpectomy, ER-poor	48	33	27	25	23	65	48	40	37	34	73	59	50	45	40	56	41	34	31	27
>Lumpectomy, ER+tam- or ER-poor*	32	23	18	16	14	48	36	29	26	23	64	52	43	38	32	43	32	26	23	20
Lumpectomy, ER+tam+	23	17	13	11	10	37	28	22	19	16	57	46	38	32	27	35	27	22	18	15
T1 (1-20mm) tumours in women allocated to BCS+RT																				
Lumpectomy, ER+tam-	33	21	17	16	15	47	31	25	24	23	45	29	24	23	21	35	23	18	17	16
Lumpectomy, ER-poor	41	26	21	21	19	55	38	31	30	28	53	36	29	29	27	43	28	22	22	20
>Lumpectomy, ER+tam- or ER-poor*	22	14	11	10	10	32	20	16	16	14	30	19	15	15	14	23	14	11	11	10
Lumpectomy, ER+tam+	11	7	5	5	5	16	10	8	8	7	15	9	7	7	7	11	7	5	5	5
T2 (21-50mm) tumours in women allocated to BCS																				
Lumpectomy, ER+tam-	71	57	48	44	39	89	78	69	63	57	97	93	88	82	75	86	75	66	59	52
Lumpectomy, ER-poor	65	48	39	37	34	81	65	56	53	49	88	75	66	61	56	73	57	48	44	40
>Lumpectomy, ER+tam- or ER-poor*	46	33	27	25	22	65	50	42	38	33	80	68	58	52	46	59	46	38	33	29
Lumpectomy, ER+tam+	34	25	20	17	15	51	40	32	28	24	73	62	52	45	38	49	38	31	27	22
T2 (21-50mm) tumours in women allocated to BCS+RT																				
Lumpectomy, ER+tam-	48	32	26	25	24	64	45	37	36	34	62	43	36	35	32	51	34	28	27	25
Lumpectomy, ER-poor	57	39	32	31	29	73	54	45	44	41	71	52	43	42	39	59	41	34	33	31
>Lumpectomy, ER+tam- or ER-poor*	33	21	17	16	15	46	31	25	24	22	44	29	23	23	21	35	22	18	17	16
Lumpectomy, ER+tam+	17	10	8	8	7	25	16	12	12	11	24	15	12	11	10	18	11	9	8	8

* No tamoxifen planned for pN0 women in these trials

Webtable 3c. **Numbers of pathologically node negative women in trials of radiotherapy after breast-conserving surgery according to prognostic and other factors.** When all the factors that are influential in determining the absolute reduction in the 10-year risk of recurrence are considered simultaneously, the numbers of women in each individual category are too small to provide meaningful estimates based only on the women in that category. Therefore, the dependence of the effect of radiotherapy on all the independently prognostic and other factors simultaneously was estimated using the regression model given in webappendix p20. The 10 parameters in that model summarise the overall trends with respect to age, grade, tumour size, etc in the whole data set and they have been used to provide much more stable estimates of the likely effect of radiotherapy for specific combinations of age, grade, tumour size etc than would be the case if the estimate for each individual category used only the women in that category as given in the table below.

Tumour size T1 (1-20 mm)

	Low grade					Intermediate grade					High grade					Unknown grade				
	Age (years)					Age (years)					Age (years)					Age (years)				
	<40	40	50	60	70+	<40	40	50	60	70+	<40	40	50	60	70+	<40	40	50	60	70+
Lumpectomy, ER+tam-	7	60	168	173	34	21	64	85	82	22	28	46	50	42	5	23	59	111	110	35
Lumpectomy, ER-poor	4	11	14	9	3	9	18	24	13	5	30	31	24	21	1	14	18	17	15	7
>Lumpectomy, ER+tam- or ER-poor*	0	5	9	11	9	2	15	29	46	28	12	37	45	68	41	55	282	437	506	132
Lumpectomy, ER+tam+	8	73	309	286	188	7	53	232	341	261	8	19	37	37	22	10	45	130	136	378

Tumour size T2 (21-50 mm)

	Low grade					Intermediate grade					High grade					Unknown grade				
	Age (years)					Age (years)					Age (years)					Age (years)				
	<40	40	50	60	70+	<40	40	50	60	70+	<40	40	50	60	70+	<40	40	50	60	70+
Lumpectomy, ER+tam-	3	12	16	15	3	13	22	27	47	14	19	27	33	38	3	11	15	34	24	19
Lumpectomy, ER-poor	1	3	0	1	1	3	13	10	13	1	17	37	35	18	3	4	10	14	16	2
>Lumpectomy, ER+tam- or ER-poor*	0	0	0	0	0	0	0	2	1	1	1	2	2	3	2	6	42	47	46	13
Lumpectomy, ER+tam+	0	0	5	12	22	1	6	16	30	51	0	3	4	6	4	4	3	24	27	17

Tumour size unknown

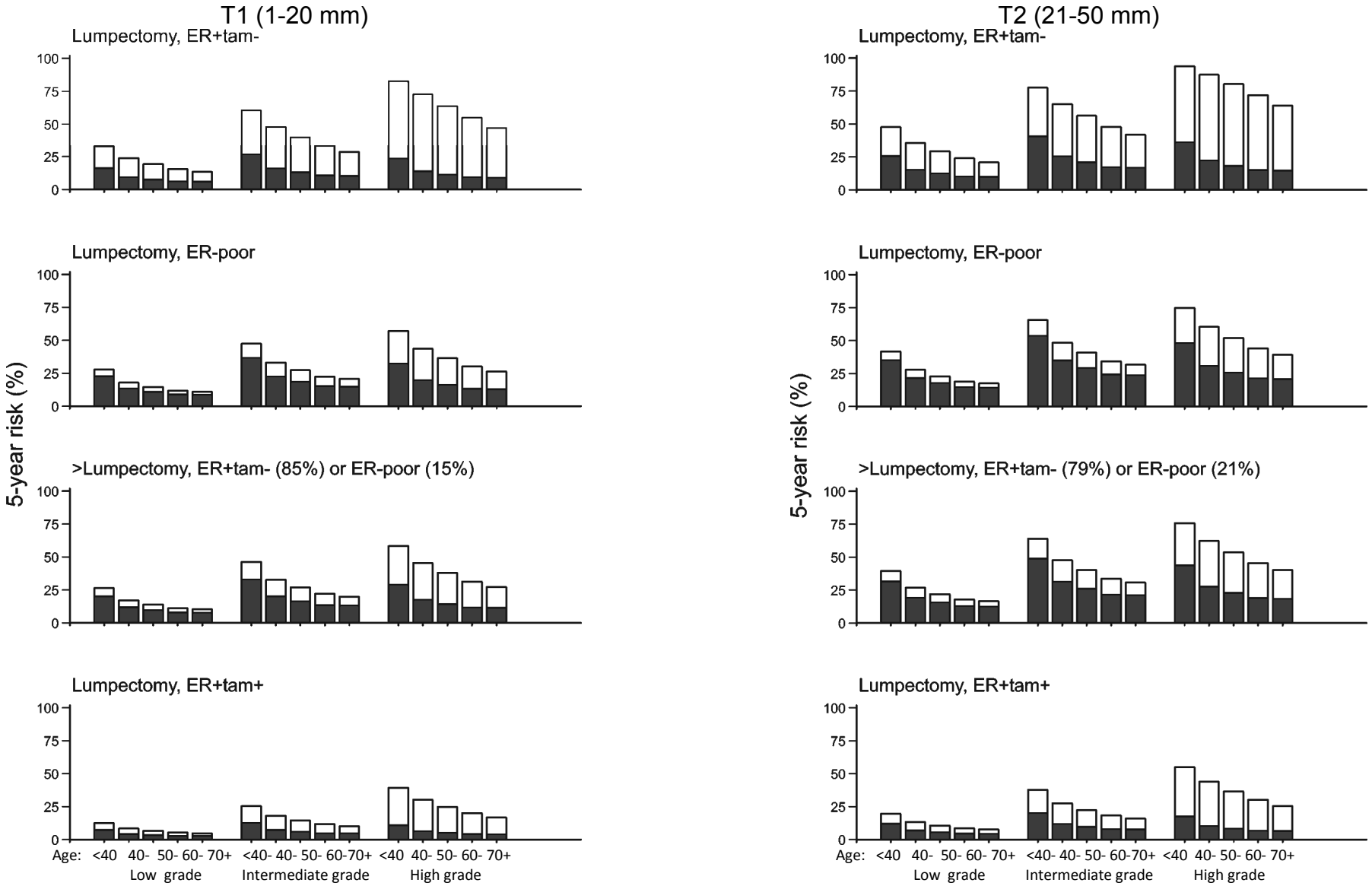
	Low grade					Intermediate grade					High grade					Unknown grade				
	Age (years)					Age (years)					Age (years)					Age (years)				
	<40	40	50	60	70+	<40	40	50	60	70+	<40	40	50	60	70+	<40	40	50	60	70+
Lumpectomy, ER+tam-	0	2	3	2	1	1	3	1	1	0	1	0	0	0	0	1	4	9	7	0
Lumpectomy, ER-poor	0	0	0	0	0	0	0	0	1	0	0	1	2	1	0	19	31	16	14	0
>Lumpectomy, ER+tam- or ER-poor*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	4	10	3	1
Lumpectomy, ER+tam+	1	5	7	9	2	2	6	7	5	4	0	5	4	3	1	16	66	72	66	4

Webtable 4. **Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on 5-year risk (%) of first recurrence of any type (locoregional or distant) in 7287 pathologically node-negative women according to prognostic and other factors.**

Factor*	Events/woman-year in years 0-4 (5-yr risk %)				Test for trend or heterogeneity‡	
	Allocated BCS+RT		Allocated BCS		Unadjusted§	Adjusted¶
Age at entry (years)						
< 40	66/711	33.0	86/547	51.8	X^2_1=28.1,	X^2_1=11.6,
40 – 49	94/2531	15.4	193/2242	34.0	2p<0.001	2p <0.001
50 – 59	118/4899	15.0	218/4285	22.3		
60 – 69	91/5111	8.3	202/4897	18.4		
70+	27/2928	4.4	63/2802	10.9		
Tumour grade						
Low	30/3321	4.6	78/3315	11.5	X^2_1=54.9,	X^2_1=29.6,
Intermediate	97/3485	11.5	176/3311	23.4	2p<0.001	2p <0.001
High	103/1823	22.0	193/1381	45.8		
Unknown**	166/7551	9.9	315/6767	20.6		
Tumour size						
T1 (1-20 mm)	240/13211	8.0	513/12313	18.9	X^2_1=10.0,	X^2_1=5.2,
T2 (21-50 mm)	122/2047	23.3	205/1601	43.5	2p=0.002	2p=0.02
Other/unknown**	34/921	17.5	44/860	22.5		
ER status & trial policy of tamoxifen use††						
ER-poor	109/1830	24.9	158/1553	37.1		
ER+Tam-	225/7499	12.7	448/6453	28.6	2p<0.001	2p<0.001
ER+Tam+	62/6851	4.5	156/6768	11.2	X^2_2=39.4,	X^2_2=16.8,
Trial policy of additional therapy**						
No	190/6646	11.8	361/5944	25.9	X^2_1=11.0,	X^2_1=0.3,
Yes	198/9310	9.6	388/8602	20.2	2p<0.001	2p=0.58
Some/Unknown**	8/224	17.1	13/227	23.8		
Trial category§§						
A. Lump: original	264/5153	21.1	469/4313	39.8	A vs C:	A vs C:
B. >Lump	95/4553	9.7	183/4208	19.4	X^2_1=53.2,	X^2_1=2.0,
C. Lump: low risk	37/6474	2.9	110/6254	8.6	2p<0.001	2p=0.15
					A+C vs B: X^2_1=2.5, 2p=0.12	A+C vs B: X^2_1=17.1, 2p<0.001

* Age at entry, tumour grade, tumour size, and ER status are characteristics of the individual women or their tumours; tamoxifen use, trial policy of additional therapy, and trial category are characteristics of the trials in which they were entered.
‡ Test for trend/heterogeneity in absolute reduction in recurrence rate.
§ Unadjusted: each factor alone.
¶ Adjusted: each factor adjusted for all others using regression modelling.
** Category excluded from test for trend/heterogeneity.
†† Tamoxifen use: tamoxifen given to both trial arms. ER unknown included with ER+.
‡‡ Chemotherapy (usually CMF) given to both trials arms and/or nodal RT or boost given to those allocated BCS+RT.
§§ See table 1 in main paper for explanation of trial categories.

Webfigure 8. Absolute reduction in 5-year risk (%) of any (locoregional or distant) first recurrence from radiotherapy (RT) after breast-conserving surgery (BCS) in pathologically node-negative women: dependence on prognostic and other factors suggested by modelling data from 7287 women. Black bars give 5-year risks in women allocated to BCS+RT, black+white bars give 5-year risks in women allocated to BCS only, and white bars give absolute reduction with RT.



Webtable 5a. 5-year risk (%) of any (locoregional or distant) first recurrence according to prognostic and other factors: Absolute reduction with radiotherapy (RT) after breast-conserving surgery (BCS) in pathologically node negative women. Reductions of 20% and above are shown in dark boxes, 10-19% in light boxes, and less than 10% in clear boxes.

	Absolute reduction in 5-year risk of recurrence with radiotherapy (%)																			
	Low grade					Intermediate grade					High grade					Unknown grade				
	Age (years)					Age (years)					Age (years)					Age (years)				
	<40	40	50	60	70+	<40	40	50	60	70+	<40	40	50	60	70+	<40	40	50	60	70+
T1 (1-20mm) tumours																				
Lumpectomy, ER+tam-	17	14	12	9	7	34	32	27	23	18	59	59	53	46	38	37	34	28	23	19
Lumpectomy, ER-poor	5	5	4	3	2	11	11	9	7	6	25	24	20	17	14	13	11	9	8	6
>Lumpectomy, ER+tam- or ER-poor*	6	5	4	3	3	13	13	11	9	7	29	28	24	20	16	15	14	11	9	7
Lumpectomy, ER+tam+	5	4	3	3	2	13	11	9	7	5	28	24	20	16	13	13	11	9	7	5
T2 (21-50mm) tumours																				
Lumpectomy, ER+tam-	22	20	17	14	11	37	40	35	31	25	58	65	62	57	49	44	44	38	32	27
Lumpectomy, ER-poor	7	6	5	4	3	12	14	12	10	8	27	30	26	23	19	16	16	13	11	9
>Lumpectomy, ER+tam- or ER-poor*	8	8	6	5	4	15	16	14	12	10	32	35	31	27	22	19	19	16	13	10
Lumpectomy, ER+tam+	8	6	5	4	3	18	16	13	10	8	37	34	28	23	19	19	16	13	11	8

* No tamoxifen planned for pN0 women in these trials

Webtable 5b. 5-year risk (%) of any (locoregional or distant) first recurrence according to prognostic and other factors: Absolute risks in pathologically node negative women allocated to breast-conserving surgery (BCS) and BCS+ radiotherapy (RT).

	5-year risk of recurrence (%)																			
	Low grade					Intermediate grade					High grade					Unknown grade				
	Age (years)					Age (years)					Age (years)					Age (years)				
	<40	40	50	60	70+	<40	40	50	60	70+	<40	40	50	60	70+	<40	40	50	60	70+
T1 (1-20mm) tumours in women allocated to BCS																				
Lumpectomy, ER+tam-	33	24	19	16	13	60	48	40	33	29	82	73	64	55	47	55	44	37	30	26
Lumpectomy, ER-poor	28	18	15	12	11	48	33	27	23	21	57	44	36	30	26	38	27	22	18	16
>Lumpectomy, ER+tam- or ER-poor*	26	17	14	11	10	46	33	27	22	20	58	45	38	31	27	38	27	22	18	16
Lumpectomy, ER+tam+	12	8	7	5	5	25	18	14	12	10	39	30	25	20	17	21	16	13	10	8
T1 (1-20mm) tumours in women allocated to BCS+RT																				
Lumpectomy, ER+tam-	16	9	8	6	6	27	16	13	11	10	23	14	11	9	9	18	11	9	7	7
Lumpectomy, ER-poor	23	13	11	9	9	37	22	18	15	15	32	20	16	13	13	25	15	12	10	10
>Lumpectomy, ER+tam- or ER-poor*	20	12	10	8	8	33	20	16	13	13	29	17	14	12	11	23	13	11	9	9
Lumpectomy, ER+tam+	7	4	3	3	3	12	7	6	5	5	11	6	5	4	4	8	5	4	3	3
T2 (21-50mm) tumours in women allocated to BCS																				
Lumpectomy, ER+tam-	48	36	29	24	21	78	65	56	48	42	94	87	80	72	64	72	61	52	44	38
Lumpectomy, ER-poor	42	28	23	19	18	66	48	41	34	32	75	60	52	44	39	54	40	33	27	25
>Lumpectomy, ER+tam- or ER-poor*	40	27	22	18	16	64	48	40	34	31	76	62	54	46	40	54	40	33	27	24
Lumpectomy, ER+tam+	20	13	11	9	8	38	27	22	18	16	55	44	36	30	25	32	24	19	16	13
T2 (21-50mm) tumours in women allocated to BCS+RT																				
Lumpectomy, ER+tam-	26	15	12	10	10	41	25	21	17	17	36	22	18	15	15	29	17	14	11	11
Lumpectomy, ER-poor	35	21	18	15	14	53	35	29	24	24	48	31	26	21	21	39	24	20	16	16
>Lumpectomy, ER+tam- or ER-poor*	31	19	16	13	12	49	31	26	22	21	44	27	23	19	18	35	21	18	14	14
Lumpectomy, ER+tam+	12	7	6	4	4	20	12	10	8	8	17	10	8	7	7	13	8	6	5	5

* No tamoxifen planned for pN0 women in these trials

Webtable 6. Risks of any (locoregional or distant) first recurrence and breast cancer mortality in 7287 pathologically node-negative women given breast-conserving surgery (BCS) according to predicted absolute benefit with radiotherapy (RT) in 10-year risk suggested by modelling of predictive factors.

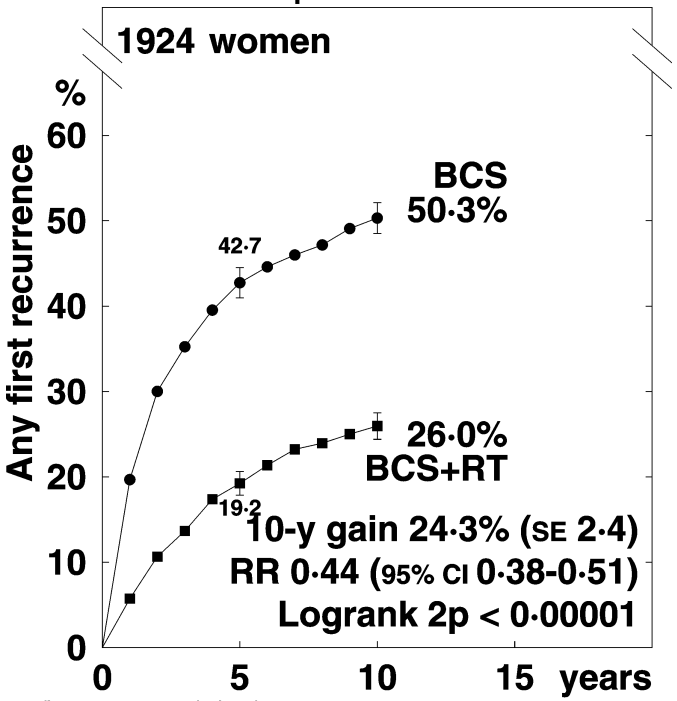
Predicted absolute benefit*	Total number of women	Number of women by trial category			Number of women with follow-up at least:			Any first recurrence 10-year risk (%)†			Breast cancer mortality 15-year risk (%)†		
								Allocated		Gain with RT‡ (95% CI)	Allocated		Gain with RT‡ (95% CI)
		A (%)	B (%)	C (%)	5y	10y	15y	BCS+RT	BCS		BCS+RT	BCS	
Large	1924	1342 (56)	322 (16)	260 (9)	1672	1198	581	26.0	50.3	24.3 (19.6, 29.0)	23.2	31.0	7.8 (3.1, 12.5)
Intermediate	3763	784 (32)	1436 (74)	1543 (53)	3096	1850	525	12.4	24.8	12.4 (9.7, 15.1)§	13.9	15.0	1.1 (-2.0, 4.2)¶
Lower	1600	294 (12)	198 (10)	1108 (38)	1084	458	118	12.0	18.9	6.9 (2.2, 11.6)§	16.5	16.6	0.1 (-7.5, 7.7)¶
Total	7287	2420 (100)	1956 (100)	2911 (100)	5852	3506	1224						
2p for trend										<0.00001			0.03

* Women allocated to categories using regression-based estimates of absolute reduction in 10-year risk of any first recurrence in main paper figure 4 and webappendix p28.
† 10-year risks of any first recurrence and 15-year risks of breast cancer mortality calculated directly from data on individual women.
‡ ie, reduction in absolute risk.
§ For intermediate and lower categories combined, 10-year risks for any first recurrence: BCS+RT: 12.1%, BCS:23.1%, gain with RT 11.0% (95% CI: 8.6, 13.4).
¶ For intermediate and lower categories combined, 15-year risk for breast cancer mortality: BCS+RT: 14.4%, BCS:15.1%, gain with RT 0.7% (95% CI: -2.2, 3.6)

Webfigure 9a. Risks of any (locoregional or distant) first recurrence in 7287 pathologically node-negative women given breast-conserving surgery (BCS) according to predicted absolute benefit with radiotherapy (RT) in 10-year risk suggested by modelling of prognostic and other factors. Women allocated to categories of predicted absolute benefit using the results of the modelling of prognostic and other factors (see figure 4). Risks calculated directly from data on individual women. Vertical lines indicate 1 SE above or below the 5 and 10 year percentages.

Predicted absolute benefit: Large (20+ %)

1924 pN0 women

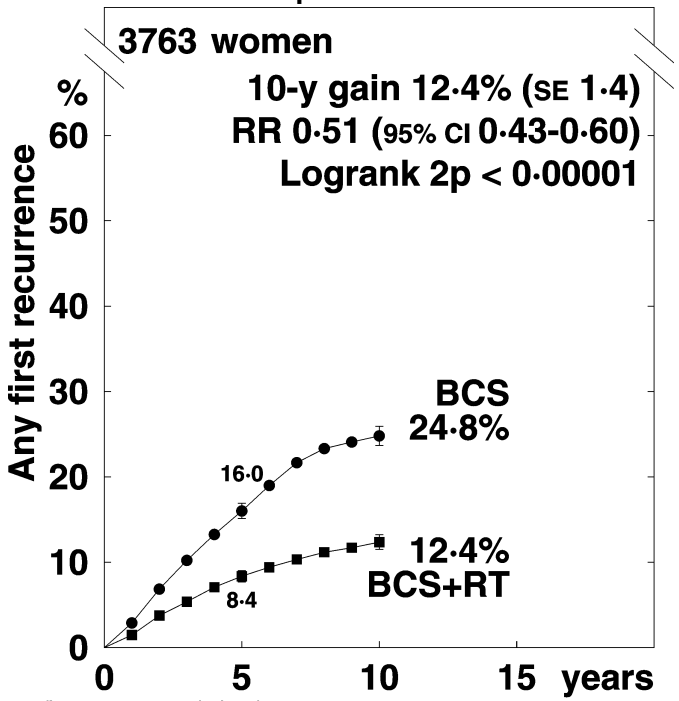


any first recurrence rates (% / year) and logrank analyses

	Years 0 - 4	Years 5 - 9	Year 10+
BCS+RT	4·78 (198 / 4146)	1·87 (57 / 3054)	0·93 (26 / 2810)
BCS	12·29 (396 / 3223)	3·00 (61 / 2036)	0·90 (17 / 1894)
Rate ratio, from	0·38 SE 0·06	0·63 SE 0·15	1·06 SE 0·32
(O-E) / V	-123·2 / 127·8	-12·7 / 27·4	0·5 / 10·1

Predicted absolute benefit: Intermediate (10-19%)

3763 pN0 women

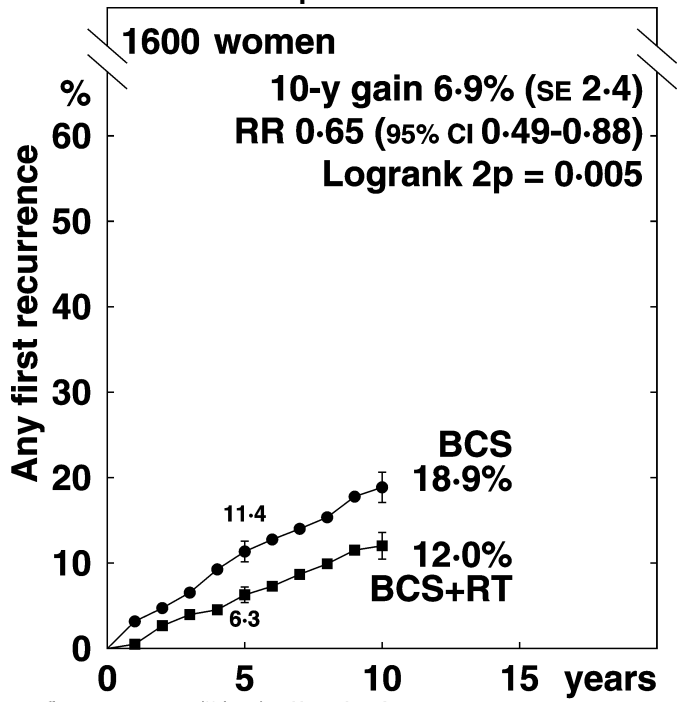


any first recurrence rates (% / year) and logrank analyses

	Years 0 - 4	Years 5 - 9	Year 10+
BCS+RT	1·81 (156 / 8632)	1·00 (57 / 5688)	0·82 (26 / 3178)
BCS	3·49 (283 / 8098)	2·40 (117 / 4870)	0·60 (16 / 2650)
Rate ratio, from	0·51 SE 0·07	0·41 SE 0·10	1·26 SE 0·36
(O-E) / V	-69·5 / 103·6	-37·5 / 41·6	2·3 / 9·8

Predicted absolute benefit: Lower (<10%)

1600 pN0 women



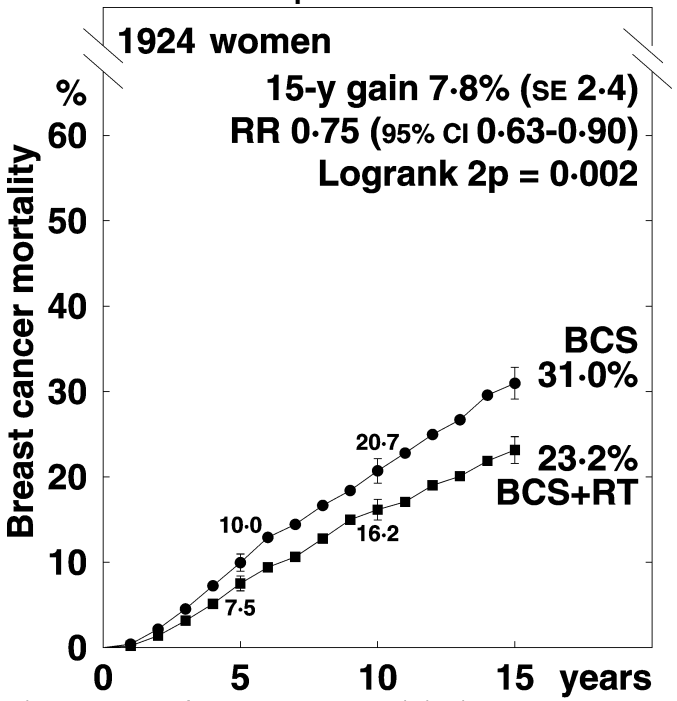
any first recurrence rates (% / year) and logrank analyses

	Years 0 - 4	Years 5 - 9	Year 10+
BCS+RT	1·24 (42 / 3394)	1·32 (21 / 1588)	1·67 (11 / 657)
BCS	2·44 (84 / 3442)	1·69 (27 / 1595)	1·10 (7 / 637)
Rate ratio, from	0·55 SE 0·14	0·73 SE 0·26	1·50 SE 0·61
(O-E) / V	-17·0 / 28·9	-3·5 / 11·2	1·7 / 4·1

Webfigure 9b. Risks of breast cancer mortality in 7287 pathologically node-negative women given breast-conserving surgery (BCS) according to predicted absolute benefit with radiotherapy (RT) in 10-year risk suggested by modelling of prognostic and other factors. Women allocated to categories of predicted absolute benefit using the results of the modelling of prognostic and other factors (see main text figure 4). Risks calculated directly from data on individual women. Vertical lines indicate 1 SE above or below the 5 and 10 year percentages.

Predicted absolute benefit: Large (20+ %)

1924 pN0 women

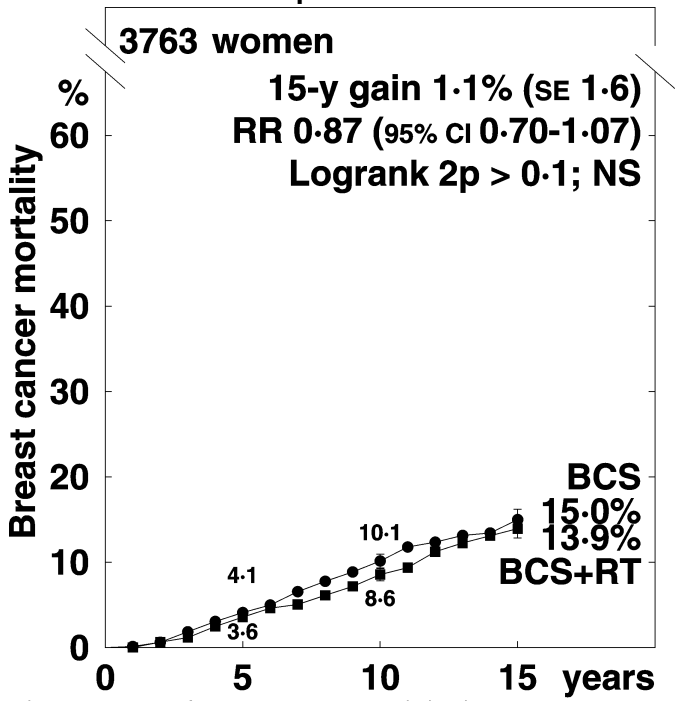


After-recurrence or possible-breast-cancer death rates (% / year) and logrank analyses

	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
BCS+RT	1·52 SE 0·18	1·83 SE 0·22	1·59 SE 0·27	2·18 SE 0·36
BCS	2·09 SE 0·22	2·72 SE 0·28	2·94 SE 0·38	2·73 SE 0·43
Rate ratio, from (O-E) / V	0·74 SE 0·14 -11·7 / 39·2	0·77 SE 0·14 -10·3 / 39·5	0·62 SE 0·17 -10·9 / 22·6	0·94 SE 0·23 -1·0 / 17·7

Predicted absolute benefit: Intermediate (10-19%)

3763 pN0 women

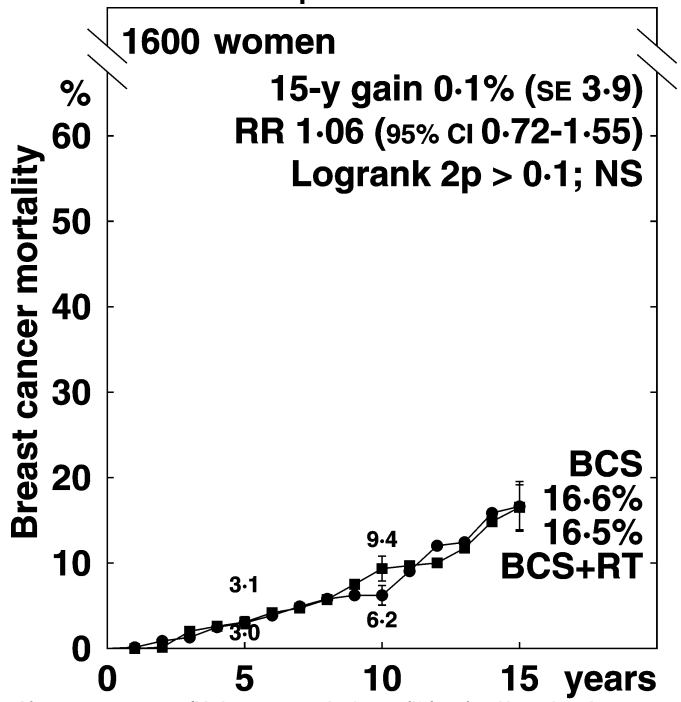


After-recurrence or possible-breast-cancer death rates (% / year) and logrank analyses

	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
BCS+RT	0·71 SE 0·09	0·98 SE 0·12	1·15 SE 0·20	1·58 SE 0·46
BCS	0·82 SE 0·10	1·35 SE 0·15	1·22 SE 0·21	2·30 SE 0·56
Rate ratio, from (O-E) / V	0·87 SE 0·16 -4·6 / 32·5	0·80 SE 0·15 -7·7 / 34·3	1·11 SE 0·26 1·7 / 16·4	0·71 SE 0·33 -2·3 / 6·7

Predicted absolute benefit: Lower (<10%)

1600 pN0 women

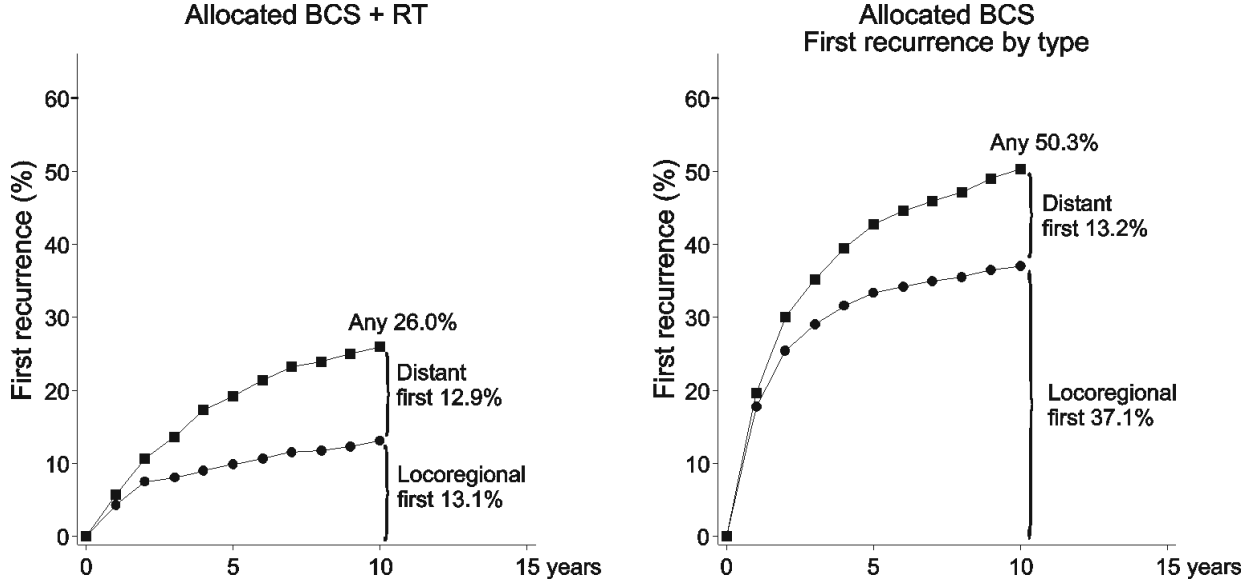


After-recurrence or possible-breast-cancer death rates (% / year) and logrank analyses

	Years 0 - 4	Years 5 - 9	Years 10 - 14	Year 15+
BCS+RT	0·55 SE 0·13	1·16 SE 0·26	0·99 SE 0·40	3·92 SE 1·39
BCS	0·66 SE 0·13	0·84 SE 0·21	2·71 SE 0·62	3·17 SE 1·30
Rate ratio, from (O-E) / V	1·03 SE 0·32 0·3 / 9·9	1·65 SE 0·46 4·0 / 8·0	0·56 SE 0·33 -3·1 / 5·3	1·05 SE 0·59 0·2 / 3·1

Webfigure 9c. 10-year risk of any first recurrence in 7287 pathologically node-negative women in trials of radiotherapy (RT) after breast-conserving surgery (BCS) according to predicted absolute benefit with radiotherapy in 10-year risk suggested by modelling of prognostic and other factors, type of first recurrence and allocated treatment. Women found to have both a locoregional and a distant recurrence at the time of their first recurrence are classified as having a distant recurrence. This figure does not provide evidence that radiotherapy increases the risk of distant recurrence, see legend on webappendix p9. Women allocated to categories of predicted absolute benefit using the results of the modelling of prognostic and other factors (see main text figure 4). Risks calculated directly from data on individual women.

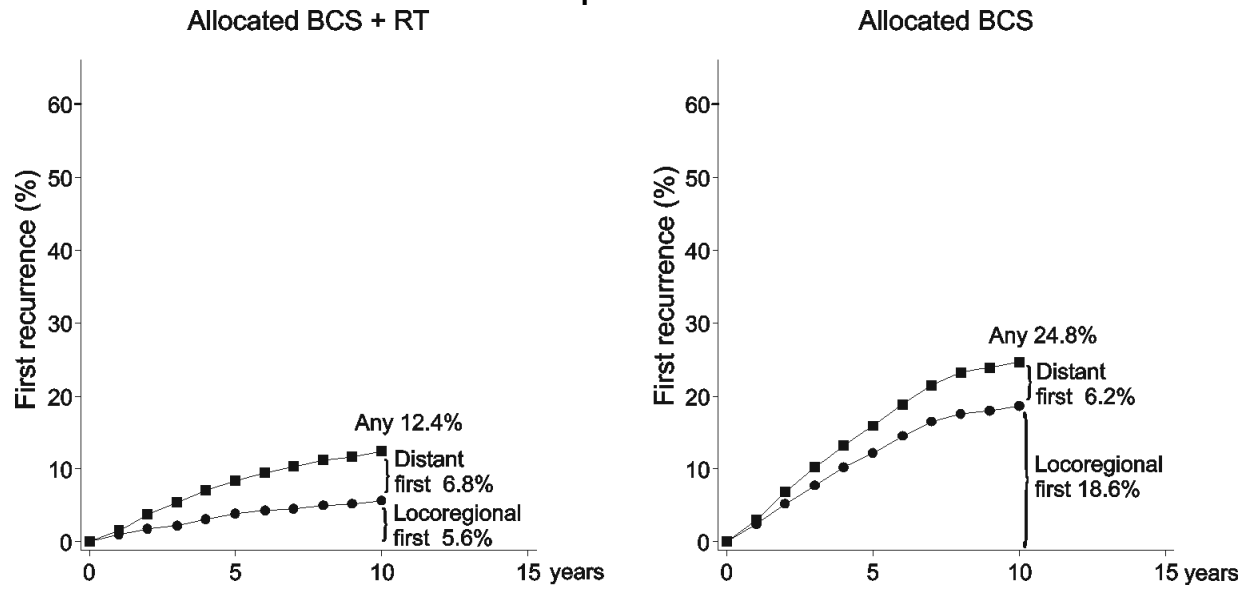
Predicted absolute benefit: Large (20+ %)
1924 pN0 women



Numbers of women with first recurrence by 10 years according to type of first recurrence and allocated treatment (BCS+RT /BCS):

a. Ipsilateral breast	b. Ipsilateral axilla	c. Other locoregional site	d. Locoregional, site unknown	Any locoregional (ie a+b+c+d)	Distant	Any recurrence
95/244	2/7	16/16	21/70	134/337	121/120	255/457

Predicted absolute benefit: Intermediate (10-19%)
3763 pN0 women

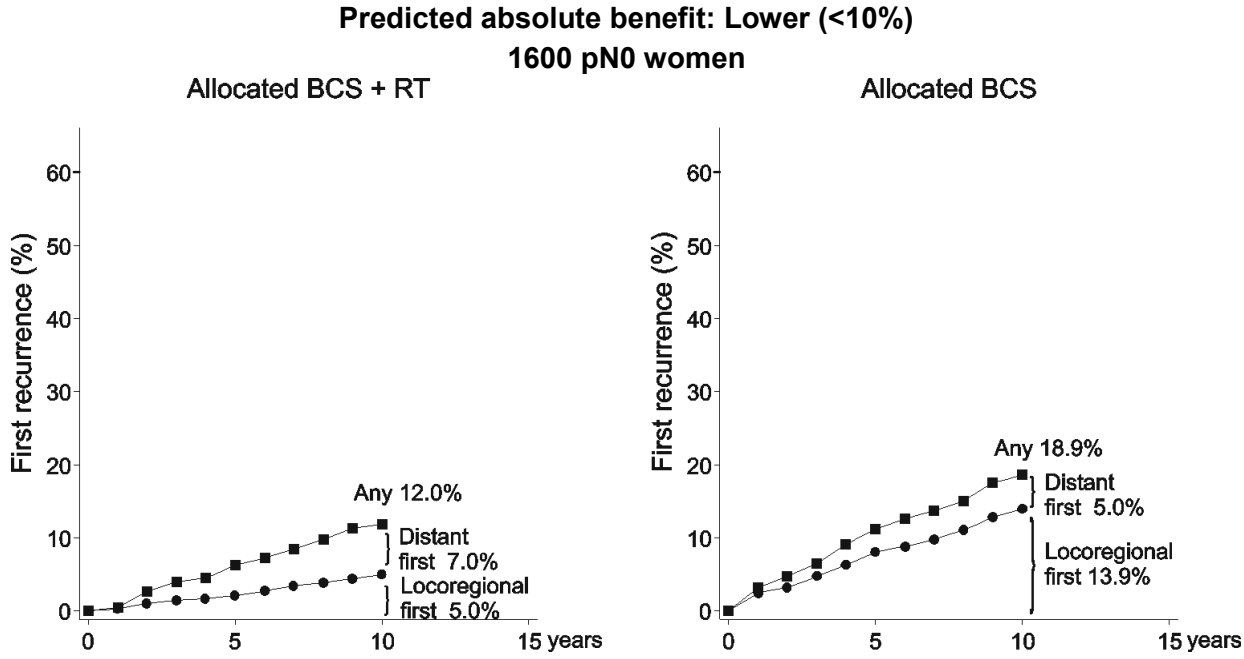


Numbers of women with first recurrence by 10 years according to type of first recurrence and allocated treatment (BCS+RT /BCS):

a. Ipsilateral breast	b. Ipsilateral axilla	c. Other locoregional site	d. Locoregional, site unknown	Any locoregional (ie a+b+c+d)	Distant	Any recurrence
55/167	4/8	5/6	34/122	98/303	115/97	213/400

continued overleaf

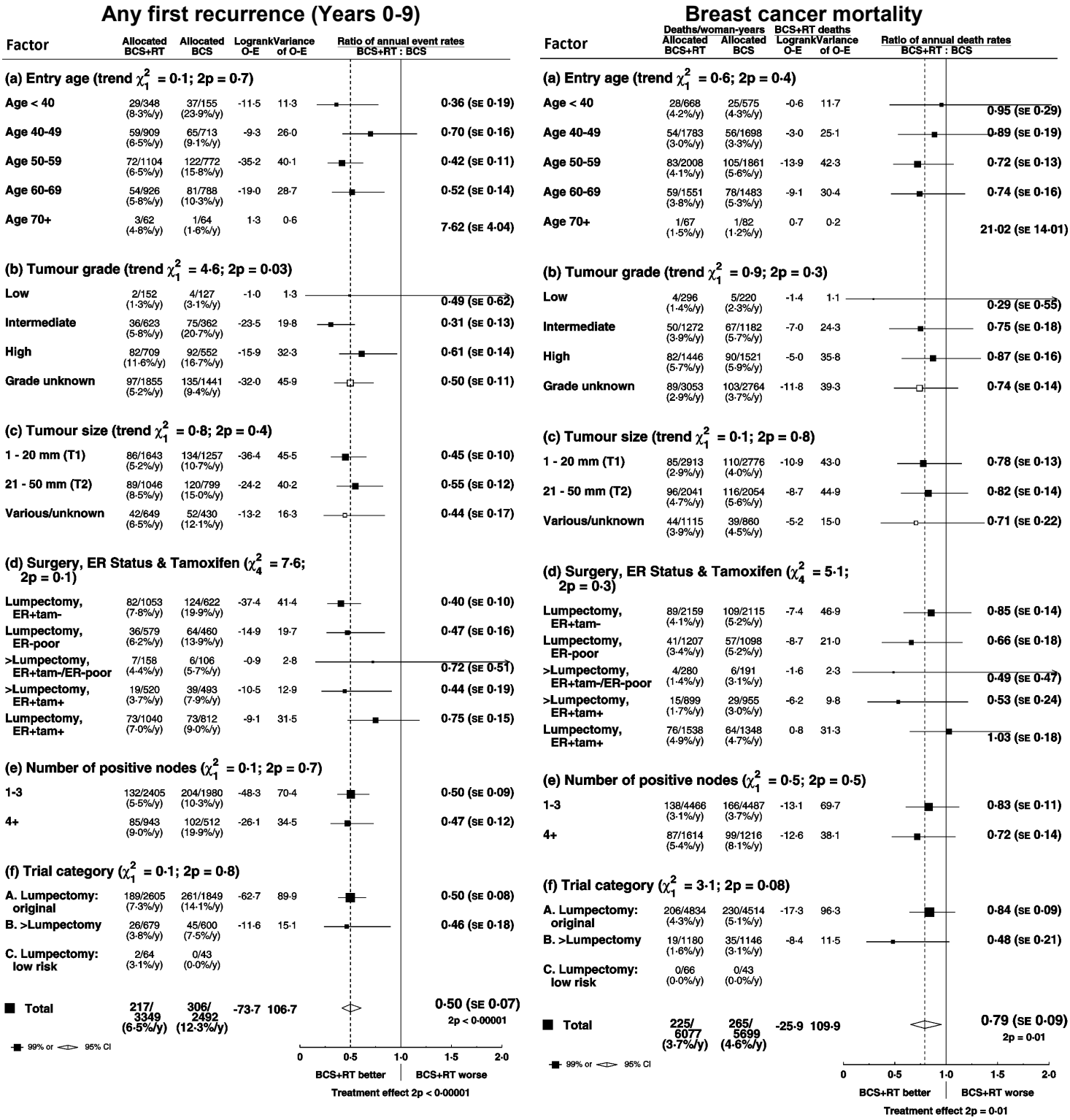
Webfigure 9c, continued.



Numbers of women with first recurrence by 10 years according to type of first recurrence and allocated treatment (BCS+RT /BCS):

a. Ipsilateral breast	b. Ipsilateral axilla	c. Other locoregional site	d. Locoregional, site unknown	Any locoregional (ie a+b+c+d)	Distant	Any recurrence
14/40	0/0	2/3	9/37	25/80	38/31	63/111

Webfigure 10. Proportional effect of radiotherapy (RT) after breast-conserving surgery (BCS). Event rate ratios for any (locoregional or distant) first recurrence, during years 0-9, and for breast cancer mortality in women with pathologically node-positive disease by prognostic and other factors.



Categories including unknowns excluded from tests for trend and heterogeneity.

See Table 1 in main paper for definitions of trial categories.

Webtable 7a. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on 10-year risk (%) of first recurrence of any type (locoregional or distant) in 1050 pathologically node-positive women according to prognostic and other factors.

Factor*	Events/woman-year in years 0-9 (10-year risk)				Test for trend or heterogeneity‡	
	Allocated BCS+RT		Allocated BCS		Unadjusted§	Adjusted¶
Age at entry (years)						
< 40	29/349	49.5	37/156	76.3	X^2_1=3.8,	X^2_1=0.3,
40 – 49	58/906	44.7	65/715	53.7	2p=0.05	2p =0.56
50 – 59	72/1108	43.2	122/776	70.7		
60+	57/992	40.6	82/858	57.7		
Tumour grade						
Low/ Intermediate	38/782	35.6	79/497	69.2	X^2_1=2.2,	X^2_1=3.3
High	82/713	63.4	92/555	71.8	2p=0.14	2p =0.07
Unknown**	96/1860	37.5	135/1454	57.5		
Tumour size						
T1 (1-20 mm)	86/1652	38.4	134/1264	60.2	X^2_1=0.0,	X^2_1=1.1,
T2 (21-50 mm)	89/1053	51.8	120/805	68.6	2p=0.94	2p=0.30
Other/unknown**	41/651	39.6	52/438	66.3		
Number of positive nodes						
1-3	132/2411	38.3	204/1988	58.2	X^2_1=4.3,	X^2_1=0.6,
4+	84/944	54.7	102/518	76.4	2p=0.04	2p=0.44
ER status & trial policy of tamoxifen use††††						
ER-poor	43/742	40.3	70/571	61.5		
ER+Tam-	82/1054	49.4	124/623	73.9	2p<0.001	2p=0.08
ER+Tam+	91/1560	42.2	112/1312	55.0	X^2_2=21.5,	X^2_2=4.9,
Trial policy of additional therapy**						
No	0/0	-	0/0	-	-	-
Yes	112/1925	41.5	147/1556	57.6		
Some/Unknown**	104/1431	47.1	159/951	69.3		
Trial category§§					A vs B:	A vs B:
A. Lump: original	188/2609	46.0	261/1861	66.7	X^2_1=3.0,	X^2_1=0.6,
B. >Lump	26/680	31.6	45/601	53.0	2p=0.08	2p=0.43
C. Lump: low risk	2/66	-	0/44	-		

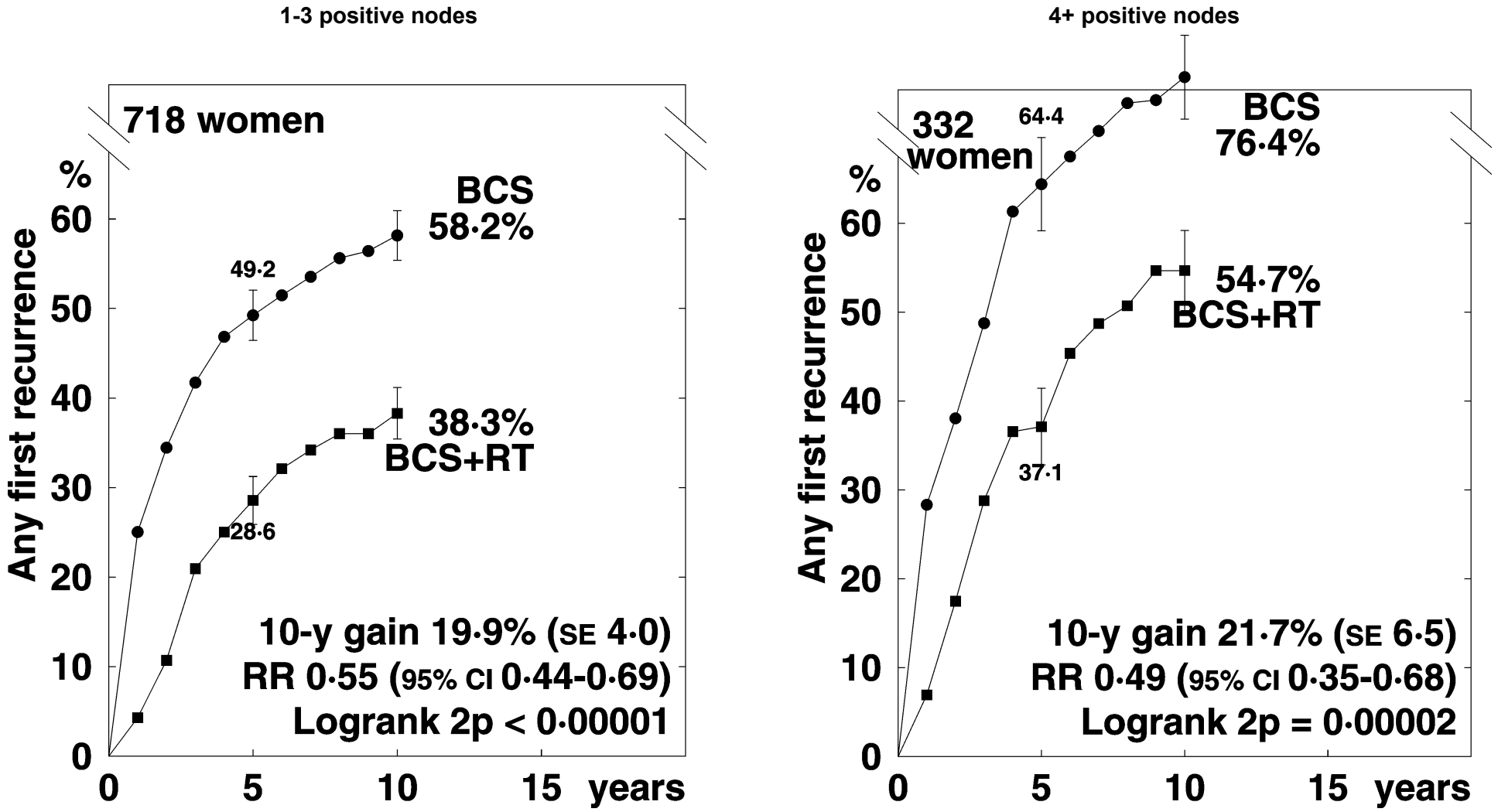
* Age at entry, tumour grade, tumour size, and ER status are characteristics of the individual women or their tumours; tamoxifen use, trial policy of additional therapy, and trial category are characteristics of the trials in which they were entered.
‡ Test for trend/heterogeneity in absolute reduction in recurrence rate.
§ Unadjusted: each factor alone.
¶ Adjusted: each factor adjusted for all others using regression modelling as described on webappendix p20.
** Category excluded from test for trend/heterogeneity.
†† Tamoxifen use: tamoxifen given to both trial arms. ER unknown included with ER+.
‡‡ Chemotherapy (usually CMF) given to both trials arms and/or nodal RT or boost given to those allocated BCS+RT.
§§ See table 1 in main paper for explanation of trial.

Webtable 7b. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on 5-year risk (%) of first recurrence of any type (locoregional or distant) in 1050 pathologically node-positive women according to prognostic factors.

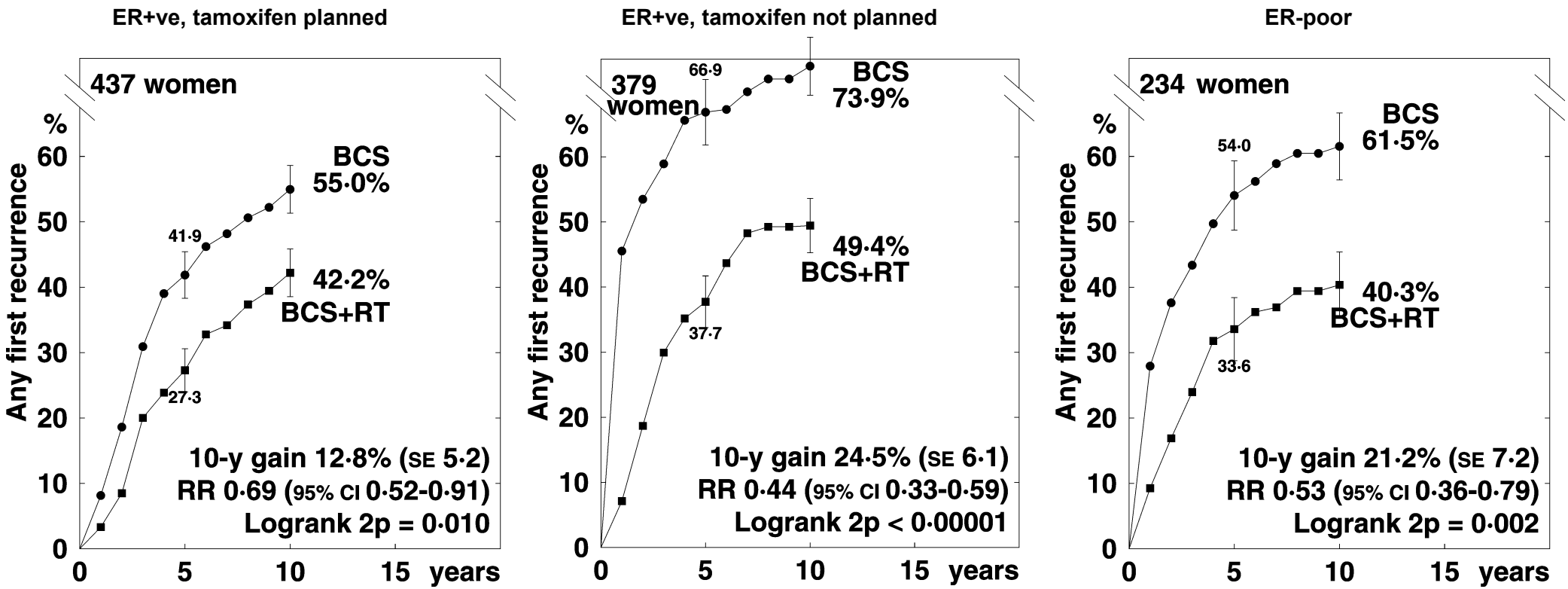
Factor*	Events/woman-year in years 0-4 (5-year risk)				Test for trend or heterogeneity‡	
	Allocated BCS+RT		Allocated BCS		Unadjusted§	Adjusted¶
Age at entry (years)						
< 40	24/213	39.9	36/102	72.9	X^2_1=7.2,	X^2_1=2.5,
40 – 49	44/543	33.2	56/415	45.3	2p=0.007	2p =0.11
50 – 59	53/659	30.4	106/517	61.1		
60+	41/603	27.3	65/543	44.6		
Tumour grade						
Low/ Intermediate	30/457	27.9	72/318	61.5	X^2_1=1.3,	X^2_1=2.5
High	70/475	54.2	85/341	65.1	2p=0.25	2p =0.11
Unknown**	62/1085	23.0	106/918	43.9		
Tumour size						
T1 (1-20 mm)	52/983	22.0	111/788	48.4	X^2_1=0.2,	X^2_1=1.7,
T2 (21-50 mm)	75/649	43.1	105/505	59.9	2p=0.64	2p=0.20
Other/unknown**	35/386	31.2	47/284	59.8		
Number of positive nodes						
1-3	101/1415	28.6	174/1206	49.2	X^2_1=4.2,	X^2_1=1.2,
4+	61/603	37.1	89/371	64.4	2p=0.04	2p=0.27
ER status & trial policy of tamoxifen use††††						
ER-poor	36/434	33.6	62/357	54.0		
ER+Tam-	64/663	37.7	114/402	66.9	2p<0.001	2p=0.05
ER+Tam+	62/921	27.3	87/819	41.9	X^2_2=25.6,	X^2_2=5.9,
Trial policy of additional therapy**						
No	0/0	-	0/0	-	-	-
Yes	77/1134	27.0	118/986	45.5		
Some/Unknown**	85/884	38.4	145/591	62.4		
Trial category§§					A vs B:	A vs B:
A. Lump: original	151/1593	36.3	233/1182	58.5	X^2_1=3.2	X^2_1=1.6,
B. >Lump	11/380	13.2	30/365	34.8	2p=0.07	2p=0.21
C. Lump: low risk	0/45	-	0/30	-		

* Age at entry, tumour grade, tumour size, and ER status are characteristics of the individual women or their tumours; tamoxifen use, Trial policy of additional therapy, and trial category are characteristics of the trials in which they were entered.
‡ Test for trend/heterogeneity in absolute reduction in recurrence rate.
§ Unadjusted: each factor alone.
¶ Adjusted: each factor adjusted for all others using regression modelling as described on webappendix p20.
** Category excluded from test for trend/heterogeneity.
†† Tamoxifen use: tamoxifen given to both trial arms. ER unknown included with ER+.
‡‡ Chemotherapy (usually CMF) given to both trials arms and/or nodal RT or boost given to those allocated BCS+RT.
§§ See table 1 in main paper for explanation of trial categories.

Webfigure 11a. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) in pathologically node-positive women — 10-year risks of any (locoregional or distant) first recurrence by number of positive axillary nodes. Vertical lines indicate 1 SE above or below the 5 and 10 year percentages.

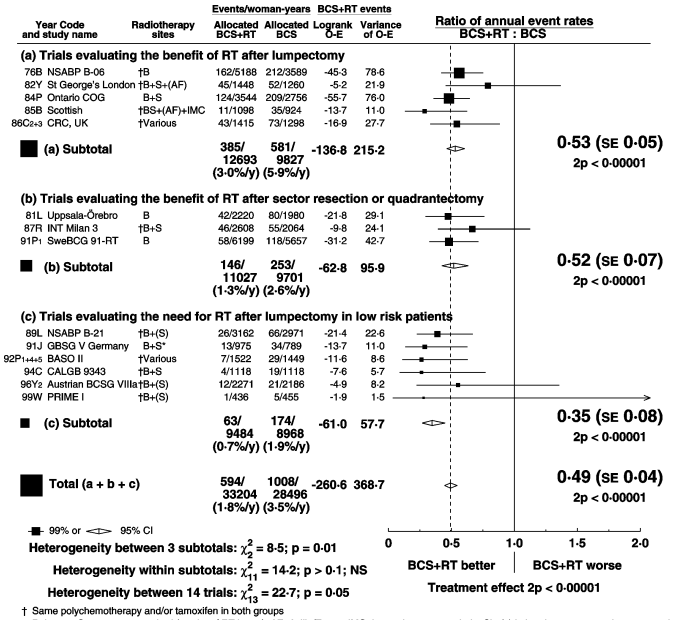


Webfigure 11b. Effect of radiotherapy (RT) after breast-conserving surgery (BCS) in pathologically node-positive women — 10-year risks of any (locoregional or distant) first recurrence by ER status and tamoxifen use. Vertical lines indicate 1 SE above or below the 5 and 10 year percentages.



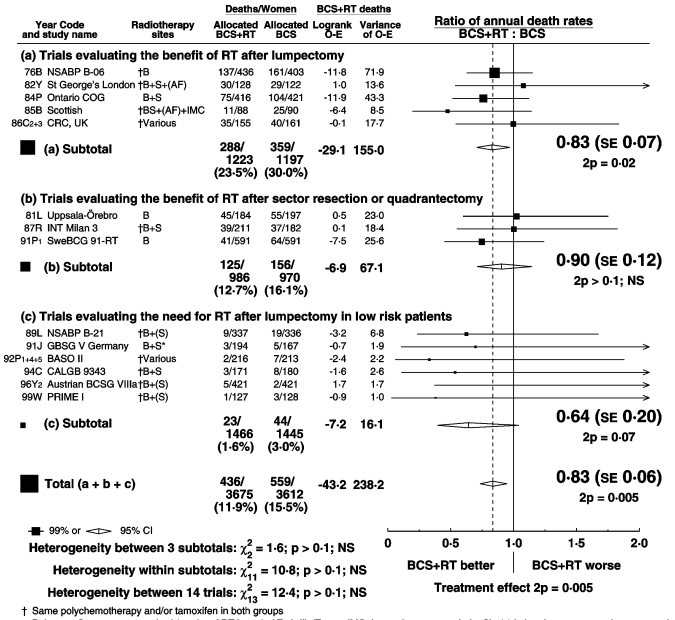
Webfigure 12a. Effect of radiotherapy after breast-conserving surgery on any (locoregional or distant) first recurrence, breast cancer mortality and all-cause mortality in 7287 women with pathologically node-negative disease. Event rate ratios, one line per trial.

Any first recurrence



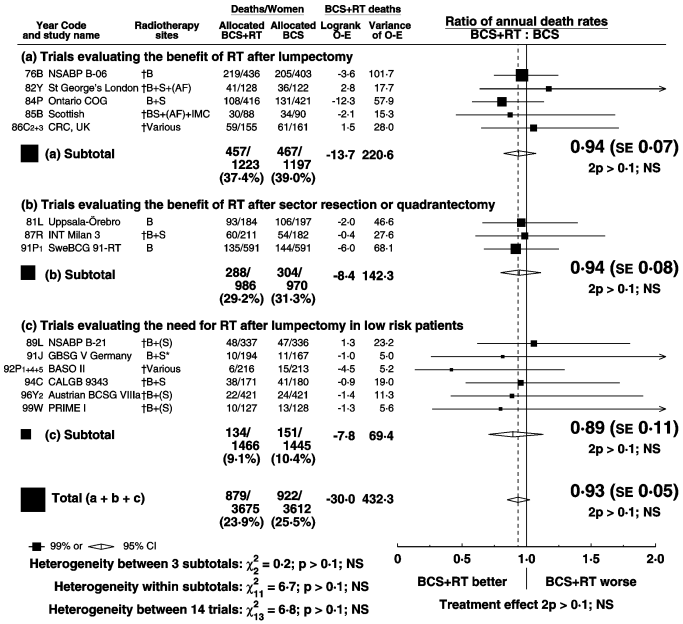
† Same polychemotherapy and/or tamoxifen in both groups
B=breast, S=scar or tumour bed (as site of RT boost), AF=Axilla/Fossa, IMC=Internal mammary chain. Site(s) in brackets were not always treated.

Breast cancer mortality



† Same polychemotherapy and/or tamoxifen in both groups
B=breast, S=scar or tumour bed (as site of RT boost), AF=Axilla/Fossa, IMC=Internal mammary chain. Site(s) in brackets were not always treated.

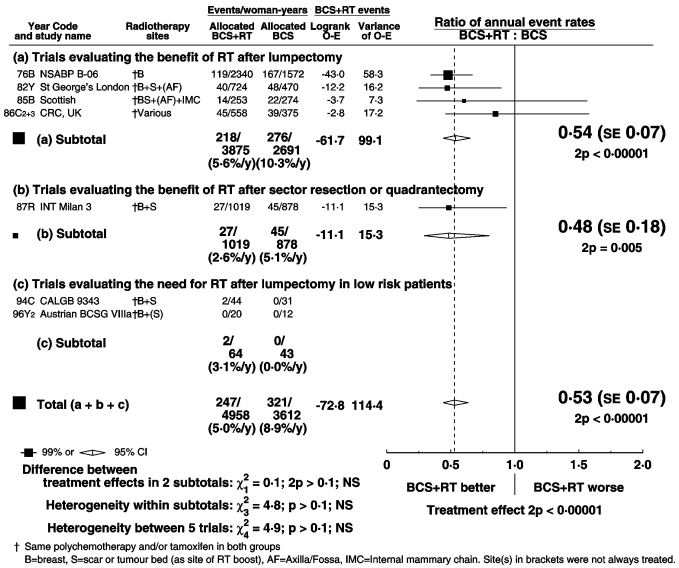
Any death



† Same polychemotherapy and/or tamoxifen in both groups
B=breast, S=scar or tumour bed (as site of RT boost), AF=Axilla/Fossa, IMC=Internal mammary chain. Site(s) in brackets were not always treated.

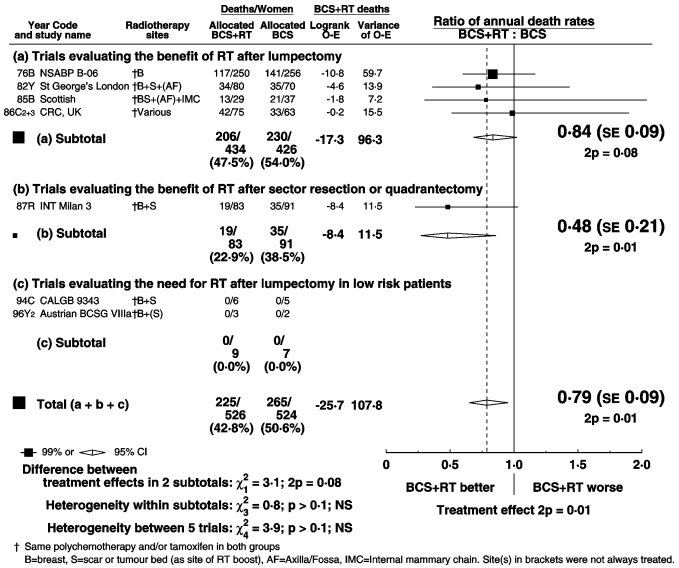
Webfigure 12b. Effect of radiotherapy after breast-conserving surgery on any (locoregional or distant) first recurrence, breast cancer mortality and all-cause mortality in 1050 women with pathologically node-positive disease. Event rate ratios, one line per trial.

Any first recurrence



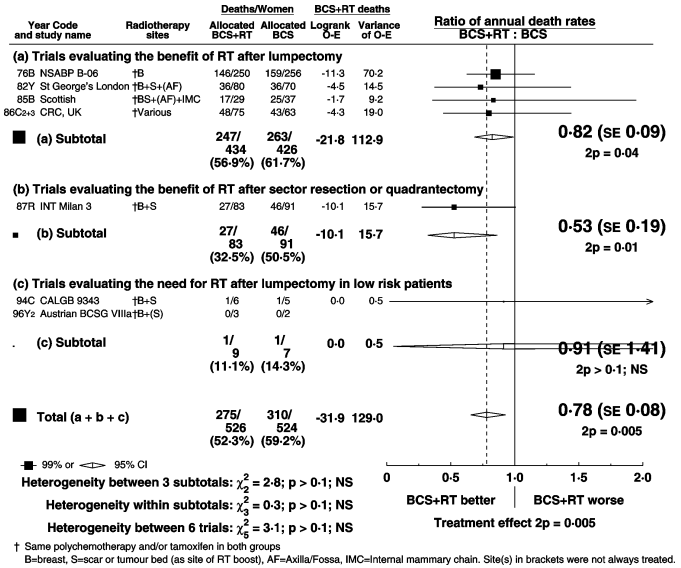
† Same polychemotherapy and/or tamoxifen in both groups
B=breast, S=scar or tumour bed (as site of RT boost), AF=Axilla/Fossa, IMC=Internal mammary chain. Site(s) in brackets were not always treated.

Breast cancer mortality



† Same polychemotherapy and/or tamoxifen in both groups
B=breast, S=scar or tumour bed (as site of RT boost), AF=Axilla/Fossa, IMC=Internal mammary chain. Site(s) in brackets were not always treated.

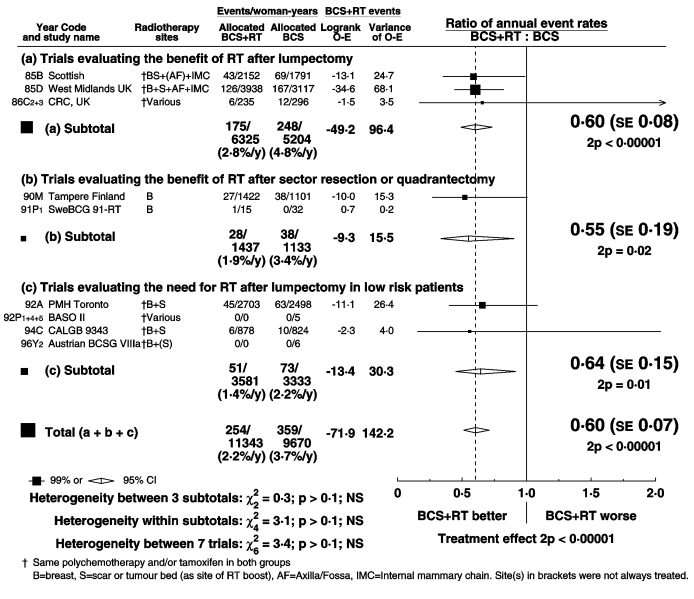
Any death



† Same polychemotherapy and/or tamoxifen in both groups
B=breast, S=scar or tumour bed (as site of RT boost), AF=Axilla/Fossa, IMC=Internal mammary chain. Site(s) in brackets were not always treated.

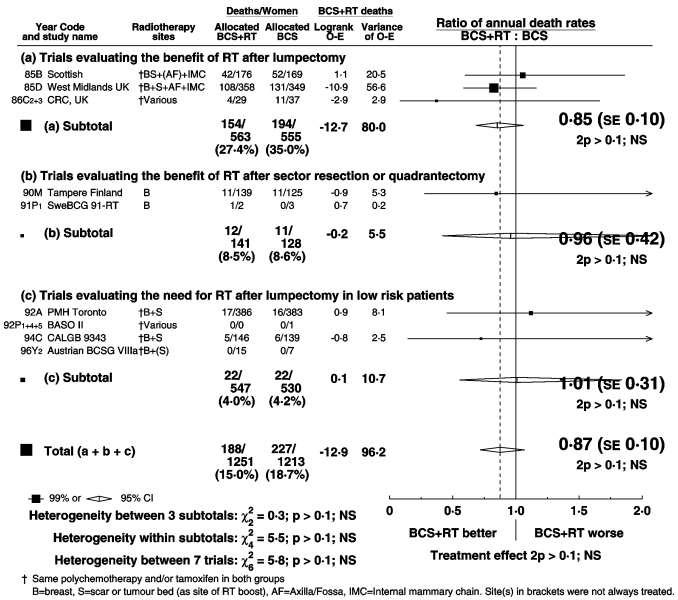
Webfigure 12c. Effect of radiotherapy after breast-conserving surgery on any (locoregional or distant) first recurrence, breast cancer mortality and all-cause mortality in 2464 women with unknown pathological nodal status disease. Event rate ratios, one line per trial.

Any first recurrence



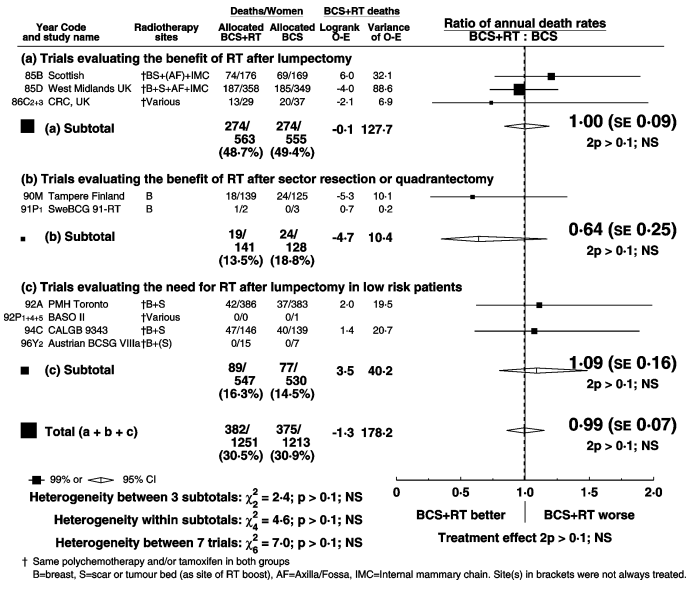
† Same polychemotherapy and/or tamoxifen in both groups
B=breast, S=scar or tumour bed (as site of RT boost), AF=Axilla/Fossa, IMC=Internal mammary chain. Site(s) in brackets were not always treated.

Breast cancer mortality



† Same polychemotherapy and/or tamoxifen in both groups
B=breast, S=scar or tumour bed (as site of RT boost), AF=Axilla/Fossa, IMC=Internal mammary chain. Site(s) in brackets were not always treated.

Any death



† Same polychemotherapy and/or tamoxifen in both groups
B=breast, S=scar or tumour bed (as site of RT boost), AF=Axilla/Fossa, IMC=Internal mammary chain. Site(s) in brackets were not always treated.

Webfigure 13. EBCTCG collaborators, listed alphabetically by institution and then alphabetically by name.

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ATLAS Trial Collaborative Study Group, Oxford, UK—V Collett, C Davies, A Delmestri, J Sayer.
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