Contents of Lancet website material for EBCTCG local therapy comparisons (also available, with powerpoints of selected graphs, on www.ctsu.ox.ac.uk/projects/ebctcg)

Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005; 366: 2087-2106.

- Webtables 1-2 Brief design details of every separate trial, including anatomic sites treated surgically, radiotherapy fields and doses, and concurrent chemotherapy and endocrine therapy
- Webtable 3 Comparisons that involved little (<10%), or substantial (>10%), absolute reduction in 5-year local recurrence risk 15-year outcome
- Webtable 4 Proportional breast cancer mortality reductions in years 0-4 and 5+, by absolute reduction in 5-year local recurrence risk (calculated by subtraction of logrank statistics for non-breast-cancer mortality from logrank statistics for any mortality)
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Webtable 1: Randomised trials comparing radiotherapy versus the same management without radiotherapy — treatment details

Type of surgery, yearBreast/chest wall (BW)code and study nameirradiation		Axilla and supraclavicular fossa (AF) irradiation	Internal mammary chain (IMC) irradiation	Boost irradiation to scar (S)	Common systemic chemoendocrine therapy
Breast-conserving surgery	(BCS), generally with axillary clear	rance			
76B NSABP B-06	50 Gy (2 Gy/f) c or m	None	None	None	pN+: FMel
81L Uppsala-Örebro	54 Gy (2 Gy/f) c or m	None	None	None	None
82Y St George's	54 Gy md (2 Gy/f) m	0-50 Gy (2 Gy/f) m	None	None	ER+: tamoxifen; ER-: CMF
84P Ontario COG	40 Gy (2.5 Gy/f) c	None	None	12.5 Gy (2.5 Gy/f) c	None
85B Scottish	50 Gy (2-2.5 Gy/f) m	0-45 Gy (2.3 Gy/f) m	50 Gy (2-2.5 Gy/f) m	10-30 Gy (2-3 Gy/f) o,e or i	ER+: tamoxifen; ER-: CMF
85D West Midlands	40-50 Gy md (2-2.7 Gy/f) c	40-50 Gy (2-2.7 Gy/f) c	40-50 Gy md (2-2.7 Gy/f) c	15 Gy (3 Gy/f) e or c	Tamoxifen
86C CRC UK	Various	Various	Various	Various	None required
87R INT Milan 3	50 Gy (2 Gy/f) c or m	None	None	10 Gy (2 Gy/f) o or e	pN+: CMF or tamoxifen
89L NSABP B-21	50 Gy (2 Gy/f) c or m	None	None	10 Gy (2 Gy/f) o	Tamoxifen
91P Swedish BCCG	48-54 Gy (1.9-2.2 Gy/f) m	None	None	None	None required
Mastectomy with axillary cl		None	None	None	None required
		FF Cy (u Cy/f) a	FF Cyr (yr Cyr/f) c	None	None
62B Berlin-Buch ABC	55 Gy (u Gy/f) c 25-41 Gy (1.3-2.1 Gy/f) o	55 Gy (u Gy/f) c 36 Gy (1.8 Gy/f) o	55 Gy (u Gy/f) c	None None	None Overige irrediction
64B Oslo X-ray			25-41 Gy (1.3-2.1 Gy/f) o		Ovarian irradiation
64E Oslo Co-60	None	50 Gy de (2.5 Gy/f) c	50 Gy de (2.5 Gy/f) c	None	Ovarian irradiation
69A Heidelberg XRT	None	65 Gy (2.2-2.7 Gy/f) c	65 Gy (2.2-2.7 Gy/f) c	None	None
71B Stockholm A	45 Gy (1.8 Gy/f) c or e	45 Gy de (1.8 Gy/f) c	45 Gy (1.8 Gy/f) c or e	None	None
71D SASIB	0-45 Gy (4.5 Gy/f) o or c	45-60 Gy (2-4.5 Gy/f) c	40-60 Gy (2-4 Gy/f) c or e	None	None
73C Mayo 70-56-32	0-50 Gy (2.1 Gy/f) m	50 Gy de (2.1 Gy/f) m	50 Gy de (2.1 Gy/f) m	None	CFP vs not
73E INT Milan 1	None	40-45 Gy (1.8-2 Gy/f) c or m	40-45 Gy (1.8-2 Gy/f) c or m	None	None
74D DFCI Boston	45 Gy (2.3 Gy/f) c or m	45 Gy (2.3 Gy/f) c or m	None	None	Either AC 6 vs AC 12 cycles, or CMF vs MF
74Q Piedmont OA	0-45 Gy (1.5 Gy/f) u	45 Gy (1.5-2.8 Gy/f) u	45 Gy (1.5-2.8 Gy/f) u	None	Mel vs CMF
76A SECSG 1	50 Gy (2 Gy/f) m	50 Gy (2 Gy/f) m	50 Gy (2 Gy/f) m	None	CMF
76C Glasgow	37.8 Gy (2.5 Gy/f) o	37.8 Gy (2.5 Gy/f) o	37.8 Gy (2.5 Gy/f) o	None	CMF
77J MD Ander. 7730B	45-50 Gy (1.8-1.9 Gy/f) c	45-50 Gy (1.8-1.9 Gy/f) c	45-50 Gy (1.8-1.9 Gy/f) c	12 Gy (u Gy/f) u	BCG+FAC vs FAC
78A S Swedish BCG	38 Gy (1.9 Gy/f) e,o,m or c	48-60 Gy (2.4 Gy/f) c or m	48 Gy (2.4 Gy/f) e, c or m	None	Premen: C; Postmen: tamoxifen
78B Toronto-Edmont.	None	40 Gy de (2.5 Gy/f) c	40 Gy de (2.5 Gy/f) c	None	CMF+ovarian irradiation+P±BCG
78G BCCA Vancouver	40 Gy (2.5 Gy/f) c or m	37.5 Gy de (2.3 Gy/f) c or m	37.5 Gy (2.3 Gy/f) c or m	None	CMF+ovarian irradiation+P vs CMF
78Q Düsseldorf U.	40 Gy (2 Gy/f) c	40 Gy (2 Gy/f) c	40 Gy (2 Gy/f) c	None	LMF
79F Coimbra	36 Gy (3 Gy/f) o or m	39-45 Gy (3.3-3.8 Gy/f) m	39 Gy (3.3 Gy/f) m	None	AC
79G Metaxas Athens	45-60 Gy (2 Gy/f) m	50 Gy (2 Gy/f) m	50 Gy (2 Gy/f) m	None	Various
80S Helsinki	45 Gy (3 Gy/f) c	45 Gy (3 Gy/f) c	30 Gy (3 Gy/f) c	None	CAFt
80W NSABC Israel	46-50 Gy (2 Gy/f) c or m	46-50 Gy (2 Gy/f) c or m	40 Gy (2 Gy/f) c or m	None	CMF
82B Danish BCG 82b pre	48-50 Gy (2-2.2 Gy/f) e	48-50 Gy (2-2.2 Gy/f) m	48-50 Gy (2-2.2 Gy/f) e	None	CMF
82C Danish BCG 82c post	48-50 Gy (2-2.2 Gy/f) e	48-50 Gy (2-2.2 Gy/f) m	48-50 Gy (2-2.2 Gy/f) e 48-50 Gy (2-2.2 Gy/f) e	None	Tamoxifen
82Q ECOG EST3181	46 Gy (2 Gy/f) c or m	46-50 Gy (2 Gy/f) c or m	46 Gy (2 Gy/f) c, m or e	None	CAF+H+tamoxifen
84A GBSG 03 Germany	50 Gy (2 Gy/f) m	50 Gy (2 Gy/f) m	44 Gy (1.8 Gy/f) m	None	CMF
	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	50 Gy (2 Gy/I) III	44 Gy (1.8 Gy/l) III	None	CIMIF
Mastectomy with axillary sa			40 0 (0 0 0 (6) -	Nana	News
73A Wessex	46 Gy (2.3 Gy/f) c	55 Gy (2.5 Gy/f) c	46 Gy (2.3 Gy/f) c	None	None
74B Edinburgh I	45 Gy md (4.5 Gy/f) m	42.5 Gy md (4.3 Gy/f) m	None	None	None
85F Nottingham	45 Gy (3 Gy/f) u	45 Gy (3 Gy/f) u	None	None	Various
86C CRC UK	Various	Various	Various	Various	None required
Mastectomy alone					
61H NSABP B-03	None	35-45 Gy (1.8-2.3 Gy/f) o or c	35-45 Gy (1.8-2.3 Gy/f) o or c	None	None
70A Manchester RBS1	30-37 Gy (2-2.5 Gy/f) o	37-40 Gy (2.5-2.7 Gy/f) o or m	37-40 Gy (2.5-2.7 Gy/f) o or m	None	Ovarian ablation
70B Kings/Cambridge	28.5-46 Gy (1.5-3.2 Gy/f) o or s	28.5-46 Gy (1.5-3.2 Gy/f) o or s	28.5-46 Gy (1.5-3.2 Gy/f) o or s	None	None
71C NSABP B-04	50 Gy (2 Gy/f) s	45-50 Gy de (1.8-2.0 Gy/f) s	45 Gy de (1.8 Gy/f) s	None	None
78D Scottish D	37-45 Gy (2.3-3.7 Gy/f) o or m	38.4-45.9 Gy (2.3-3.8 Gy/f) o or m	40-45 Gy (2.3-2.7 Gy/f) o or m	None	Tamoxifen vs not
85Z Tokyo CIH PS	None	42-48 Gy (2-3 Gy/f) u	42-48 Gy (2-3 Gy/f) u	None	CMF
88U Tokyo CIH CZ	None	42-48 Gy (2-3 Gy/f) u	42-48 Gy (2-3 Gy/f) u	None	CMF

c=cobalt-60, e=electron, i=iridium-192, m=megavoltage (linear accelerator), o=orthovoltage, s=supervoltage, u=unknown, de=dose at depth (of nodes), f=fraction, Gy=Gray (intended dose), md=maximum tissue dose. A=doxorubicin (adriamycin), BCG=bacillus Calmette-Guérin, C=cyclophosphamide, ER=oestrogen receptor, F=fluorouracil, Ft=futrafur, H=halotestin, L=chlorambucil, M=methotrexate, Mel=melphalan, P=prednisone, (p)N+=(pathologically) node-positive, (p)N-=(pathologically) node-negative, vs=versus (at random), ±=randomising the addition of.

Webtable 2: Randomised trials comparing more extensive surgery versus less extensive surgery — treatment details

Comparison, year Surgery 1 Surgery 2 code and study name Active arm Control arm			Local recurrence definition	Notes (including common RT or systemic therapy)
Internal mammary chain	removal (both groups v	vith mastectomy an	d axillary clearance)	
63D Internat. Co-op	M+AC+Pec+IMNC	M+AC+Pec	Parasternal, axilla or supraclavicular	Data from Lima and Warsaw centres not avaliable.
73D Chicago U.	M+AC+Pec+IMNC	M+AC+Pec	Within operative field (supraclavicular taken as distant)	Endocrine or chemotherapy to ~20%.
Pectoral muscle removal	(both groups with mas	tectomy and axillar	y clearance)	
67C Groote Schuur	M+AC+Pec	M+node picking	Scar, skin flap, axilla or supraclavicular	Node picking = local excision of enlarged nodes. Trial terminated after 3 years due to high rate of axillary recurrence.
69D Northwest UK	M+AC+Pec	M+AC	Skin flap, related chest wall or axilla	
76Q Berlin-Buch	M+AC+Pec	M+AC	Local tumour relapse	Unknown if adjuvant treatment given.
91R CAMS China	M+AC+Pec	M+AC	Recurrences not generally collected	RT to ~50%, CMF to ~90%, tamoxifen to ~70%.
Axillary clearance in N+v	e disease (both groups	with mastectomy a	ind radiotherapy)	
58B Addenbrooke's	M+AC+Pec+(IMNC)	M+(AS)	Unspecified	Some axilla nodes removed in surgery 2, but no block dissection. RT (BW+AF+IMC).
72A WSSA Glasgow	M+AC	Μ	Scar, chest wall, supraclavicular or axilla (enlarged nodes)	RT (BW).
Axillary clearance in N-ve	e disease (both groups	with mastectomy a	nd no axillary radiotherapy)	
67B Cardiff N-	M+AC+(Pec)	M+AS	Chest wall, axilla, supraclavicular or IMN	Used only the 122 N- (as in the 78 N+ there was more RT in surgery 1).
67C Groote Schuur	M+AC+Pec	Μ	Scar, flap, axilla or supraclavicular	(
71C NSABP B-04	M+AC+Pec	Μ	Chest wall, scar, axilla, supra- and subclavicular or IMN	Axilla recurrences were excluded in some other reports. Some in surgery 2 (68/384) got AC after local recurrence.
72A WSSA Glasgow	M+AC	Μ	Scar, chest wall, supraclavicular or axilla (enlarged nodes)	RT (BW)
*80Y Edinburgh N-	M+AC	M+AC1	Chest wall, axilla, or supraclavicular	Some women randomised into other trials.
Mastectomy versus brea	st-conserving surgery (both groups with a	xillary clearance and no radiotherapy)	
76B NSAPB B-06	M+AC	BCS+AC1+2	Residual breast, chest wall, scar, axilla, supraclavicular or IMN	Residual breast recurrences were excluded in some other reports. Clear tissue margins required in surgery 2 (if not [64/719], M).
Mastectomy versus breas	st-conserving surgery (both groups with a	xillary clearance and radiotherapy)	
82A CRC, ŬK	M+AC1	BČS+ÁC1	Not specified	No information on tissue margin requirement available. RT (BW+AF+IMC) compulsory, except for last 20 pN- in surgery 1. Optional tamoxifen \pm chemotherapy.
83J Danish BCG 82TM (high-risk group)	M+AC1+2	BCS+AC1+2	Residual breast, chest wall or axilla	Clear tissue margins required in surgery 2. RT (BW+AF+IMC) in surgery 1 and 2, but different technique. Premen: CMF, postmen: tamoxifen.

AC=axillary clearance (AC1, 2 or 3, shows levels cleared), AS=axillary sampling, BCS=breast-conserving surgery, IMN(C)=internal mammary node (clearance), M=mastectomy, Pec=pectoral muscle excision. Treatments in parentheses () were given to only some women; parentheses after RT denote irradiated sites. Other abbreviations defined in footnote to webtable 1.

* Note added in proof: 80Y Edinburgh N- (8/123 vs 9/116 local recurrences) should have been in webfigure 9a, not 10a, and not in Table 4 or webfigure 7. Correction, however, would make no material difference.

Webtable 3: Randomised trials comparing extensive surgery versus less extensive surgery plus radiotherapy — treatment details

Comparison, year code and study name	Surgery 1 Active arm	Surgery 2 Control arm			Local recurrence definition	Notes (including common RT or systemic therapy)
Nodal surgery versus ra	diathoropy					
†51A Copenhagen	M+AC+ Pec+IMNC	М	BW: 42-45 Gy md (2.3-2.5 Gy/f) o AF: 40 Gy (2.2 Gy/f) o	IMC: 28-30 Gy (1.6-1.7 Gy/f) o S: None	Parasternal, chest wall, axilla or supraclavicular	Very high local recurrence rates in both arms: webfigure 10.
†64D SE Scotland	M+AC+Pec	М	BW: 45 Gy (4.5 Gy/f) m AF: 42.5 Gy md (4.3 Gy/f) m	IMC: 45 Gy (4.5 Gy/f) m S: None	Skin, axilla, supraclavicular or IMN	Age <60: ovarian ablation.
†70A Manchester RBS2	M+AC+(Pec)	Μ	BW: 30-37 Gy (2-2.5 Gy/f) o AF: 37-40 Gy (2-2.7 Gy/f) o or m	IMC: 37-40 Gy (2.5-2.7 Gy/f) o or m S: None	Axilla, supraclavicular or chest wall	Premen: ovarian ablation.
71C NSABP B-04	M+AC+Pec	Μ	BW: 50 Gy (2 Gy/f) s AF: 45 Gy (1.8 Gy/f) s	IMC: 45 Gy (1.8 Gy/f) s S: None	Chest wall, scar, supra- and subclavicular, IMN or axilla	
72A WSSA Glasgow	M+AC	Μ	BW: 42 Gy (2.1 Gy/f) o AF: 42 Gy (2.1 Gy/f) c or m	IMC: None S: None	Scar, chest wall, supraclavicular or axilla (enlarged nodes)	RT (BW).
72H CMN Mexico	M+AC+Pec	Μ	BW: u AF: u	IMC: u S: u	Unknown	Unknown if adjuvant therapy given.
76Q Berlin-Buch	M+AC+ Pec+IMNC	M+AC+Pec		IMC: u S: None	"Local relapse"	Only women with medial or central tumours were entered, and all got IMN biopsy.
*80Y Edinburgh N+	M+AC	M+AC1	BW: u Gy (u Gy/f) m AF: 40-42.5 Gy (2-2.1 Gy/f) m	IMC: u Gy (u Gy/f) m S: None	Chest wall, axilla or supraclavicular	Some women randomised into other trials. Node-negative in webtable 2.
82K Ins.Curie Paris	BCS+AC	BCS	BW: 55 Gy (1.8 Gy/f) c AF: 50 Gy (1.7 Gy/f) c	IMC: 45 Gy (1.5 Gy/f) c S: 10-15 Gy (u Gy/f) c	Breast, axilla or supraclavicular	Medial or central: AC vs RT (AF), with other RT (BW+S+IMC) to both. Lateral or tail: AC vs RT (AF+IMC), with other RT (BW+S) to both. Postmen ER+: tamoxifen.
Mastectomy with axillary	v clearance and	radiotherapy	versus breast-conserving surger	y without axillary clearance plus mo	re extensive radiotherapy	
†61E Guy's London	M+AC+Pec	BCS	BW: 30-38 Gy (2.3-3 Gy/f) m AF: 30 Gy (3 Gy/f) o	IMC: 30-38 Gy (2.3-3 Gy/f) m S: None	Skin, axilla, breast, supraclavicular or IMN	RT (AF+IMC). Axillary radiation dose low, axillary recurrence rate high after RT without AC. First half of trial: thiotepa.
Mastectomy versus brea	ast-conservina s	uraerv plus ra	adiotherapy, both with axillary cle	earance		
72G IGR Villejuif	M+AC1+ (AC2+3)	BCS+AC1	BW: 45 Gy (2.5 Gy/f) c AF: N-: none, N+: see note	IMC: N-: none, N+: see note S: 15 Gy (2.5 Gy/f) c or e	Breast, chest wall or lymph nodes	N-: AC1 only. pN+: AC \pm extra RT (AF+IMC).
73E INT Milan 1	M+AC+Pec	BCS+AC	BW: 50 Gy (2 Gy/f) c or m AF: N-: none, N+: see note	IMC: N-: none, N+: see note S: 10 Gy (u Gy/f) o	Breast: recurrence or 2nd 1ry Regional: unknown	pN+ 1st half: \pm extra RT (AF+IMC). pN+ 2nd half of trial: CMF.
76B NSABP B-06	M+AC	BCS+ AC1+2	BW: 50 Gy (2 Gy/f) u AF: None	IMC: None S: None	Scar, breast, chest wall, axilla, supraclavicular or IMN	Breast recurrences excluded in some other reports. pN+: MF.
79J NCI Bethesda	M+AC	BCS+AC	BW: 48.6 Gy (1.8 Gy/f) m AF: 0-45 Gy de (1.8 Gy/f) m	IMC: 0-48.6 Gy (1.8 Gy/f) m S: 15-20 Gy (u Gy/f) e or i	Breast, chest wall, axilla, supraclavicular or IMN	Breast recurrences excluded in some other reports. Surgery 2, medial or pN+: RT (IMC), pN+: RT (AF). Postmen pN+ (1985-87): tamoxifen.
80G EORTC 10801	M+AC+(Pec)	BCS+AC	BW: 50 Gy (2 Gy/f) u AF: 50 Gy (2 Gy/f) u	IMC: 50 Gy de (2 Gy/f) u S: 25 Gy (u Gy/f) e or i	No information available	Central, medial or pN+: RT (IMC). Residual tumour after surgery: RT (BW+AF).
83J Danish BCG 82TM (low-risk group)	M+AC	BCS+AC	BW: 48-50 Gy (2-2.2 Gy/f) m or e AF: None	IMC: None S: 10-25 Gy (2 Gy/f) e	Breast, chest wall or axilla	
84A GBSG 01 Germany	BCS+AC1+2 and then M	BCS+ AC1+2	BW: 50 Gy (2 Gy/f) c or m AF: 50 Gy de (2 Gy/f) c or m	IMC: 50 Gy de (2 Gy/f) m or e S: 10-12 Gy (2-3 Gy/f) e	"Local", axilla or supraclavicular	Central, medial: RT (IMC+supraclavicular).

BW=breast or chest wall, M= mastectomy. Other abbreviations (and asterisked footnote) as in webtables 1 and 2.

† The local recurrence rate after RT was relatively high with the RT regimens actually given in the four oldest of these trials (51A, 61E, 64D, 70A), particularly in the earliest two of these (which started in 1951 and 1961).

Webtable 4: Proportional breast cancer mortality reductions in years 0-4 and 5+, by absolute reduction in 5-year local recurrence risk (with the 24 types of local treatment comparison categorised into those producing <10%, 10-20%, or >20% reduction) Logrank statistics are given for any death, for mortality from causes other than breast cancer and, by subtraction, for breast cancer mortality

Active	Il woman-years Control years 0-4 after 1726/ 36 839	O-E		Ratio, active/ _ control (SE)		s/years ecurrence Control	<u>st cancer*</u> Statis O-E	stics V	Ratio, active/ control _ (SE)	Statist O-E	tics** V	Ratio, active/ control (SE)
(a) Mortality in 1680/ 36 574 2354/	years 0-4 after 1726/ 36 839	r randomis	ation		Active	Control	0-Е	V		O-E	V	
1680/ 36 574 2354/	1726/ 36 839											
36 574 2354/	36 839	-21.2	774 5									
	0.4004		774.5	0.97 (0.04)	165/ 30 618	158/ 30 862	2.8	78.7	1.04 (0.11)	-23.9	695.8	0.97 (0.04)
	2482/ 43 699	-50.6	1070.0	0.95 (0.03)	244/ 35 444	201/ 32 063	16.9	101.9	1.18 (0.11)	-67.6	968.2	0.93 (0.03)
677/ 10 667	729/ 10 856	-21.7	296.0	0.93 (0.06)	64/ 8736	650/ 7251	-3.7	26.9	0.87 (0.18)	-18.0	269.1	0.93 (0.06)
4711/ 90 816	4937/ 91 385	-93.5	2140.5	0.96 (0.02)	473/ 74 793	424/ 70 172	16.0	207.5	1.08 (0.07)	-109.5	1933.1	0.94 (0.02)
(b) Mortality in	n years 5+ afte	er randomis	sation									
2301/ 50 812	2305/ 51 305	-3.2	1043.3	1.00 (0.03)	749/ 41 975	708/ 41 488	10.4	330.5	1.03 (0.06)	-13.6	712.8	0.98 (0.04)
2779/ 59 993	2849/ 56 977	-84.7	1212.4	0.93 (0.03)	885/ 49 440	692/ 41 416	54.4	327.5	1.18 (0.06)	-139.1	884.9	0.85 (0.03)
795/ 16 509	854/ 15 458	-43.8	357.6	0.88 (0.05)	232/ 13 373	174/ 9687	6.5	84.8	1.08 (0.11)	-50.3	272.8	0.83 (0.06)
5875/ 127 310	6008/ 123 732	-131.7	2613.3	0.95 (0.02)	1866/ 104 787	1574/ 92 587	71.3	742.8	1.10 (0.04)	-203.0	1870.5	0.90 (0.02)
10 586/ 218 446	10 945/ 215 451	-225.2	4753.8	0.95 (0.01)	2339/ 179 852	1998/ 163 029	87.3	950.3	1.10 (0.03)	-312.5	3803.6	0.92 (0.02)
(677/ 10 667 4711/ 90 816 b) Mortality in 2301/ 50 812 2779/ 59 993 795/ 16 509 5875/ 127 310	677/ 729/ 10 667 10 856 4711/ 4937/ 90 816 91 385 b) Mortality in years 5+ after 2301/ 2305/ 50 812 51 305 2779/ 2849/ 59 993 56 977 795/ 854/ 16 509 15 458 5875/ 6008/ 127 310 123 732	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	43 58043 69933 44432 063 $677/$ $729/$ -21.7 296.0 $0.93 (0.06)$ $64/$ $650/$ $10 667$ $10 856$ -21.7 296.0 $0.93 (0.06)$ 8736 7251 $4711/$ $4937/$ 93.5 2140.5 $0.96 (0.02)$ $473/$ $424/$ $90 816$ $91 385$ -93.5 2140.5 $0.96 (0.02)$ $473/$ $424/$ $90 816$ $91 385$ -93.5 2140.5 $0.96 (0.02)$ $473/$ $424/$ $50 816$ $91 385$ -3.2 1043.3 $1.00 (0.03)$ $749/$ $708/$ $50 812$ $51 305$ -3.2 1043.3 $1.00 (0.03)$ $749/$ $41 488$ $2779/$ $2849/$ -84.7 1212.4 $0.93 (0.03)$ $885/$ $692/$ $59 993$ $56 977$ -84.7 1212.4 $0.93 (0.03)$ $885/$ $692/$ $16 509$ $15 458$ -43.8 357.6 $0.88 (0.05)$ $232/$ $174/$ $16 509$ $15 458$ -43.8 357.6 $0.88 (0.05)$ $232/$ $174/$ $127 310$ $123 732$ -131.7 2613.3 $0.95 (0.02)$ $1866/$ $1574/$ $10 586/$ $10 945/$ -225.2 4753.8 $0.95 (0.01)$ $2339/$ $1998/$ $128 446$ $215 451$ -225.2 4753.8 $0.95 (0.01)$ $2339/$ $1998/$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$

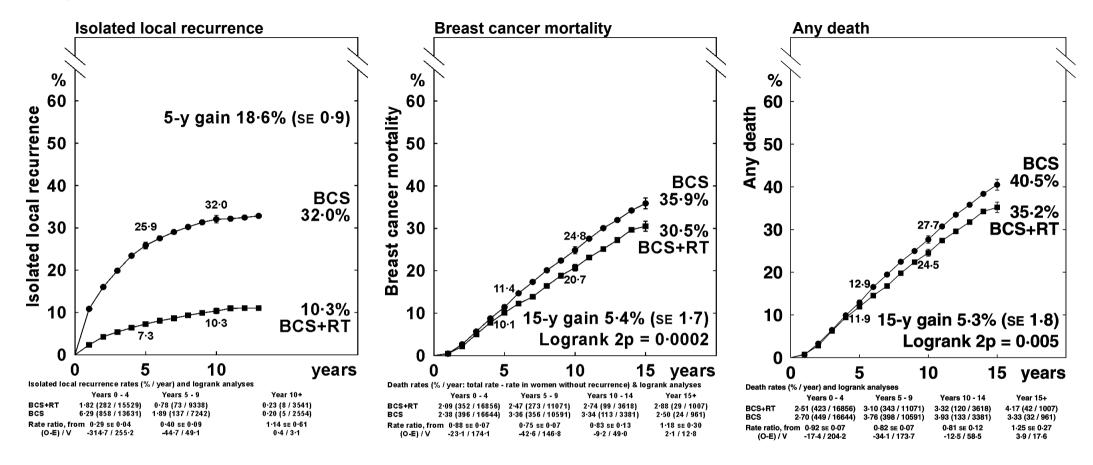
O-E is the logrank Observed minus Expected, V is its variance, and the estimated ratio, active versus control, of the annual mortality rates is exp([O-E]/V).

* Defined as mortality from all causes before breast cancer recurrence.

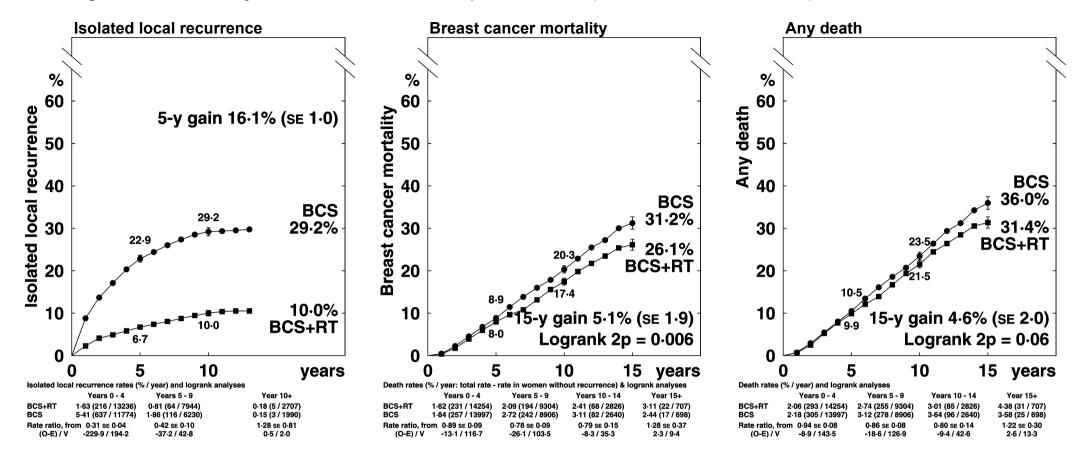
** Statistics for breast cancer mortality are calculated by "logrank subtraction," ie, subtraction of the statistics for mortality from causes other than breast cancer (O-E and V in the table above) from the corresponding statistics for any death.

Note added in proof: A paper on possible ways of improving logrank subtraction is being prepared by NSABP statistician John Byrant (bryant@nsabp.pitt.edu).

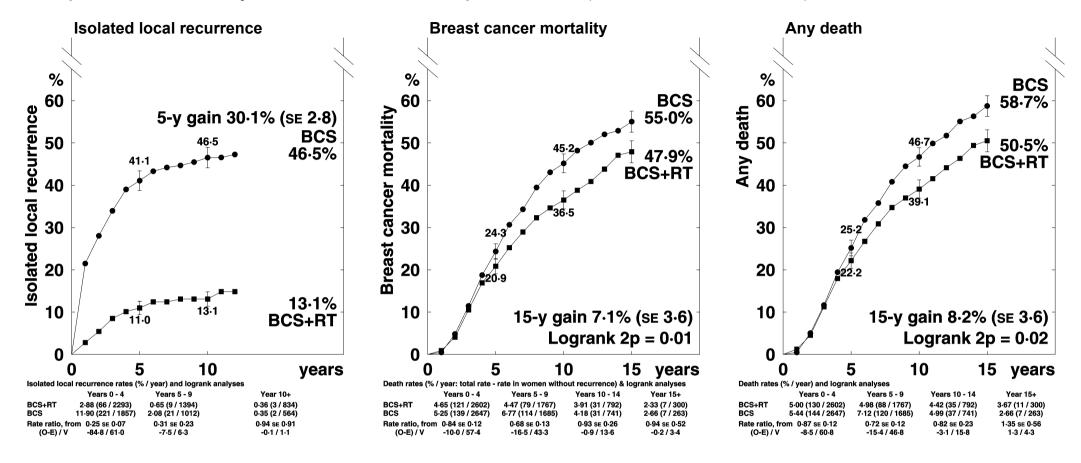
Webfigure 1a: Radiotherapy after breast-conserving surgery, generally with axillary clearance (BCS±RT) in all women — 15-year outcome, where follow-up is sufficient (life-table curves: 7311 women, 17% with node-positive disease)



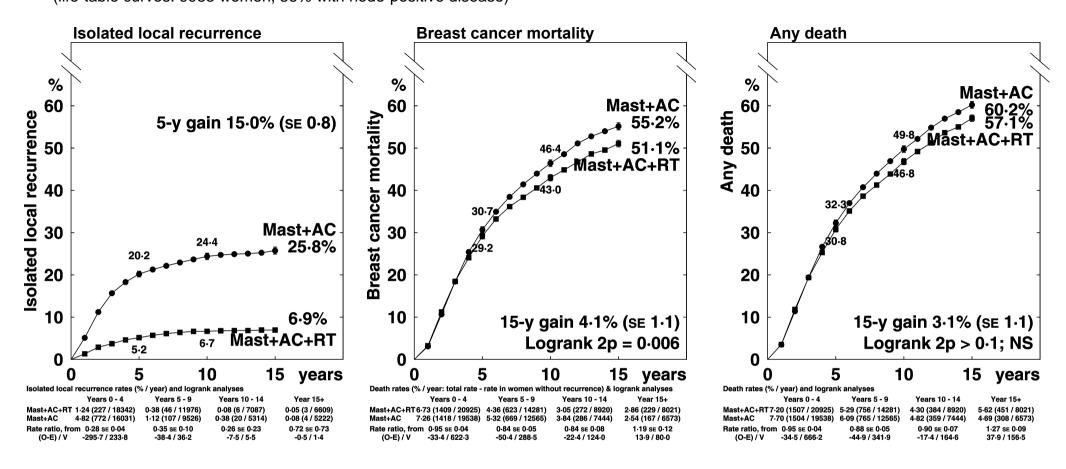
Webfigure 1b: Radiotherapy after breast-conserving surgery, generally with axillary clearance (BCS±RT) in women with node-negative disease — 15-year outcome, where follow-up is sufficient (life-table curves: 6097 women)



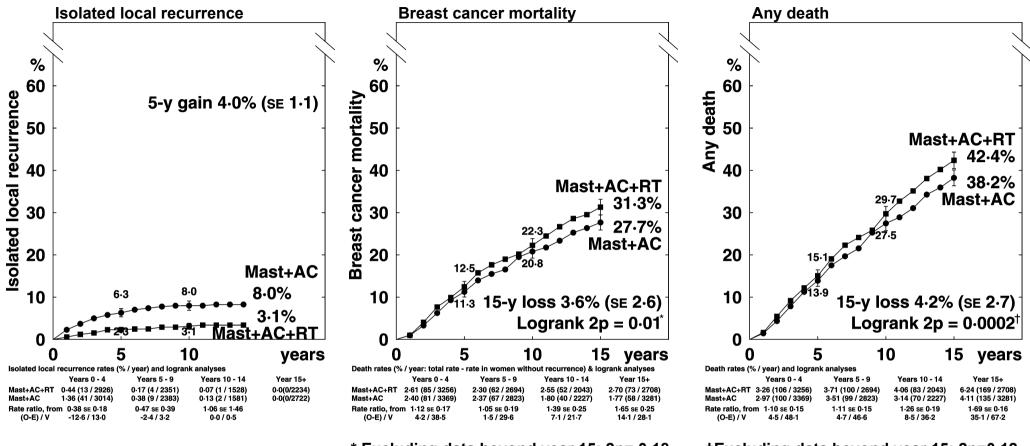
Webfigure 1c: Radiotherapy after breast-conserving surgery, generally with axillary clearance (BCS±RT) in women with node-positive disease — 15-year outcome, where follow-up is sufficient (life-table curves: 1214 women)



Webfigure 2a: Radiotherapy after mastectomy with axillary clearance (Mast+AC±RT) in all women — 15-year outcome (life-table curves: 9933 women, 86% with node-positive disease)



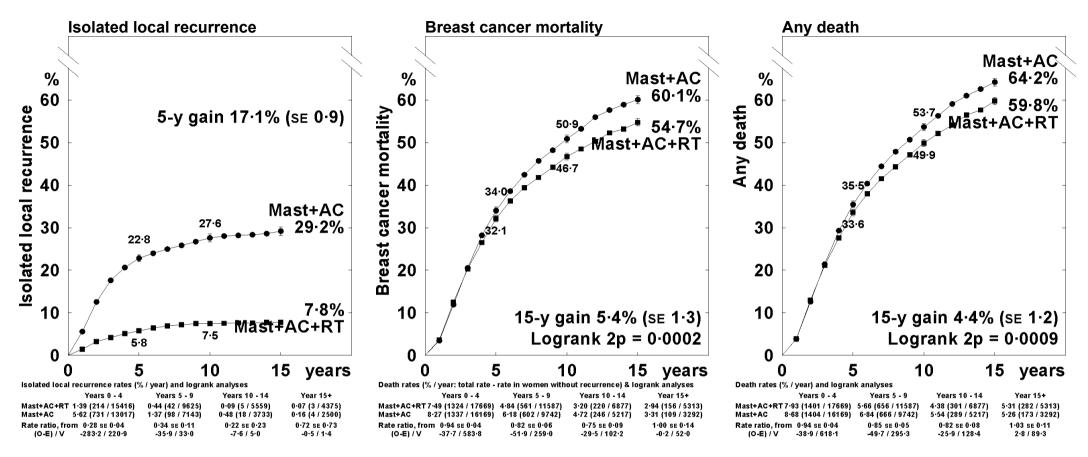
Webfigure 2b: Radiotherapy after mastectomy with axillary clearance (Mast+AC±RT) in women with node-negative disease — 15-year outcome (life-table curves: 1428 women)



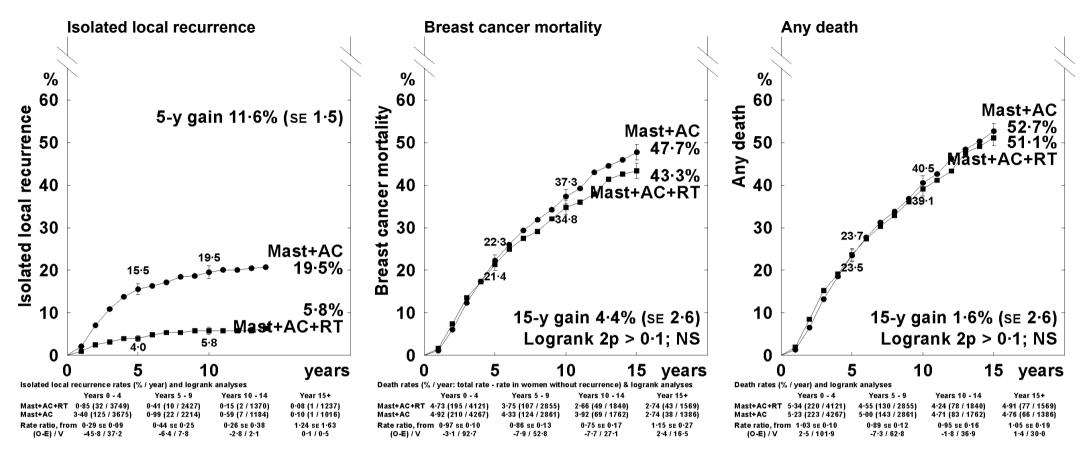
* Excluding data beyond year 15: 2p= 0.18

†Excluding data beyond year 15: 2p=0.12

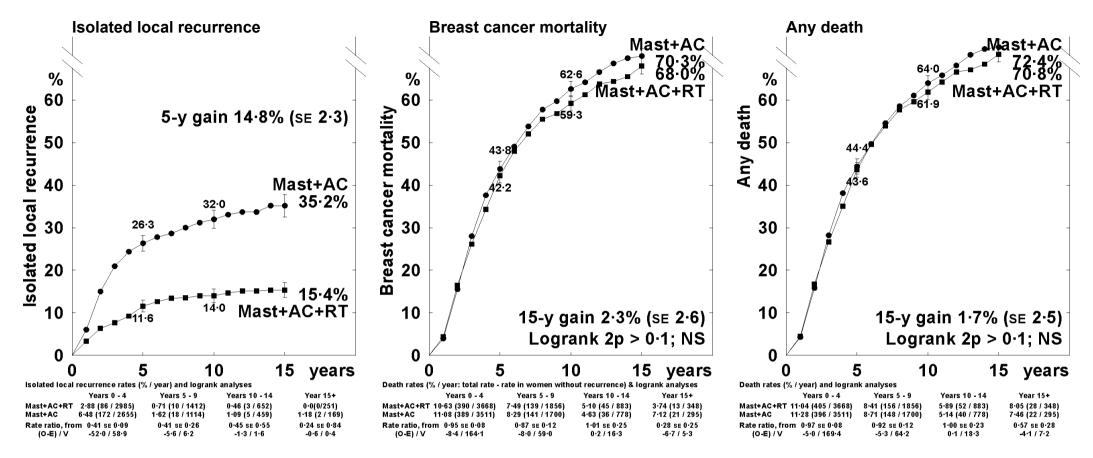
Webfigure 2c: Radiotherapy after mastectomy with axillary clearance (Mast+AC±RT) in all women with node-positive disease — 15-year outcome (life-table curves: 8505 women, many with the actual number of involved nodes unknown)



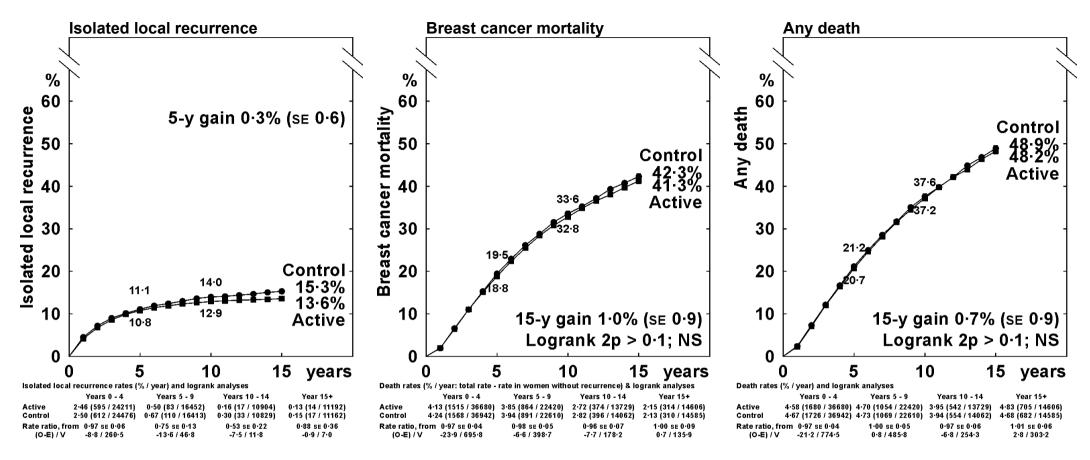
Webfigure 2d: Radiotherapy after mastectomy with axillary clearance (Mast+AC±RT) in women with 1-3 involved lymph nodes (pN1-3) — 15-year outcome (life-table curves:1890 women)



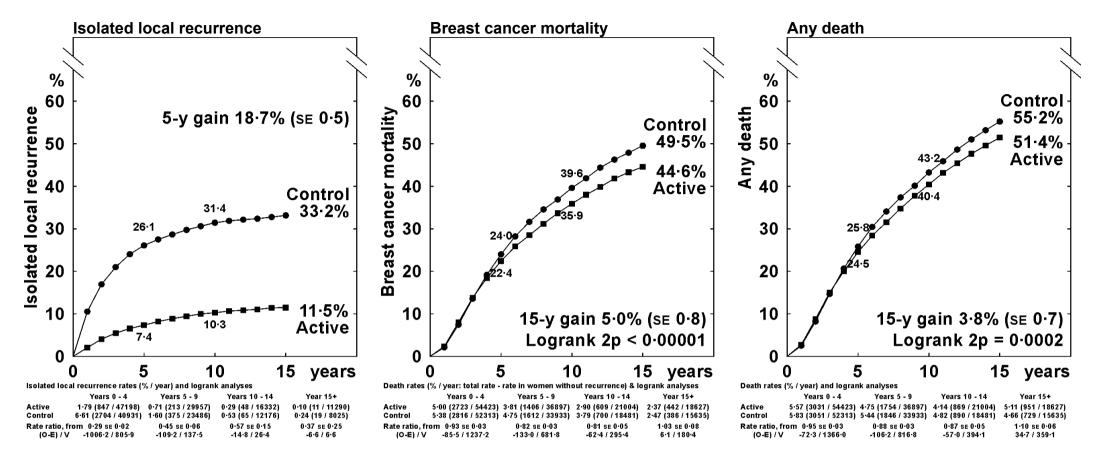
Webfigure 2e: Radiotherapy after mastectomy with axillary clearance (Mast+AC±RT) in women with 4 or more involved lymph nodes (pN4+) — 15-year outcome (life-table curves: 1868 women)



Webfigure 3a: 12 types of treatment comparison that yield <10% isolated local recurrence risk reduction — 15-year outcome (life-table curves: 16 804 women, 43% with node-positive disease)

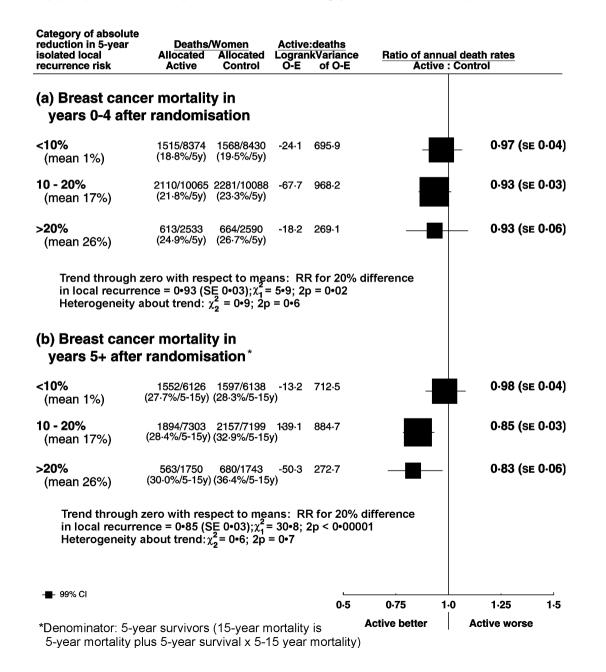


Webfigure 3b: 12 types of treatment comparison that yield >10% isolated local recurrence risk reduction — 15-year outcome (life-table curves: 25 276 women, 51% with node-positive disease)



Webfigure 4: Breast cancer mortality rate ratio by time since randomisation and by category of absolute reduction in 5-year local recurrence risk (from webtable 4)

Numerators are deaths after recurrence (from any cause), but percentages are life-table estimates of the probabilities of death just from breast cancer (in the absence of any other causes) during the first 5 years (upper part) or, for 5-year survivors, during years 5-15 (lower panel)



Webfigure 5: Homogeneity of 24 breast cancer mortality rate ratios, given the category (<10%, 10-20%, or >20%) of absolute reduction in 5-year local recurrence risk (numerators and denominators as in webfigure 4)



and treatment	Deaths/ Active (Logra	ve:deaths nk Variance	death rat			/Women Control	Logra	ve:deaths nk Variance	death	f annual rates
comparison			O-E	of O-E	Active:Con	trol	Active	Control	0-E	of O-E	Active:	Control
a) <10% (mean 1%) is reduction — early	heterog	geneity	/ betw	ence een						between 1 = 18·1; p	= 0-08	
12 comparisons: χ [*] -ve, Mast+AC ± RT (9 trials)	1 = 3·t 85/ 706	9; p = 1 81/ 722	4.2	38-5			187/ 597	165/ 622	22-8	79-4		
-ve, IMC removal vs. not, neither with RT (2 trials)	30/ 243	27/ 251	2.6	13-3			69/ 209	69/ 222	-1.0	30-9		
-ve, PecM removal vs. not, some with RT (2 trials)	91/ 1026	98/ 1034	-3-0	45-8	-		58/ 733	58/ 729	1.5	27-4		•
-ve, Mast+AC vs. BCS+AC, both with RT (2 trials)	7/ 59	5/ 60	0.9	2-9 —		• •	14/ 51	13/ 54	0-5	5-9 —		•
Hwe, Nodal surg vs. RT (6 trials)	214/ 1343	229/ 1329	-10-8	101-6			256/ 1040	285/ 1000	-24-5	121-9		
I-ve, Mast vs. BCS+RT, both with AC (7 trials)	123/ 1432	127/ 1438	-1.8	60-4			249/ 1233	266/ 1242	-1.5	122-8	-	—
I+ve, IMC removal vs. not, neither with RT (2 trials)	121/ 286	127/ 302	0.5	53-8			101/ 165	106/ 172	-1-3	43-8		
I+ve, PecM removal vs. not, some with RT (4 trials)	276/ 1444	301/ 1421	-14-5	134-1			154/ 930	172/ 880	-18-3	74.7	-	-
+ve, AC vs. not, in N+ve diseas both with some RT (2 trials)	e, 53/ 129	53/ 137	0.5	21.9			34/ 73	37/ 83	2-6	14-0		•
V+ve, Mast+AC vs. BCS+AC, both with RT (2 trials)	35/ 153	36/ 156	0-4	16-1			29/ 103	34/ 108	-2-7	14-1 -	•	
N+we, Nodal surg vs. RT (8 triats)	347/ 943	346/ 935	-4-1	145-5			245/ 557	212/ 548	10-8	101-5	-	-
N+ve, Mast vs. BCS+RT, both with AC (5 trials)	133/ 610	138/ 645	1.0	62-0	-		156/ 435	180/ 478	-2-1	76-1	_	
(a) Subtotal	1515/ 8374	1568/ 8430	-24-1	695-9	4	0-97 (se 0-04)	1552/ 6126	1597/ 6138	-13-2	712-5	¢	0.98 (se 0.04)
b) 10 - 20% (mean 15% reduction — early 7 comparisons: χ_6^2	hetero = 7.1:	geneit p = 0.3	cal re y betv 3	currence veen			Later h 7 comp	eterog parison	eneity s: χ ₆	/ between = 8-0; p = 0	•2	
N-ve, BCS ± RT (10 trials)	231/ 3071	3026	-13-1	116-7	-		284/ 2522	341/ 2455	-32-1	148-3		
+ve, Mast+AS ± RT (3 trials)	37/ 225	33/ 224	2.1	16-5	•	>	37/ 180	57/ 189	-6-9	20-6 –	•	
I-ve, Mast alone ± RT (5 trials)	327/ 1617	364/ 1701	-7.9	157-3	_		407/ 1174	440/ 1226	1.9	194-4	-	
I-ve, AC vs. not, in N-ve disease neither with axillary RT (4 trials)	572	134/ 582	4.4	59-0			118/ 392	154/ 409	-15-7	60-9	-	-
I-ve, Mast+AC vs. BCS alone + RT (Guy's Hospital)	43/ 241	64/ 233	-10-4	24-4	-		79/ 192	78/ 168	-3-5	34-3	-	
I+ve, Mast+AC ± RT (25 trials)	1324/ 4254	1403/ 4251	-37.7	583-8			937/ 2784	1059/ 2708	-81-6	413-1	-	
I+ve, Mast+AC vs. BCS alone + RT (Guy's Hospital)	21/ 85	26/ 71	-5-1	10-5 —	-	_	32/ 59	28/ 44	-1-2	13-1	•	
(b) Subtotal	2110/ 10065	2281/ 10088	3 ^{-67.7}	968-2	0	0-93 (se 0-03)	1894/ 7303	2157/_ 7199	139-1	884-7	¢	0-85 (se 0-03)
c) >20% (mean 26%) i reduction — early f 5 comparisons: χ_4^2	solated terog	d local jeneity o = 0.6	recur betw	rence een			5 comp	parison	s: χ ₄ ²	between = 1·9; p = 0	-8	
I-ve, Mast+AC vs. BCS+AC, neither with RT (NSABP B-06)	39/ 432	49/ 432	-4-5	21-3			92/ 379	108/ 373	-5-1	48-1	-	
I+ve, BCS ± RT (5 trials)	121/ 602	139/ 612	-10-0	57-4			117/ 438	152/ 437	-17.7	60-3	-	
+ve, Mast+AS ± RT (3 trials)	38/ 95	42/ 103	-1.7	16-7			25/ 51	29/ 57	-3-9	9.6 —	•	
+ve, Mast alone ± RT (6 trials)	350/ 1123	374/ 1156	-6-4	144-8	-		260/ 698	303/ 675	-15-5	118-5	-	_
I+ve, Mast+AC vs. BCS+AC, neither with RT (NSABP B-06)	65/ 281	60/ 287	4.4	28-9			69/ 184	88/ 201	-8-1	36-2	-	
(c) Subtotal	613/ 2533	664/ 2590	-18-2	269-1	\Leftrightarrow	0-93 (se 0-06)	563/ 1750	680/ 1743	-50-3	272.7	\Rightarrow	0-83 (se 0-06)
							*Done					
								ominato ar survi				

Sum of 6 heterogeneity test statistics: χ^{2}_{42} = 41·2; p=0·5

Footnote to webfigure 5

Contribution from different types of treatment

comparison — The evidence in webfigures 4 and 5 that breast cancer mortality after the first 5 years can be reduced comes almost entirely from the two categories of treatment comparison that involved absolute reductions of more than 10% (ie, 10-20% or >20%) in the 5-year isolated local recurrence risk. These two categories comprise 12 of the 24 types of treatment comparison, including 5 comparisons of post-mastectomy radiotherapy. These 5 comparisons yield in total a logrank O-E of -106.0 (-6.9 + 1.9 - 81.6 - 3.9 - 15.5) with variance 756.2, and hence a breast cancer mortality rate ratio of 0.87 SE 0.03, 2p=0.0001. This accounts for about two-thirds of the evidence on breast cancer mortality after the first 5 years. The remainder of the evidence comes in approximately equal measure from the 2 comparisons of post-BCS radiotherapy (O-E -49.8, variance 208.6, breast cancer mortality rate ratio 0.79 SE 0.06, 2p=0.0006) and from the 5 comparisons of more versus less surgery to the breast or axilla (or both) without effective radiotherapy to the conserved tissue (O-E -33.6, variance 192.6, breast cancer mortality rate ratio 0.84 SE 0.07, 2p=0.015). The breast cancer mortality rate ratios corresponding to these 3 groups of comparisons (0.87, 0.79 and 0.84) are not significantly different from each other, even though post-mastectomy radiotherapy and post-BCS radiotherapy usually prevent different types of local recurrence. (The 5 comparisons of more versus less surgery without effective control of local recurrence by radiotherapy included not only mastectomy versus BCS and axillary clearance versus not, both without radiotherapy, but also the Guy's trial of mastectomy with axillary clearance versus BCS+RT that began in 1961, in which the radiotherapy actually given still left a high risk of local recurrence not only around the conserved breast but also in the conserved axilla.)

Webfigure 6a: Radiotherapy after breast conserving surgery in node-negative disease — subgroup analyses

(event rate ratios for all three endpoints, with 5-year risks of local recurrence, 10-year breast cancer mortality risks and crude % for any death; subdivisions by entry age, tumour grade, tumour size, use of systemic therapy in both arms, ER status and time period)

Category	Events/woman-years Allocated Allocated LogrankVariand BCS+RT BCS O-E of O-E	e Ratio of annual event ra BCS+RT : BCS	tes Ca	ategory	Allocated BCS+RT	nan-years Allocated BCS	LogrankVa O-E of	riance	Ratio of annual de BCS+RT : BC	eath rates S	Category	Allocated BCS+RT	Women Allocated BCS	BCS+RT (Logrank\ O-E	Varlance	Ratio of annual BCS+RT : B	death rates ICS
	and $\chi_1^2 = 0.4$; 2p = 0.5)			i) Entry age (tre							(a) Entry age (tre						
Age < 50	128/7297 308/5547 -110-7 95-6 (10-9%/5y) (33-1%/5y)		od (o oo)	ge < 50	170/8682	181/8223	-10-8 8	3-7		0-88 (se 0-10)	Age < 50	179/876	192/852		88-4		- 0.86 (SE 0.10)
Age 50 - 59	78/7224 222/5923 -79-2 70-5		-33 (SE 0-07)	ae 50 - 59	(18-3%/10y) (132/8162	(21-4%/10y) 178/7662	-24-6 74	4-6		0.72 (se 0.10)	Age 50 - 59	(20·4%) 166/928	(22·5%) 199/899	-21-6	87.9		0·78 (se 0·09)
Age 60 - 69	(7·0%/5y) (22·7%/5y) 66/7556 190/6923 -64·3 61·1		9E (on 0 08)	ge 60 - 69	(15·0%/10y) ((19·7%/10y) 183/8448	-9-3 8	0.0	_	0-89 (se 0-11)	Age 60 - 69	(17·9%) 234/987	(22·1%) 235/1005	-2-0 1	112-0		
Age 70+	(4-2%/5y) (16-3%/5y) 13/1833 36/1626 -12-4 11-8	0	.35 (e= 0.18)	ge 70+	(16-6%/10y) (55/1992	(18-5%/10y) 56/1929	-0.6 2			0.00 (02.011)	Age 70+	(23·7%) 85/280	(23·4%) 78/270		37.8	T.	
	(2·6%/5y) (13·1%/5y)		A	ye 70+	(-%/10y)	(-%/10y)	-0-6 2:	9-8		0-98 (se 0-19)		(30.4%)	(28.9%)	2.7	0,0		1.07 (SE 0.17
b) Tumour grade	e (trend χ ₁ ² = 0·0; 2p = 0·9)		(h) Tumour grad	e (trend γ'	² = 0.1: 2	2n = 0·8)				(b) Tumour grad	e (trend	$\chi^2_{\star} = 0.1;$	2p = 0·7	7)		
ell differentiated/	18/2373 55/2309 -17-4 17-4 (4-3%/5y) (13-5%/5y)	0	-37 (SE 0-15)	ell differentiated		1 32/2789	3-0 1				Well differentiated	52/320 (16·3%)	47/337		23-6		■ 1.18 (se 0.2
loderately differentiated	68/4537 168/3944 -54-9 52-6 (9-2%/5y) (26-1%/5y)		-35 (SE 0-09)	oderately	(15·1%/10y) ((11·6%/10y)	-14.7 6	1.8		1.21 (SE 0.28) 0.79 (SE 0.11)	Moderately	146/609	(13·9%) 165/620	-12-1	73-9		- 0.85 (SE 0.1
oorly differentiated	75/4040 160/3135 -48-6 49-7 (12-1%/5y) (33-5%/5y)		-38 (se 0-09)	differentiated	(18-3%/10y) (differentiated Poorly	(24-0%) 190/499	(26·6%) 201/494		89-9		0.97 (se 0.1)
Grade unknown	124/12961 373/10625 -141-4 118-3 (5-0%/5y) (20-0%/5y)	0	-30 (se 0-05)	differentiated	(28·0%/10y) ((30·8%/10y)	-6-2 73			- 0.92 (SE 0.11)	differentiated Grade unknown	(38-1%) 276/1643	(40·7%) 291/1575	-19-7 1	105.0		0.86 (se 0.08
	(0.070009) (20.070009)		G	rade unknown	211/14141 (14·3%/10y) (-25-4 11	1.5		0-80 (SE 0-08)	Glade unknown	(16-8%)	(18.5%)	-19-7 1	33-3		0.00 (35 0.00
	(trend $\chi_1^2 = 4.4$; 2p = 0.04)		1-) Tumour circ	(trend v ²	- 0.4.0m	- 0 5)				(c) Tumour size (trend γ^2	= 0.8: 20	o = 0·4)			
- 20 mm (T1)	149/15603 462/13318 -173-6 143-4 (5-3%/5y) (20-4%/5y)	0		:) Tumour size (- 20 mm (T1)	(trend χ ₁ : 266/17401		-32-4 14			0.80 (se 0.07)	1 - 20 mm (T1)	349/2047	398/2038	-31.8 1	180-5	_	0-84 (se 0-07
:1 - 50 mm (T2)	95/4255 198/3378 -56-7 63-7 (14-2%/5y) (35-2%/5y)	- 0	•41 (SE U•08)		(14·9%/10y) ((17·5%/10y)				. ,	21 - 50 mm (T2)	(17-0%) 208/549	(19·5%) 223/563	-5.1 1	101-3		0.95 (SE 0.1)
50 mm (T3) or T4	0/9 3/38 -0-3 0-2 (-%/5y) (-%/5y)	0	·00 (se 1·74)	l - 50 mm (T2)	(28·4%/10y) (-10-4 8	6-4		0-89 (se 0-10)	> 50 mm (T3) or T4	(37·9%) 0/1	(39-6%) 3/8		0.4.		
arious/unknown	41/4042 93/3287 -32-1 31-2 (5-7%/5y) (17-3%/5y)	0	-36 (se 0·11) >	50 mm (T3) or T4	0/9 (–%/10y)	3/51 (-%/10y)	-0.6	0-4			. ,	(-%)	(-%)		•		
			Va	arious/unknown	80/4466 (16·5%/10y) (66/3976 (15·8%/10y)	3.5 34	4-1		1.11 (se 0.18)	Various/unknown	107/474 (22-6%)	80/417 (19·2%)	7.9	43-5		1.20 (SE 0.1
d) Chemo. (C) o 2p = 0⋅2)	r Tamoxifen (T) ($\chi_1^2 = 1.7;$										(d) Chemo. (C) o	r Tamovi	ifen (T) («	² - 0.8 ¹	· 2n - 0.4	۰ I	
oth with C or T	31/4814 106/4194 -42-7 32-2 (3-5%/5v) (13-6%/5v)		-27 (SE U-1U)	I) Chemo. (C) o							Both with C or T	84/676	71/640	1-0-0,		, 	
either with C or T	254/19096 650/15825 -223-9 206-8	0	-34 (se 0-04)	oth with C or T	60/5167 (10·9%/10y) (54/4861 (11·7%/10y)	-0.4 20	6-6		0-98 (se 0-19)	Neither with C or T	(12-4%) 580/2395	(11·1%) 633/2386	-35-4 2			1.03 (SE 0.1 0.88 (SE 0.0
	(7·7%/5y) (25·3%/5y)		N	either with C or T	455/21949 (19·0%/10y) (544/21401 (22·4%/10y)	-44-7 23	8-4	-#-	0-83 (se 0-06)		(24.2%)	(26.5%)	004 2			000 (02 0 0
e) ER status (ER-poor ve EE	R-positive: χ ₁ ² = 2·7; 2p = 0·1)		,		_		. ,				(e) ER status (EF	l-poor ve	s ER-posi	itive: χ^2_{\star}	= 0·7; 2r	o = 0·4)	
R-poor	57/3402 133/2965 -40-5 43-0		00 (0 10)	e) ER status (EF			•) = 0.4)	– 0.89 (se 0.13)	ER-poor	123/415	133/428		60-3		0.97 (se 0.1
R-positive	(12·3%/5y) (30·4%/5y) 118/10527 340/8372 -129·3 104·4		20 (a= 0.06)	R-poor	(22·3%/10y) (-6-1 5				ER-positive	(29·6%) 279/1276	(31·1%) 300/1232	-22-4 1	139-1		0-85 (SE 0-0
R-unknown	(6·0%/5y) (25·2%/5y) 110/9985 283/8683 -95-9 92-5		-35 (SE 0-06)	R-positive	212/12085 (16-9%/10y) (-27-4 11:	2-1		0·78 (se 0·08)	ER-unknown	(21.9%) 262/1380	(24·4%) 271/1366	-5-6 1	127-9		— 0.96 (se 0.0
- unknown	(5-9%/5y) (18-1%/5y)		55 (82 0.00) El	R-unknown	199/11026 (17·2%/10y) (-6-9 9	9.9		0.93 (se 0.10)		(19-0%)	(19-8%)				
) Period of follo 2p = 0·04)	w-up (trend $\chi_1^2 = 4.3;$		(f)) Period of follo	ow-up (tre	nd $\chi_1^2 = 0$	0∙0; 2p =	: 0.9)			(f) Period of folio Denominator: n						
ear 0	80/2953 254/2826 -88-9 71-6 (2-7%/y) (9-0%/y)		·29 (SE 0·07) Ye	ears 0-2	118/8904 (1·3%/y)	134/8748 (1·5%/y)	-8-7 6	0-1		0-87 (SE 0-12)	Years 0-2	159/3071 (5·2%)	162/3026 (5·4%)	-3-4	76-9		
ears 1-2	83/5453 236/4870 -85-3 75-2 (1-5%/y) (4-8%/y)		-32 (se 0-07) Ye	ears 3-4	113/5306 (2·1%/y)	123/5205 (2-4%/y)	-4-5 50	6-6		— 0·92 (se 0·13)	Years 3-4	(3 270) 134/2821 (4-8%)	143/2770 (5·2%)	-5-5	66-6		0·92 (se 0·1
ears 3-4	53/4745 147/4000 -55-7 47-4 (1-1%/y) (3-7%/y)		-31 (se 0-09) Ye	ears 5-9	194/9288	242/8894	-26-1 103	3-5		0·78 (se 0·09)	Years 5-9	255/2522	278/2455	-18-6 1	126-9		0-86 (se 0-0
ears 5-9	(1-1 %y) (3-7 %y) 64/7924 116/6214 -37-2 42-8 (0-8%/y) (1-9%/y)		-42 (se 0·10) γe	ears 10-14	(2·1%/y) 68/2814	(2·7%/y) 82/2628	-8-3 3	5-3		0-79 (se 0-15)	Years 10-14	(10·1%) 85/1090	(11·3%) 96/1025	-9-4	42-6		— 0·80 (se 0·1
ears 10+	(0-8%/y) (1-9%/y) 5/2709 3/1996 0-5 2-0 (0-2%/y) (0-2%/y)		Ye	ears 15+	(2·4%/y) 22/718 (3·1%/y)	(3·1%/y) 17/709 (2·4%/y)	2.3	9-4		1.28 (SE 0.37)	Years 15+	(7·8%) 31/280 (11·1%)	(9·4%) 25/255 (9·8%)	2.6	13-3		- 1.22 (SE 0.3
Total	285/ 756/ -266-6 239-0 23910 20019 (6-7%/5y) (22-9%/5y)		33 (se 0·04) _{2p < 0·00001}	Total	515/ 27116 17-4%/10y) (-45·2 265	5-0	\diamond	0-84 (se 0-06) 2p = 0-006	Total	664/ 3071 (21·6%)	704/ 3026 (23·3%)	-34-3 32	26-2	\diamond	0•90 (se 0• 2p = 0•06
				(*	17.4%/10y)/	(∠∪∙3%/10∖	9					(21.0%)	(23.3%)				

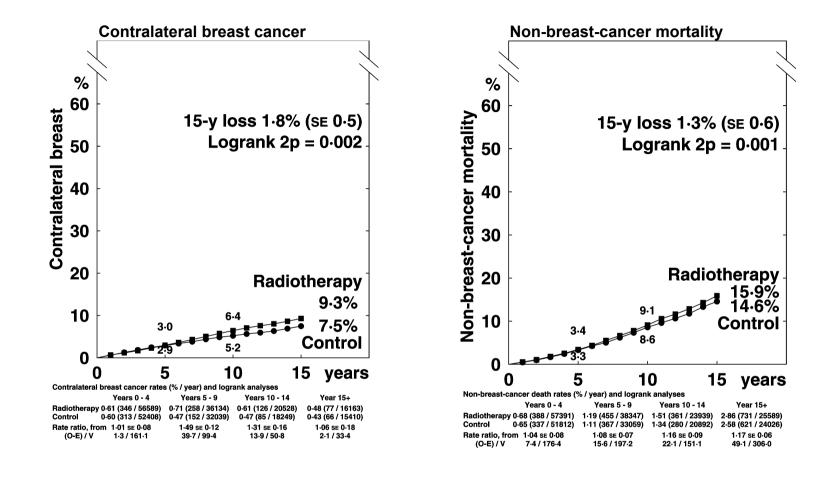
Webfigure 6b: Radiotherapy after mastectomy and axillary clearance in node-positive disease — subgroup analyses (event rate ratios for all three endpoints, with 5-year risks of local recurrence, 15-year breast cancer mortality risks and crude % for any death; subdivisions by entry age, tumour grade, tumour size, use of systemic therapy in both arms, ER status, no. of nodes, and time period)

	Events/woman-yearsMast+AC+RT events		Breast	cancer mortality	Ratio of annual (death rates	Any dea	Deathe/Wo	men Mast+AC+RT deaths	Ratio of annual d	eath rates
Category	Allocated Allocated LogrankVariance Mast+AC+RT Mast+AC O-E of O-E	Mast+AC+RT : Mast+AC	Category	Allocated Allocated LogrankVariance Mast+AC+RT Mast+AC O-E of O-E	Mast+AC+RT : M	ast+AC			Iocated LogrankVariance ast+AC O-E of O-E	Mast+AC+RT : Ma	st+AC
a) Entry age (tre	end χ ₁ ² = 0·2; 2p = 0·6)			rend $\chi_1^2 = 2.1$; 2p = 0.1)			(a) Entry age (tre				
\ge < 50	121/16148 404/14020 -149-9 120-0 (6-0%/5y) (22-6%/5y)	● 0-29 (SE 0-05)	Age < 50	947/19116 1085/17919 -84-3 442-0 (50-5%/15y) (58-7%/15y)		0-83 (SE 0-04)	Age < 50	1004/1911 11 (52-5%) (33/1912 -81·9 464·4 59·3%)		0-84 (se 0-0
lge 50 - 59	77/8970 232/7904 -78-5 66-9 (6-5%/5y) (23-7%/5y)	0-31 (SE 0-07)	Age 50 - 59	586/10804 599/10243 -14-3 245-8	_	0-94 (se 0-06)	Age 50 - 59		73/1052 -9-5 279-5 64-0%)	- # -	0-97 (se 0-0
ge 60 - 69	61/9437 256/8136 -95-2 70-0	0-26 (SE 0-07)	Age 60 - 69	(56-3%/15y) (59-6%/15y) 679/11039 717/10608 -11-5 293-1		0-96 (se 0-06)	Age 60 - 69	888/1204 8	34/1199 -10-8 367-9		0-97 (se 0-0
ge 70+	(4-8%/5y) (22-8%/5y) 5/436 15/367 -3-5 3-4 -	0-36 (se 0-34)	Age 70+	(59-7%/15y) (61-8%/15y) 49/507 61/492 -9-2 16-1		0.57 (se 0.19)	Age 70+		73-7%) 73/88 -9-5 19-5		0.61 (SE 0.1
	(8·9%/5y) (18·6%/5y)		Agerot	(-%/15y) (-%/15y)	_	0.01 (32 0.13)	Age i ei	(84-6%) (83-0%)	-	
b) Tumour grad	le (trend χ ₁ ² = 0·2; 2p = 0·6)		(b) Tumour grad	de (trend χ ₁ ² = 1·1; 2p = 0·3)			(b) Tumour grad	e (trend χ^2_1	= 1·6; 2p = 0·2)		
/ell differentiated	16/3162 91/2692 -39-5 26-0	■ 0·22 (SE 0·10)	Well differentiated	I 143/3537 181/3377 -22-4 75-3	_	0-74 (se 0-10)	Well differentiated	163/359 2	08/375 -27·7 86·7 55-5%)		0.73 (SE 0.0
loderately	(3-8%/5y) (21-6%/5y) 37/4837 190/3693 -84-1 54-0	0.21 (SE 0.07)	Moderately	(43·1%/15y) (56·3%/15y) 384/5588 450/4880 -52·2 186·5	_	0-76 (se 0-06)	Moderately	423/697 4	83/690 -53-8 203-9	- B	0.77 (se 0.0
differentiated oorly	(4-5%/5y) (30-0%/5y) 19/1663 93/1188 -42-3 25-6 -	0.19 (se 0.10)	differentiated Poorly	(60-8%/15y) (70-1%/15y) 215/1978 213/1671 -12-5 88-8		0-87 (se 0-10)	differentiated Poorly	224/321 2	70-0%) 19/288 -12-3 92-4		0-88 (SE 0-1
differentiated	(5·9%/5y) (40·4%/5y)		differentiated Grade unknown	(-%/15y) (-%/15y)	_	. ,	differentiated Grade unknown		76-0%) 53/2898 -24-4 764-1		0-97 (se 0-0
arade unknown	192/25355 533/22880 -164-0 156-8 (6-4%/5y) (19-3%/5y)	0-35 (SE 0-05)	Grade unknown	1519/30393 1618/29364 -40-0 657-1 (53-4%/15y) (56-2%/15y)		0-94 (se 0-04)		(63-6%) (63-9%)	甲	
	$(trend x^2 = 0.0, 2n = 0.2)$			•			(-) -	a			
- 20 mm (T1)	(trend $\chi_1^2 = 0.9$; 2p = 0.3) 42/5927 158/5018 -62.1 47.7	0.27 (SE 0.08)		$\chi_1^2 = 0.7; 2p = 0.4$			(c) Tumour size 1 - 20 mm (T1)		0·8; 2p = 0·4) 96/686 -38·3 170·2	_	0-80 (se 0-0
	(4·8%/5y) (22·1%/5y)		1 - 20 mm (T1)	303/6835 355/6348 -33-2 150-8 (47-8%/15y) (56-8%/15y)		0-80 (se 0-07)		(50-1%) (57.7%)		
1 - 50 mm (T2)	49/5571 227/4494 -96-7 65-3 (5-9%/5y) (30-3%/5y)	■ 0·23 (SE 0·06)	21 - 50 mm (T2)	523/6663 562/6292 -26-0 240-1 (65-0%/15y) (68-4%/15y)		0-90 (SE 0-06)	21 - 50 mm (T2)	(64-5%) (02/864 -27-3 260-5 69-7%)		0-90 (SE 0-0
50 mm (T3) or T4	15/1438 79/1168 -32-0 21-3 - (8-4%/5y) (35-6%/5y)	■ 0·22 (SE 0·11)	> 50 mm (T3) or T	183/1837 211/1730 -10-4 80-9 (70-8%/15y) (78-2%/15y)		0-88 (SE 0-10)	> 50 mm (T3) or T4	190/271 2 (70·1%) (19/289 -11-7 84-5 75-8%)		0-87 (SE 0-1
arious/unknown/	158/22072 443/19766 -135-2 127-0 (6-0%/5y) (18-8%/5y)	⊡- 0-34 (se 0-05)	Various/unknown	1252/26151 1334/24910 -41-8 529-5 (51-8%/15y) (55-4%/15y)		0-92 (se 0-04)	Various/unknown		46/2412 -25-0 625-3 64-1%)		0-96 (se 0-0
				(31.6 % 139) (33.4 % 139)						T	
d) Chemo. (C) o 2p = 0.6)	or Tamoxifen (T) ($\chi_1^2 = 0.2$;		(d) Chemo. (C)	or Tamoxifen (T) (χ ₁ ² = 1·7; 2p = 0·	2)		(d) Chemo. (C) c		ι (T) (χ ₁ ² = 2·5; 2p = 0	0-1)	
Both with C or T	197/21346 698/18349 -268-4 211-1	0-28 (se 0-04)	Both with C or T	1615/25746 1805/24517 -107-9 756-4		0-87 (se 0-03)	Both with C or T	1788/3042 19 (58-8%) (46/3058 -105-6 829-4 63-6%)		0-88 (SE 0-0
leither with C or T	(6·4%/5y) (24·8%/5y)	0-30 (SE 0-08)		(57-2%/15y) (63-5%/15y)			Neither with C or T	852/1212 8	17/1193 -6-1 301-8		0-98 (se 0-0
	(4·1%/5y) (17·3%/5y)	0.00 (35 0.00)	Neither with C or	646/1212 657/1193 -11-4 240-7 (48-6%/15y) (51-1%/15y)	_	0-95 (se 0-06)		(70-3%) (68-5%)		0.00 (05 0.0
e) ER status			(a) ED atatus /E	R-poor vs ER-positive: $\chi_1^2 = 0.3$; 2	- 0 6		(e) ER status (El	R-poor vs E	R-positive: $\chi_1^2 = 1.1$;	2p = 0·3)	
(ER-poor vs El	R-positive: $\chi_1^2 = 0.7$; 2p = 0.4)		ER-poor	371/4993 454/5090 -19-4 175-3	p=0•0)	0-90 (se 0-07)	ER-poor	403/680 4	71/744 -11-8 186-8 63-3%)	· _	0-94 (se 0-0
R-poor	52/4035 178/3838 -62-1 52-7 (8-3%/5y) (28-0%/5y)	- 0-31 (SE 0-08)	ER-positive	(60-9%/15y) (65-4%/15y) 567/9920 638/9282 -45-0 268-3		0-85 (se 0-06)	ER-positive	637/1126 7	00/1121 -47-6 299-6	-	0-85 (se 0-0
ER-positive	69/8267 258/6832 -102-8 77-2 (5-7%/5y) (24-2%/5y)	- 0-26 (SE 0-06)		(56-3%/15y) (61-3%/15y)		. ,	ER-unknown		62-4%) 92/2386 -40-7 651-4		0-94 (se 0-0-
R-unknown	143/22689 471/19762 -164-1 129-6 (4-9%/5y) (20-6%/5y)	0-28 (SE 0-05)	ER-unknown	1323/26560 1370/24895 -42-9 556-2 (52-8%/15y) (57-3%/15y)		0-93 (SE 0-04)		(65-4%) (66-7%)	Щ.	
	(4-8-%-3 y) (20-0-%-3y)						(f) Nedel Invelve		0 1. 0 0 7)		
f) Nodal involve	ement (χ ₁ ² = 2·0; 2p = 0·2)			ement ($\chi_1^2 = 0.0$; 2p = 0.9)			(f) Nodal involve pN1-3		0·1; 2p = 0·7) 15/954 -5·2 231·6		0-98 (SE 0-0
N1-3	45/8800 155/8101 -54-8 47-5 (4-0%/5y) (15-5%/5y)	0-32 (SE 0-09)	pN1-3	394/10395 441/10280 -16-2 189-1 (43-3%/15y) (47-7%/15y)	-	0-92 (SE 0-07)	pN4+	(54-0%) (54-0%) 06/917 -14-2 259-2		
N4+	99/5298 197/4404 -59-4 67-1 (11-6%/5y) (26-3%/5y)		pN4+	587/6750 587/6283 -22-9 244-6 (68-0%/15y) (70-3%/15y)		0-91 (se 0-06)	-	(67-4%) (66-1%)		0-95 (SE 0-0
ther N+ or N?	120/20895 555/17930 -217-2 145-7	0-23 (SE 0-04)	Other N+ or N?	1280/24321 1434/22699 -95-0 561-4 (54-0%/15y) (61-5%/15y)		0-84 (se 0-04)	Other N+ or N?		42/2380 -106-2 641-1 69-0%)		0·85 (se 0·0
	(4-3%/5y) (24-9%/5y)			(0.0.0.0)) (0.0.0.0))					•		
g) Period of foll	low-up (trend $\chi_1^2 = 0.4$;		(g) Period of fo	low-up (trend $\chi_1^2 = 4.3$; 2p = 0.04)			(g) Period of foll Denominator: n	ow-up (tren umber enter	d χ ² = 1·1; 2p = 0·3) na time period		
° 2p = 0·5)		0 20 (0= 0.07)	Years 0-2	845/11507 845/11523 -2-2 364-4 (7-3%/y) (7-3%/y)	-	0-99 (SE 0-05)	Years 0-2	884/4254 8	90/4251 -4-5 383-1		0-99 (se 0-0
'ear O	63/3881 228/3819 -77-3 63-8 (1-6%/y) (6-0%/y)	• 0-30 (se 0-07)	Years 3-4	479/6033 558/5939 -35-5 219-4		0-85 (SE 0-06)	Years 3-4		20-9%) 90/3330 -34-4 235-0		0-86 (se 0-0
ears 1-2	102/6353 406/5855 -153-6 113-7 (1-6%/y) (6-9%/y)	0-26 (SE 0-05)	Years 5-9	(7-9%/y) (9-4%/y) 561/11548 639/10783 -51-9 259-0		0-82 (SE 0-06)		(15-5%) (17-7%)		-
ears 3-4	49/4989 144/4356 -52·2 43·4 (1·0%/y) (3·3%/y)			(4-9%/y) (5-9%/y)			Years 5-9	(23-6%) (11/2708 -49-7 295-3 26-3%)		0-85 (SE 0-0
ears 5-9	42/9589 105/7999 -35-9 33-0 (0-4%/y) (1-3%/y)	0-34 (se 0-11)	Years 10-14	220/6827 272/6066 -29-5 102-2 (3-2%/y) (4-5%/y)		0-75 (SE 0-09)	Years 10-14	(15-6%) (25/1763 -25-9 128-4 18-4%)	─■	0-82 (SE 0-0
ears 10+	8/9936 24/8146 -8-0 6-4 -	0·28 (SE 0·23)	Years 15+	156/5319 148/4698 -0·2 52·0 (2·9%/y) (3·2%/y)		1.00 (se 0.14)	Years 15+		47/805 2-8 89-3 30-7%)		1.03 (SE 0.1
	(0·1%/y) (0·3%/y)										
Total	264/ 907/ -327.1 260.2	0·28 (se 0·04)	Total	2261/ 2462/ -119-3 997-0 41466 39262	\diamond	0-89 (se 0-03)	Total	2640/ 2 4254	2763/ -111·7 1131·3 4251 55·0%)	\diamond	0-91 (SE 0-0 2p = 0-0009
	34991 30427 32771 20072 (5-8%/5y) (22-8%/5y)	2p < 0-00001		41466 39262 (54-7%/15y) (60-1%/15y)		2p = 0-0002			5-0%)		2p = 0-0009
			-∎ 99% or -==> 95% 0	Ci	0-5 1-0	1.5 2.0	🖶 99% or 🖘 95% C			0-5 1-0	1.5 24

Webfigure 6c: 12 types of treatment comparison that yield >10% isolated local recurrence risk reduction — subgroup analyses (event rate ratios for all three endpoints, with 5-year local recurrence risks, 15-year breast cancer mortality risks and crude % for any death; subdivisions by entry age, nodal status, tumour grade, tumour size, use of systemic therapy in both arms, ER status and time period)

Isolated	l local recurre		Breast cance	r mortali	ty	Any de	eath	
Category, and control % with BCS	Events/woman-years Active events Allocated Allocated LogrankVarian Active Control O-E of O-E	ce Ratio of annual event rates	Category, and % node-positive (N+)	Active deaths d LogrankVarlance Rati 0-E of 0-E	o of annual death rates Active : Control	Category	Deaths/Women Active deaths Allocated Allocated LogrankVariance Active Control O-E of O-E	Ratio of annual death rates Active : Control
	and $\chi_1^2 = 0.5$; 2p = 0.5)		(a) Entry age (trend $\chi_1^2 = 0.3$; 2p =	= 0.6)		(a) Entry age (tre	end $\chi_1^2 = 2.3$; 2p = 0.1)	
Age < 50	481/40783 1295/33048 -467-5 392-8	0-30 (se 0-03)	Age < 50 1907/51447 2059/4844 (58% N+) (42-4%/15y) (47-6%/15)	14 -110-9 887-0 jy)	0-88 (SE 0-03)	Age < 50	2099/4546 2189/4450 -95-1 960-2 (46-2%) (49-2%)	0-91 (se 0-03
(32% BCS) Age 50 - 59	(8-6%/5y) (29-7%/5y) 322/30573 936/25626 -326-0 285-8	0-32 (SE 0-04)	Age 50 - 59 1494/39041 1671/3759	95 -88-4 689-2	0-88 (se 0-04)	Age 50 - 59	1892/3719 1958/3736 -63-3 835-6 (50-9%) (52-4%)	0-93 (SE 0-03
(43% BCS) Age 60 - 69	(7-7%/5y) (26-6%/5y) 284/29772 895/26237 -317-3 271-4	0·31 (se 0·04)	(49% N+) (43.5%/15y) (49.3%/15 Age 60 - 69 1581/36057 1806/3626		0-92 (se 0-04)	Age 60 - 69	2275/3750 2371/3860 -42-6 1005-5 (60-7%) (61-4%)	0-96 (se 0-03
(40% BCS) Age 70+	(6-1%/5y) (22-8%/5y) 32/3647 93/3717 -26-0 26-5	0·38 (se 0·12)	(50% N+) (48-6%/15y) (52-4%/15)			A == 70 -		1 00 (97 0 00
(57% BCS)	(4-3%/5y) (15-2%/5y)		Age 70+ 198/4391 246/4886 (26% N+) (51.9%/15y) (55.7%/15)	6 -11-6 85-2 5y)	0-87 (SE 0-10)	Age 70+	339/583 396/632 0-6 135-0 (58-1%) (62-7%)	— — 1.00 (se 0.09
	$(\chi_1^2 = 4.9; 2p = 0.03)$		(b) Nodal status ($\chi_1^2 = 0.3$; 2p = 0-				$(\chi_1^2 = 4.1; 2p = 0.04)$	
Node-negative (62% BCS)	581/53928 1564/46010 -539-8 493-3 (7-0%/5y) (24-2%/5y)	0-33 (SE 0-03)	Node-negative 1821/67209 2079/6666 (34-8%/15y) (38-5%/15)	38 -90-7 901-8 iy)	0-90 (SE 0-03)	Node-negative	2580/6158 2688/6198 -28-0 1205-3 (41-9%) (43-4%)	0-98 (SE 0-03
Node-positive (16% BCS)	538/50847 1655/42618 -597-0 483-1 (7-8%/5y) (28-3%/5y)	0·29 (se 0·03)	Node-positive 3359/63727 3703/6051 (53-7%/15y) (59-6%/15)	19-184-2 1493-0 iy)	0-88 (se 0-02)	Node-positive	4025/6440 4226/6480 -172-4 1731-0 (62-5%) (65-2%)	0-91 (se 0-02
c) Tumour grad	e (trend χ ₁ ² = 0·8; 2p = 0·4)					() -	(mail ² 00 0 0 0)	
Well differentiated	40/6626 163/6047 -61-4 48-4	■ 0·28 (se 0·08)	(c) Tumour grade (trend $\chi_1^2 = 0.7$; Well differentiated 201/7445 236/7543		0-83 (SE 0-09)	(c) Tumour grad Well differentiated	e (trend χ_1^2 = 0.8; 2p = 0.4) 258/777 297/815 -21.9 127.8 (33-2%) (36.4%)	0-84 (se 0-08
(49% BCS) Moderately differe	(4-0%/5y) (17-6%/5y) - 171/15351 595/12379 -226-9 170-4	0·26 (se 0·04)	(51% N+) (33-1%/15y) (39-2%/15) Moderately differ- 757/18315 914/1829	5y)	0-81 (SE 0-05)	Moderately	915/1929 1026/1979 -63-6 443-3	0-87 (se 0-04
ntlated (48% BCS Poorly differe-	219/14782 587/11438 -208-2 174-1	0·30 (se 0·04)	entiated (50% N+) (44-6%/15y) (53-7%/15	ōy)	-	differentiated Poorly	(47·4%) (51·8%) 1009/1762 1029/1713 -44·1 460·8	0-91 (se 0-04
ntiated (58% BCS) Grade unknown	(11-7%/5y) (36-1%/5y) 689/68057 1874/58787 -633-3 587-3	0-34 (se 0-03)	entiated (35% N+) (48-3%/15y) (53-5%/15		0-88 (SE 0-05)	differentiated Grade unknown	(57-3%) (60-1%) 4423/8130 4562/8171 -100-5 1939-8	0-95 (se 0-02
(31% BCS)	(7-0%/5y) (23-2%/5y)		Grade unknown 3406/87265 3755/8447 (55% N+) (44-9%/15y) (46-7%/15y	/4 -139-1 1552-1 y)	0-91 (SE 0-02)		(54-4%) (55-8%)	
d) Tumour size	(trend χ ₁ ² = 0·1; 2p = 0·8)		(a) Tomorow also (from al. 2 0.7 of			(d) Tumour size	(trend χ ₁ ² = 4-0; 2p = 0-05)	
- 20 mm (T1) (73% BCS)	291/30300 890/25026 -331-9 272-5 (6-0%/5y) (23-6%/5y)	0·30 (SE 0·04)	(d) Tumour size (trend χ ² ₁ = 2·7; 2 1 - 20 mm (T1) 872/34697 1029/3322		0-82 (se 0-04)	1 - 20 mm (T1)	1109/3579 1221/3540 -92-2 544-6 (31-0%) (34-5%)	0-84 (SE 0-04
1 - 50 mm (T2) (46% BCS)	265/18371 795/14716 -280-8 232-9 (10-6%/5y) (34-9%/5y)	0-30 (se 0-04)	(29% N+) (32-3%/15y) (38-6%/15) 21 - 50 mm (T2) 1156/22427 1290/2240	5y)	0-91 (SE 0-04)	21 - 50 mm (T2)	1380/2394 1447/2434 -30-9 643-8	0-95 (se 0-0-
50 mm (T3) or T4		■ 0·26 (se 0·10)	(54% N+) (52-5%/15y) (56-3%/15	ōy)		> 50 mm (T3) or T4	(57-6%) (59-4%) 269/374 317/423 -4-7 120-2	0.96 (SE 0.05
(3% BCS) arious/unknown (17% BCS)	(100,745) 534/53964 1417/46822 -469-6 442-5 (7-1%/5y) (23-2%/5y)	0·35 (SE 0·03)	> 50 mm (T3) or T4 240/2760 285/3033 (75% N+) (66-8%/15y) (74.7%/15) Various/unknown 2912/71089 3178/685 (61% N+) (47.1%/15y) (51-0%/15	61 -110.9 1302.9	0-93 (SE 0-09) 0-92 (SE 0-03)	Various/unknown	269/374 317/423 -4-7 120-2 (71-9%) (74-9%) 3847/6251 3929/6281 -73-9 1658-7 (61-5%) (62-6%)	0-96 (SE 0-02
e) Chemo. (C) o	r Tamoxifen (T) (χ ₁ ² = 1·5;		· · ·					
2p = 0·2)	•		(e) Chemo. (C) or Tamoxifen (T) ((χ ₁ ² = 1·9; 2p = 0·2)		(e) Chemo. (C) o Both with C or T	r Tamoxifen (T) (χ ² ₁ = 5·6; 2p = 0 2718/5343 2894/5292 -148-8 1254-4	•02) 0-89 (se 0-03
Both with C or T (40% BCS)	493/41408 1414/33683 -518-2 428-7 (7-8%/5y) (27-5%/5y)	0-30 (SE 0-03)	Both with C or T 2349/49819 2625/4697 (74% N+) (49.1%/15y) (55.1%/15)	78-160-7 1110-0 iy)	0-87 (SE 0-03)	boar with c or 1	(50-9%) (54-7%)	0.03 (32 0.03
leither with C or T (37% BCS)	626/63367 1805/54945 -618·5 547·7 (7·0%/5y) (25·0%/5y)	0-32 (SE 0-03)	Neither with C or T 2831/81117 3157/8020 (34% N+) (41-2%/15y) (45-3%/15y))9 -114-2 1284-8 iy)	0-91 (SE 0-03)	Neither with C or T	3887/7255 4020/7386 -51-6 1681-9 (53-6%) (54-4%)	0-97 (SE 0-02
f) ER status		_				(f) ED status (EE	I-poor vs ER-positive: $\chi_1^2 = 1.2$; 2	n - 0.3)
(ER-poor vs El R-poor	R-positive: χ ₁ ² = 7·2; 2p = 0·00 165/10612 456/9533 -146·2 138·9	/) ■ 0.35 (se 0.05)	(f) ER status (ER-poor vs ER-pos			ER-poor	714/12871 828/13150 -28-6 336-4	0-92 (SE 0-05
(48% BCS) ER-positive	(11.5%/5y) (31.4%/5y) 281/24750 911/19145 -347-7 260-4	0.05 (SE 0.03)	ER-poor 647/12871 783/1315 (63% N+) (49.0%/15y) (53.3%/15		0-89 (SE 0-05)	ER-positive	(5-5%) (6-3%) 1225/29397 1358/28086 -94-3 585-1	0-85 (se 0-04
(60% BCS)	(6-7%/5y) (29-8%/5y)	-	ER-positive 1046/29397 1230/2808 (51% N+) (41.5%/15y) (48-0%/15)	5y)	0-82 (SE 0-04)	ER-unknown	(4-2%) (4-8%) 4666/88681 4728/85971 -83-7 2043-0	0-96 (se 0-02
ER-unknown (28% BCS)	673/69414 1852/59946 -634-5 575-7 (6-9%/5y) (23-4%/5y)	0-33 (se 0-03)	ER-unknown 3487/88681 3769/8597 (49% N+) (45-2%/15y) (49-3%/15)	/1 -121-9 1579-1 })	0-93 (SE 0-02)		(5-3%) (5-5%)	
g) Period of foll 2p < 0.00001)	ow-up (trend $\chi_1^2 = 50.5$;		(g) Period of follow-up (trend χ_1^2	= 4·7; 2p = 0·03)		(g) Period of foll Denominator:	ow-up (trend $\chi_1^2 = 0.0$; 2p = 0.9) number entering time period	
/ear 0	272/11263 1188/10798 -453-4 314-4 (2-4%/y) (11-0%/y)	0-24 (SE 0-03)	Years 0-2 1699/34827 1693/3514 (4-9%/y) (4-8%/y)	45 16-7 739-3	1-02 (SE 0-04)	Years 0-2	1868/12598 1849/12678 23-4 812-1 (14-8%) (14-6%)	1-03 (SE 0-04
ears 1-2	388/19436 1101/17309 -388-8 340-7 (2-0%/y) (6-4%/y)	0-32 (SE 0-03)	Years 3-4 1024/19250 1252/1923 (5-3%/y) (6-5%/y)	38 -102-2 497-9	0-81 (SE 0-04)	Years 3-4	1163/10472 1362/10564 -95-7 553-9 (11-1%) (12-9%)	0-84 (se 0-04
ears 3-4	187/15985 462/13514 -164-0 150-8	0·34 (se 0·05)	Years 5-9 1406/36767 1674/3541 (3-8%/y) (4-7%/y)		0-82 (SE 0-03)	Years 5-9	(17-16) (12-676) 1754/9053 1934/8942 -106-2 816-8 (19-4%) (21-6%)	0-88 (SE 0-03
ears 5-9	(1-2%/y) (3-4%/y) 213/29845 382/24266 -109-2 137-5	0.45 (se 0.06)	(3-8%/y) (4-7%/y) Years 10-14 609/20873 736/1952:		0-81 (SE 0-05)	Years 10-14		0-87 (SE 0-05
ears 10+	(0-7%/y) (1-6%/y) 59/27607 86/22086 -21-4 33-0 (0-2%/y) (0-4%/y)	0.52 (se 0.13)	Years 15+ 442/18626 427/1721 (2.9%/y) (3-8%/y) (2-4%/y) (2-5%/y)) 19 6-1 180-4	1-03 (SE 0-08)	Years 15+	869/5682 950/5397 -57-0 394-1 (15-3%) (17-6%) 951/3100 819/2842 34-7 359-1 (30-7%) (28-8%)	
Total (39% BCS)	1119/ 3219/ -1136-8 976-5 104775 88628 (7-4%/5y) (26-1%/5y)	0-31 (se 0-02) 2p < 0-0001	_		0.89 (se 0.02) 2p < 0.00001	Total	6605/ 6914/ -200-4 2936-3 12598 12678 - (52-4%) (54-5%)	0-93 (s≡ 0-0 2p = 0-0002
-∎- 99% or <:> 95% Cl	0	0-5 1-0 1-5 2-0	-∎- 99% or -==> 95% Cl	0 0-5	5 1.0 1.5 2.0	- 99% or <⇒ 95% C		0-5 1-0 1-5 2-0
		Active better Active worse		Active b	better Active worse		, in the second s	Active better Active worse

Webfigure 7: Effect of radiotherapy on contralateral breast cancer incidence and on non-breast-cancer mortality (46 trials of adding radiotherapy, and 17 trials of radiotherapy vs more surgery) — 15-year outcome (life table curves: 29 623 women)



Webfigure 8a: Radiotherapy versus not, in women with node-negative disease

(event rate ratios, one line per trial)

Isolated local recurrence

isolatea		Events/wo	man-years	Radio	. events		
Year Code and study name	Radiotherapy sites		-		k Varlance of O-E		ual event rates : Control
(a) Breast conserva	ation, general	y with a	xillary cl	earanc	e	1	
76B NSABP B-06	+BW	86/4604	152/3385	-40-8	49-1		
81L Uppsala-Örebro	BW	10/1636	43/1511	-17-7	12.7		
2Y1357 St George's Londo	n †BW	12/1202	31/1047	-11-5	9-6		
84P Ontario COG	BWS	53/3543	155/2754	-58-2	48-2		
85B Scottish	BWS+(AF)+IMC	0/2175	52/1822	-23-3	14.9	- -	
85D West Midlands, UK	BWS+AF+IMC	42/2398	104/1929	-36-8	34-2		
86C2+3 CRC, UK	Various	20/1022	52/995	-16-2	17-1		
87R INT Milan 3	†BWS	13/1802	35/1418	-14-0	11.4		
89L NSABP B-21	†BWS	6/1810	40/1729	-17-3	11.2		
91P1 Swedish BCCG	BW	33/3718	92/3429	-30-8	30.5		
(a) Subtotal		285/ 23910	756/ 20019	-266-6	238-9	4	0.33 (SE 0.04 2p < 0.00001
5-year risk	τ .	6•7%	22•9	6			2p < 0.00001
(b) Mastectomy wit	h axillary clea	rance					
64B Oslo X-ray	BW+AF+IMC	5/3390	8/3388	-1-6	3.2		<u> </u>
64E Oslo Co-60	AF+IMC	4/2843	9/3515	-2-2			
69A Heidelberg XRT	AF+IMC	-/316	-/301	(no	data)	1	
71D SASIB	(BW)+AF+IMC	1/42	0/39	0.2	0.2	1	
74Ds DFCI Boston	†BW+AF	0/61	1/15			1	
78A S Swedish BCG	†BW+AF+IMC	2/1398	5/1352	-1-6	1.7 -		
79G2+3 Metaxas Athens	†BW+AF+IMC	0/41	0/52				
82B Danish BCG 82b	†BW+AF+IMC	2/695	14/742	-4-7	3.7 -	-	+
82C Danish BCG 82c	†BW+AF+IMC	4/640	15/670	-5-1	4.7	1	<u>+</u>
 (b) Subtotal with 	-	18/ 9110	52/ 9773	-15-0	16-7		0.41 (SE 0.16 2p = 0.0002
5-year risk	C	2•3%	6•3%				
(c) Mastectomy wit	h axillary sam	pling					
73A Wessex	BW+AF+IMC	6/499	6/525	0-0	2.9		
74B Edinburgh I	BW+AF	13/1732	50/1530	-19-7	14.9		
C4+5+6 CRC, UK	Various	0/86	1/67	-0-6	0.2		
 (c) Subtotal 		19/	57/	-20-3	18-0	-	0.32 (SE 0.14
5-year risk	c	2317 6•1%	2122 24•5%	b			2p < 0.00001
(d) Mastectomy alo	ne						
1H45689 NSABP B-03	AF+IMC	-/1996	-/1039	(no	data)		
70B Kings/Cambridge	BW+AF+IMC	99/9964	278/9690	-90-8		- -	
71C1 NSABP B-04	BW+AF+IMC	18/3896	94/3335	-40-4	25-4	- - -	
78D4 Scottish D	†BW+AF+IMC	7/358	13/375	-2.7	4.5		
85Z Tokyo CIH PS	† AF+IMC	0/2	1/23	-0-3	0.2		
(d) Subtotal with	th data §	124/ 14220	386/ 13423	-134-1	121.6	\$	0.33 (SE 0.05
5-year risk	ι .	5.6%	23•3%				2p < 0.00001
Total (a + b +	c + d)	446/ 49557	1251/ 45337	-436-0	395-3	\$	0.33 (SE 0.03
5-year risk	(5•8%	21.0%	D			2p < 0.00001
🖶 99% or 🖘 95	% CI						L
Heterogeneity be		tals: χ_{g}^{2} =	= 0-8; p =	0-9	0	0-5 1	-0 1-5 2-0
Heterogeneit	y within subto	tals: χ^2_{10}	= 26-9; p) = 0·1		Radio. better	Radio. worse
Heterogeneity						Treatment effe	ect 2p < 0.00001
					allocated Ra	dio.: 2312: allocated Con	trol: 1340)

ν.	ear Code	Radiotherapy	Deaths.	Adjusted		<u>. deaths</u> . Verlence	Ratio of annual	death rates
and	study name	sites	Radio.	Control	* 0-E	of O-E	Radio. : 0	
(a) E	Breast conserva	ation, generall	y with a	killary cle	earanc	e		
	NSABP B-06	†BW	141/454	157/432	-9-7	71.5		_
	Uppsala-Örebro	BW	37/184	34/197	2.3	16-8		• •
	St George's Londor Ontario COG	BWS	24/128 91/416	25/122 123/421	-2·5 -16-4	10-9 51-5		
	Scottish	BWS+(AF)+IMC		39/219	-10-4	17-8		
	West Midlands, UK		88/358	107/349	-11-4	45-3		_
	CRC, UK	Various	30/158	43/174	-4-1	17-5		
	INT Milan 3	†BWS	28/211	21/182	1.7	11-8		• •
	NSABP B-21 Swedish BCCG	†BWS BW	8/337 32/593	8/336 41/594	0-5 -3-9	3-9 18-0		• <u> </u>
	(a) Subtotal		515/ 3071 (16-8%)	598/ 3026		265.0	Ą	0.84 (SE 0.06 2p = 0.006
<i>(</i> 1) •				(,				
	Mastectomy wit Oslo X-rav	n axillary clea BW+AF+IMC	63/175	71/174	-2-8	30-8		
	Oslo Co-60	AF+IMC	65/179	58/187	10-6	28-0		• • •
69A	Heidelberg XRT	AF+IMC	25/44	12/31	5.2	7.9		•>
	SASIB	(BW)+AF+IMC	2/6	2/5	0.2	0.7 -		>
	DFCI Boston	†BW+AF	1/8	1/2	-0-3	0.2 —		>
	S Swedish BCG	†BW+AF+IMC †BW+AF+IMC	55/145	37/149 1/5	9-5 0-3	21-5 0-2		• •
	Metaxas Athens Danish BCG 82b	TBW+AF+IMC	1/5 19/67	31/88	-3-0	11.7		
	Danish BCG 82c	†BW+AF+IMC	41/77	33/81	7.3	16-9		→
	(b) Subtotal		272/	246/	27.0	117.9	-	1.26 (SE 0.10
			706 (38∙5%)	722 (34·1%)				2p = 0-01
(c) I	lastectomy wit		pling					
	Wessex	BW+AF+IMC	15/37	16/37	-1-0	6-5		>
	Edinburgh I CRC, UK	BW+AF Various	55/173 4/15	67/175 7/12	-3-2 -0-6	28-7 1-9		
			74/	90/				0.88 (SE 0.15
•	(c) Subtotal		225 (32·9%)	224	-4.8	37.1		2p = 0.4
(d) I	Mastectomy alo	ne						
	NSABP B-03 *	AF+IMC	30/190	2(19/112)	-1-2	10-4		
	Kings/Cambridge	BW+AF+IMC	515/996	572/1049	-3-1	254-1	-	-
	NSABP B-04	BW+AF+IMC	169/386	177/384	-3-7	80-0		
	Scottish D Tokyo CIH PS	†BW+AF+IMC † AF+IMC	17/42 3/3	14/39 3/5	1-2 0-9	6-5 0-9		• • • • •
_	(d) Subtotal *		734/	804/		054.0		0.98 (SE 0.05
	(u) Subiolai		1617	1701 (47-3%)	-0-9	351-8		2p = 0-8
	Total (a + b +	- c + d) *	1595/ 5619 (28-4%)	1738/ 5673 (30-6%)	-28-8	771.9	\$	0·96 (SE 0·04) 2p = 0·3
	99% or 🖘 95					_		
He	terogeneity bet					0	0-5 1-0	1.5 2.0
		/ within subto					Radio. better	Radio. worse

Any death

		Deatna	Women	Radio	. deaths	.
Year Code and study name	Radiotherapy sites	Allocated Radio.	Adjusted Control	Lograni O-E	Variance of O-E	Ratio of annual death rates Radio. : Control
(a) Breast conserva	ation, general	ly with a	xillary cle	aranc	•	1
76B NSABP B-06	tBW	186/454	184/432	-5-0	88-7	
81L Uppsala-Örebro	BW	48/184	50/197	-0-2	23-5	
Y1357 St George's Londor		30/128	29/122	-2.4	13-2	
84P Ontario COG	BWS	108/416	131/421	-12-9	57.7	
85B Scottish	BWS+(AF)+IMC		52/219	3.1	27.1	
85D West Midlands, UK		115/358	132/349	-12-6	57-4	
6C2+3 CRC. UK	Various	30/158	43/174	-4-1	17-5	
87R INT Milan 3	TBWS	38/211	28/182	2.3	15-9	
89L NSABP B-21	TBWS	16/337	14/336	1.2	7.3	
91P1 Swedish BCCG	BW	32/593	41/594	-3.9	18-0	
(a) Subtotal		664/ 3071 (21·6%)	704/ 3026 (23·3%)	-34-3	326-2	0.90 (SE 0.0 2p = 0.06
(b) Mastectomy wit	h axillary clea	rance				1
	BW+AF+IMC	133/175	128/174	8.4	60-0	-
64B Oslo X-ray		133/175	128/174	8-4 28-9	58-7	
64E Oslo Co-60	AF+IMC AF+IMC	143/179 36/44	113/18/ 19/31	28.9	58-7 12-1	-
69A Heidelberg XRT						
71D SASIB	(BW)+AF+IMC	2/6	2/5	0.2	0.7 -	
74D5 DFCI Boston	†BW+AF	1/8	1/2	-0-3	0.2	
78A S Swedish BCG	†BW+AF+IMC	73/145	59/149	8.6	31-3	
9G2+3 Metaxas Athens	†BW+AF+IMC	1/5	1/5	0.3	0.2	
82B Danish BCG 82b	†BW+AF+IMC	20/67	36/88	-4.7	13-1	
82C Danish BCG 82c	†BW+AF+IMC	49/77	45/81	5-6	21-8	= 1:31 (s∈ 0.0
(b) Subtotal		458/ 706	404/ 722	52-8	198-2	2p = 0.0002
		• •	(56-0%)			
(c) Mastectomy wit						
73A Wessex	BW+AF+IMC	27/37	25/37	2.1	11-2	
74B Edinburgh I C4+5+6 CRC, UK	BW+AF Various	77/173 4/15	79/175 7/12	0-4 -0-6	37-0 1-9	
0110, UK	vanous		1/12	-0-0	1.9	1 04 (0 1
(c) Subtotal		108/ 225 (48·0%)	111/ 224 (49·6%)	2.0	50-1	1.04 (SE 0.1 2p = 0.8
(d) Mastectomy alo	-					1
45689 NSABP B-03 *	AF+IMC	98/190	2(58/112)	-1.5	30-9	
70B Kings/Cambridge	BW+AF+IMC	697/996	721/1049	12.6	334-4	
71C1 NSABP B-04	BW+AF+IMC	271/386	256/384	10-9	120-0	
78D4 Scottish D	†BW+AF+IMC	22/42	21/39	2.4	8-5	
85Z Tokyo CIH PS	† AF+IMC	3/3	3/5	0-9	0-9	
(d) Subtotal *		1091/ 1617 (67·5%)	1117/ 1701 (65·7%)	25-4	494.7	1.05 (SE 0.0 2p = 0.3
Total (a + b	+ c + d) *	2321/ 5619 (41·3%)	2336/ 5673 (41·2%)	45 ∙9	1069-1	⇒ 1.04 (se 0.0 2p = 0.2
🖶 99% or <> 95	% CI				<u> </u>	
Heterogeneity bet	ween 4 subto	tals: χ_3^2 =	= 17·1; p =	= 0.000	70	0-5 1-0 1-5 2-
Heterogeneity	/ within subto	tals: χ^2_{23}	= 18∙5; p	= 0.7		Radio. better Radio. worse
			= 35∙6; p			Treatment effect 2p = 0·2, adverse

§ 2 trials with no data do not contribute to subtotais on to the overall total (allocated Radio.: 2312; allocated Control: 1340) † Same polychemotherapy and/or tamoxifien in both groups BW-breast/chest will, Secard (as slot Of Th Docum), AF-a-Xill@Fossa, IMC=Internal mammary chain. Site(a) in brackets were not always treated

Webfigure 8b: Radiotherapy versus not, in women with node-positive disease

(event rate ratios, one line per trial)

Isolated local recurrence

isolated	local		man-years		events		
Year Code and study name	Radiotherapy sites		Adjusted Control			Ratio of annua Radio. :	l event rates Control
(a) Breast conserv	vation, general	ly with a	xillary cle	earance	,		
76B NSABP B-06	†BW	39/2258	133/1606	-52-6	35.7	- 	
82Y2468 St George's Lond	on †BW+AF	14/620	30/380	-10-9	9.7	I	
85B Scottish	BWS+(AF)+IM		31/438	-9.7	7.6		
86C2+3 CRC, UK 87R INT Milan 3	Various tBWS	13/582 6/676	25/459 25/587	-8-0 -11-1	8-6 6-9		
o/H INT Milan o	1DWS	0/0/0	20/06/	-11-1	0.9		
(a) Subtotal		78/ 4559	244/ 3470	-92-3	68-4		0·26 (SE 0·07 2p < 0·00001
5-year ris	k	11•0%		6			2p < 0.00001
(b) Mastectomy w							
62B1 Berlin-Buch ABC 64B Oslo X-ray	BW+AF+IMC BW+AF+IMC	8/829 7/1355	18/915 22/1046	-3·4 -8·7	5-9 7-0		
64E Oslo Co-60	AF+IMC	2/1369	10/1188	-3.9	2.8 -		
69A Heidelberg XRT	AF+IMC	-/177	-/94		data)	1	
71B Stockholm A *	BW+AF+IMC	32/9028	2(56/4013)	-28-2	18-6	I	
71D SASIB	(BW)+AF+IMC	17/836	42/752	-12-9	14.0	֥	
73C Mayo 70-56-32	†(BW)+AF+IMC	16/1112	40/1019	-14-8	12.1	-+	
73E2 INT Milan 1	AF+IMC	0/145 7/546	1/103	-5-9	6-5		
74D5 DFCI Boston 74Q Piedmont OA	†BW+AF †(BW)+AF+IMC	6/964	20/613 18/986	-5-9	5-4		_
76A2+3 SECSG 1	†BW+AF+IMC	13/567	18/528	-2.9	7.4		
76C Glasgow	†BW+AF+IMC	16/825	30/705	-7.5	10-8		_
77J2 MD Ander. 7730E		-/294	-/497		data)		
78A S Swedish BCG	†BW+AF+IMC	10/1811	38/1459	-15-3	11-4		
78B2 Toronto-Edmont.	† AF+IMC	6/222	5/188	0.0	2.3		
78G1 BCCA Vancouver 78Q2 Düsseldorf U.	+BW+AF+IMC +BW+AF+IMC	17/1622 0/92	38/1240 1/194	-12·7 -0·4	13-1 0-3 —		
79F Coimbra	†BW+AF+IMC	7/419	10/347	-0-4	4.0	_	
79G2+3 Metaxas Athens	TBW+AF+IMC	4/187	4/189	0.2	1.9		
80S1 Helsinki	†BW+AF+IMC	4/313	15/395	-4-3	4.1		
80W NSABC Israel	†BW+AF+IMC	2/472	10/478	-3-9	2.7 -	-	_
82B Danish BCG 82b	†BW+AF+IMC	44/6238	218/4899	-95-2	62-4	-∎÷	
82C Danish BCG 82c 82Q ECOG EST3181	†BW+AF+IMC †BW+AF+IMC	28/4368 13/1051	195/3575 30/1018	-88-4 -8-6	53-3 10-2	₩ ;	
84A2 GBSG 03 Germa		5/620	12/564	-8-6 -3-6	4-2		
(b) subtotal w	rith data § *	264/ 34991	907/ 30427	-327-1	260-2	÷	0.28 (SE 0.04
5-year ris	k	5•8%	22•8%				2p < 0.00001
(c) Mastectomy w	ith axillarv san	npling					
73A Wessex	BW+AF+IMC	6/379	22/171	-9-3	5.7 -		
85F Nottingham	BW+AF	7/192	20/126	-6-9	5.7		
6C4+5+6 CRC, UK	Various	1/88	5/132	-1-9	1.0 —	•	<u> </u>
 (c) Subtotal 		14/ 659	47/ 429	-18-1	12-3	4-	0-23 (SE 0-15 2p < 0-00001
5-year ris	k	13•8%	22•5%)			
(d) Mastectomy al	one						
1H45689 NSABP B-03	AF+IMC	-/1662	-/781	(no	data)	1	
70A1 Manchester RBS	1 BW+AF+IMC	54/3846	131/3093	-43-7	43-4	÷∎	
70B Kings/Cambridge	BW+AF+IMC	45/3153	141/2589	-54-7	43-2		
78D4 Scottish D 85Z Tokyo CIH PS	†BW+AF+IMC † AF+IMC	1/30 7/259	3/63 11/235	-2-3	3.7		
88U Tokyo CIH N2	† AF+IMC	6/199	7/187	-0.6	3.1		
(d) Subtotal w		113/		-101-3	93-5		0.34 (se 0.06
5-year ris	-	7487 11•6%	6167 33•5%				2p < 0∙00001
							0 00 (0 00
Total (a + b +	+ c + d) *	469/ 47696	1491/ 40493	-538-9	434-5	+	0·29 (SE 0·03 2p < 0·00001
5-year ris	k	7•3%	27•1%				2p < 0.00001
🖶 99% or 🖘 9					0	0.5 1.0) 1.5 2.0
Heterogeneity b					-	Radio. better	Radio. worse
	ty within subto					Treatment effec	
Heterogeneit	y between 34 t				(dio.: 2133; allocated Contro	-

§ 3 trials with no data do not contribute to subtotais or to the overall total (allocated Radio.: 2133; allocated Control: 1372) For balance, control patients in 3-way trials or trial strata count haif or twice in subtotal(s) and in final total of events/women.
§ Same poly-kenotherapy and/or transvien in both groups
BW=breast/chest wall, S=scar (as site of RT boost), AF=Axilla/Fossa, IMC=Internal mammary chain. Site(s) in brackets were not always treated

(a) F	study name	sites	Allocated Radio.	Control	Logrank * O-E	Variance of O-E	Radio. : C	ontrol
	Breast conserv	ation. general	lv with a	xillarv cle	earance	•		
	NSABP B-06	tBW	126/277	148/287	-10-0	63-5		_
2Y2468	St George's Londo	n †BW+AF	31/80	28/70	-2-1	12-2		
	Scottish CRC, UK	BWS+(AF)+IMC Various	2 23/61 46/101	39/77 46/87	-3-4 -4-2	12-4 20-1		
	INT Milan 3	†BWS	12/83	30/91	-7-9	9-5		
	(a) Subtotal		238/ 602 (39·5%)	291/ 612 (47-5%)	-27.5	117.7	0	0·79 (SE 0·08 2p = 0·01
(ь) І	Mastectomy wi	th axillarv clea	arance					
	Berlin-Buch ABC	BW+AF+IMC	105/123	96/132	8-2	43-1		
64B	Oslo X-ray	BW+AF+IMC	72/110	65/93	-2-4	30-5		
	Oslo Co-60	AF+IMC AF+IMC	51/99 35/41	61/98 20/27	-6-8 1-4	25-3		
	Heidelberg XRT Stockholm A *	BW+AF+IMC	35/41 295/639	20/27 2(168/321)		10-2 95-7		• • • • • • • • • • • • • • • • • • • •
	SASIB	(BW)+AF+IMC	77/180	69/186	5.2	32-2		
	Mayo 70-56-32	t(BW)+AF+IMC	79/121	83/120	-4-4	35-2		
73E2	INT Milan 1	AF+IMC	9/15	3/7	2.3	2.2		
	DFCI Boston	†BW+AF	47/103	53/105	0.2	22.6		
74Q	Piedmont OA SECSG 1	†(BW)+AF+IMC †BW+AF+IMC	76/144 58/127	68/136 67/130	3-8 -3-7	31-5 26-0		
	Glasgow	TBW+AF+IMC	67/112	76/107	-4.9	30-2		
	MD Ander. 7730B	†BWS+AF+IMC	31/43	30/54	7.7	11-1	74-	•
78A	S Swedish BCG	†BW+AF+IMC	122/241	134/233	-13-2	56-0		
	Toronto-Edmont.	† AF+IMC	14/28	14/22	-0-2	4.5		
	BCCA Vancouver Düsseldorf U.	†BW+AF+IMC †BW+AF+IMC	74/164 17/34	90/154 24/54	-13-6 3-3	38-4 7-8		
	Coimbra	TBW+AF+IMC	36/62	38/62	0-4	14-8		· · · · · · · · · · · · · · · · · · ·
	Metaxas Athens	†BW+AF+IMC	11/25	21/36	-3-0	6-2		
	Helsinki	†BW+AF+IMC	22/47	21/52	2.9	9-3		
	NSABC Israel	†BW+AF+IMC	21/54	20/58	1.3	9-1 212-6		•>
	Danish BCG 82b	†BW+AF+IMC	416/824	515/825	-67-4			
82C	Danish BCG 82c	†BW+AF+IMC	381/649	419/656	-21-3	179-2		
	ECOG EST3181 GBSG 03 German	†BW+AF+IMC v †BW+AF+IMC	104/171 41/98	92/161 47/101	4·8 -3·2	43-8 19-7		
	(b) Subtota	1*	2261/ 4254 (53·1%)	4251	-119-2	997-3	\$	0-89 (SE 0-03 2p = 0-0002
(c) I	Mastectomy wi	th axillary sam	pling					
73A	Wessex	BW+AF+IMC	26/37	33/40	-6-2	11-5		_
	Nottingham	BW+AF	23/36	30/41	-3-5	11-1		
C4+5+6	CRC, UK	Various	14/22 63/	8/22 71/	4-0	3-7		0.81 (SE 0.18
•	(c) Subtotal		95 (66-3%)	103	-5-6	26-4		2p = 0.3
	Mastectomy al							
	NSABP B-03 * Manchester RBS1	AF+IMC BW+AF+IMC	155/286 178/355	2(81/160) 212/359	3-3 -14-0	44-5 90-1		
	Kings/Cambridge	BW+AF+IMC	232/380	252/375	-10-2	109-6		-
	Scottish D	†BW+AF+IMC	2/5	3/7	0.5	0-3		
85Z	Tokyo CIH PS	† AF+IMC	18/47	21/45	-0-1	7-8		
88U	Tokyo CIH N2	† AF+IMC	25/50	27/50	-1-2	11-1		
	(d) Subtotal *		610/ 1123 (54·3%)	677/ 1156 (58-6%)	-21-8	263-3	ų.	0-92 (SE 0-06 2p = 0-2
	Total (a +	b + c + d) *	3172/ 6074 (52-2%)	3501/ 6122 (57-2%)	-174-2	1404.7	\$	0-88 (SE 0-0 2p < 0-00001
-	99% or 🖘 9	5% CI						
He	terogeneity be	tween 4 subto	tals: χ^2_{γ} :	= 2·1; p =	0.6	0	0-5 1-0	1.5 2.0

* 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.

Any death

Year Code and study name	Radiotherapy	Allocated	Women Adjusted Control		deaths Variance	Ratio of annual death rates	
	sites	Radio.	Control	* Ŏ-E	of O-E	Radio. : Control	
	servation, genera						
76B NSABP B-06	†BW	141/277	158/287	-9.7	69-4		
2468 St George's I 85B Scottish	ondon †BW+AF BWS+(AF)+IN	32/80 MC 29/61	28/70 43/77	-1-6 -3-1	12-4 14-7		
C2+3 CRC, UK	Various	46/101	46/87	-4-2	20.1		
87R INT Milan 3	TBWS	16/83	33/91	-7.0	11-1		
_						0.90 (0= 0	00
(a) Subtota	d	264/ 602	308/ 612	-25.7	127.7	0-82 (SE 0 2p = 0-03	
		(43-9%)	(50-3%)				_
(b) Mastectom	y with axillary cle	arance					
62B1 Berlin-Buch A		105/123	96/132	8.2	43-1		
64B Oslo X-ray	BW+AF+IMC	96/110	80/93	0.3	39-4		
64E Oslo Co-60	AF+IMC	81/99	73/98	-2-4	33-8		
69A Heidelberg X	RT AF+IMC	38/41	24/27	0-8	11-8		->
71B Stockholm A	* BW+AF+IMC	431/639	2(231/321)	-20-6	134-9		
71D SASIB	(BW)+AF+IM0		72/186	8-2	35-0		-
73C Mayo 70-56-		0 93/121	92/120	-5-2	38-5		
3E2 INT Milan 1	AF+IMC	10/15	3/7	2.3	2.2		\rightarrow
4Ds DFCI Boston	†BW+AF	57/103	55/105	4.0	25-2		-
74Q Piedmont OA A2+3 SECSG 1	tBW+AF+IMC	C 85/144 60/127	75/136 69/130	5·4 -3·7	35-0 26-9		
76C Glasgow	TBW+AF+IMC	78/112	87/107	-5-1	26-9		
77J2 MD Ander. 7	30B †BWS+AF+IMC		30/54	7.7	11-1		•>
78A S Swedish B	CG †BW+AF+IMC	154/241	151/233	-10-4	67-0	_	
78B ₂ Toronto-Edm	ont. † AF+IMC	15/28	14/22	0.3	4.7		->
8G1 BCCA Vanco		78/164	92/154	-13-1	39-9		
8Q2 Düsseldorf U	tBW+AF+IMC	17/34	24/54	3.3	7-8		\rightarrow
79F Coimbra G2+3 Metaxas Athe	†BW+AF+IMC ens †BW+AF+IMC	41/62 11/25	43/62 21/36	0.4	17-2		
32+3 Metaxas Atri IOS1 Helsinki	TBW+AF+IMC TBW+AF+IMC	24/47	25/52	-3-0	10-6		~
30W NSABC Israe		23/54	20/58	2.0	9-5		_
82B Danish BCG		441/824	528/825	-63-6	221.9		
82C Danish BCG		428/649	480/656	-33.7	205-4		
320 ECOG EST3		111/171	99/161	4.9	47.2		
	rmany †BW+AF+IMC	46/98	48/101	-1.6	21.1		
	-						
(b) Sub	total *	2640/	2763/	-111.7	1131.3		1.03
(-)		4254	4251			2p = 0.000	60
		(62-1%)	(65-0%)				
	y with axillary sa	molina					
			04/40	4-	10.1		
73A Wessex	BW+AF+IMC BW+AF	32/37 23/36	34/40 30/41	-4-5 -3-5	12-1		
OFF Mattingh		23/36 14/22	30/41 8/22	-3·5 4·0	11-1 3-7		
85F Nottingham	Various		0/22		0.1	1	
	Various	14/22					\rightarrow
1+5+6 CRC, UK		14/22 69/	72/	-4.0	27.0	0.86 (SE 0	→)•18
			72/ 103	-4-0	27.0		
+5+6 CRC, UK		69/	103	-4-0	27.0	0.86 (SE 0 2p = 0.4	
₊₅₊₆ CRC, ÜK I (c) Subtot a	al	69/ 95	103	-4-0	27.0		
uter (c) Subtota (c) Subtota (d) Mastectom	al y alone	69/ 95 (72-6%)	103 (69-9%)				
4+5+6 CRC, ÜK ■ (c) Subtota (d) Mastectom 45689 NSABP B-03	al y alone * AF+IMC	69/ 95 (72-6%) ^{205/286}	103 (69-9%) 2(109/160)	2.7	58-9		
4+5+6 CRC, ÜK ■ (c) Subtota (d) Mastectom 45689 NSABP B-03 70A1 Manchester F	al y alone * AF+IMC RBS1 BW+AF+IMC	69/ 95 (72-6%) 205/286 272/355	103 (69-9%) 2(109/160) 285/359	2.7 -11.4	58-9 129-1		
	al y alone * AF+IMC ABS1 BW+AF+IMC idge BW+AF+IMC	69/ 95 (72.6%) 205/286 272/355 294/380	103 (69-9%) 2(109/160) 285/359 304/375	2:7 -11:4 -12:6	58-9 129-1 135-5		
cr CRC, UK (c) Subtota (c) Subtota (d) Mastectom	y alone * AF+IMC ABS1 BW+AF+IMC Idge BW+AF+IMC TBW+AF+IMC	69/ 95 (72-6%) 205/286 272/355 294/380 4/5	103 (69-9%) 2(109/160) 285/359 304/375 3/7	2.7 -11.4 -12.6 0.5	58-9 129-1 135-5 0-3		
	y alone • AF+IMC BBS1 BW+AF+IMC idge BW+AF+IMC †BW+AF+IMC \$ t AF+IMC	69/ 95 (72-6%) 205/286 272/355 294/380 4/5 20/47	103 (69-9%) 2(109/160) 285/359 304/375 3/7 23/45	2.7 -11.4 -12.6 0.5 0.4	58-9 129-1 135-5 0-3 8-5		
cr CRC, UK (c) Subtota (c) Subtota (d) Mastectom	y alone • AF+IMC BBS1 BW+AF+IMC idge BW+AF+IMC †BW+AF+IMC \$ t AF+IMC	69/ 95 (72-6%) 205/286 272/355 294/380 4/5	103 (69-9%) 2(109/160) 285/359 304/375 3/7	2.7 -11.4 -12.6 0.5	58-9 129-1 135-5 0-3	2p = 0.4	¦ →
(c) Subtot: (c) Subtot: (c) Nastectom (d) Mastectom (sease NSABP B-03 70A1 Manchester H 70B Kings/Cambr 85Z Tokyo Cil P 88U Tokyo Cil N	y alone * AF+IMC aBS1 BW+AF+IMC tidge BW+AF+IMC 1BW+AF+IMC \$ † AF+IMC 2 † AF+IMC	69/ 95 (72-6%) 205/286 272/355 294/380 4/5 20/47 26/50	103 (69-9%) 2(109/160) 285/359 304/375 3/7 23/45 28/50	2:7 -11:4 -12:6 0:5 0:4 -1:3	58-9 129-1 135-5 0-3 8-5 11-6	2p = 0.4	¦ →
(c) Subtot: (c) Subtot: (c) Subtot: (d) Mastectom (d) Mastectom (d) Mastectom (d) Mastectom (d) Mastector	y alone * AF+IMC aBS1 BW+AF+IMC tidge BW+AF+IMC 1BW+AF+IMC \$ † AF+IMC 2 † AF+IMC	69/ 95 (72-6%) 205/286 272/355 294/380 4/5 20/47 26/50 821/	103 (69-9%) 2(109/160) 285/359 304/375 3/7 23/45 28/50 861/	2.7 -11.4 -12.6 0.5 0.4	58-9 129-1 135-5 0-3 8-5 11-6	2p = 0.4	⊶)•05
(d) Mastectom (d) Mastectom ISS88 NSABP B-03 70A1 Manchester H 70B Kings/Cambr 845Z Tokyo CiH P. 88U Tokyo CiH N	y alone * AF+IMC aBS1 BW+AF+IMC tidge BW+AF+IMC 1BW+AF+IMC \$ † AF+IMC 2 † AF+IMC	69/ 95 (72-6%) 205/286 272/355 294/380 4/5 20/47 26/50 821/ 1123	103 (69-9%) 2(109/160) 285/359 304/375 3/7 23/45 28/50 861/ 1156	2:7 -11:4 -12:6 0:5 0:4 -1:3	58-9 129-1 135-5 0-3 8-5 11-6	2p = 0.4	-→ 0-05
(c) Subtot: (c) Subtot: (c) Nastectom (d) Mastectom (sease NSABP B-03 70A1 Manchester H 70B Kings/Cambr 85Z Tokyo Cil P 88U Tokyo Cil N	y alone * AF+IMC aBS1 BW+AF+IMC tidge BW+AF+IMC 1BW+AF+IMC \$ † AF+IMC 2 † AF+IMC	69/ 95 (72-6%) 205/286 272/355 294/380 4/5 20/47 26/50 821/ 1123	103 (69-9%) 2(109/160) 285/359 304/375 3/7 23/45 28/50 861/	2:7 -11:4 -12:6 0:5 0:4 -1:3	58-9 129-1 135-5 0-3 8-5 11-6	2p = 0.4	⊶)•05
(c) Subtot: (c) Subtot: (c) Nastectom (d) Mastectom (sease NSABP B-03 70A1 Manchester H 70B Kings/Cambr 85Z Tokyo Cil P 88U Tokyo Cil N	y alone * AF+IMC aBS1 BW+AF+IMC tidge BW+AF+IMC 1BW+AF+IMC \$ † AF+IMC 2 † AF+IMC	69/ 95 (72-6%) 205/286 272/355 294/380 4/5 20/47 26/50 821/ 1123	103 (69-9%) 2(109/160) 285/359 304/375 3/7 23/45 28/50 861/ 1156	2:7 -11:4 -12:6 0:5 0:4 -1:3	58-9 129-1 135-5 0-3 8-5 11-6	2p = 0.4	→ 0-05
	I y alone * AF+IMC IBS1 BW+AF+IMC #BW+AF-IMC 15W+AF-IMC 2 † AF+IMC al *	69/ 95 (72-6%) 205/286 272/355 294/380 4/5 20/47 26/50 821/ 1123	103 (69.9%) 22(109/160) 225/359 304/375 3/7 23/45 28/50 861/ 1156 (74.5%)	2:7 -11:4 -12:6 0:5 0:4 -1:3 -21:7	58-9 129-1 135-5 0-3 8-5 11-6 343-8	2p = 0.4	→ 0-05
(d) Mastectom (d) Mastectom (see NSABP B-03 (An Manchester 1 708 Kings/Cambr 7804 Soctish D 882 Tokyo CH P 880 Tokyo CH N (d) Subtor	y alone * AF+IMC aBS1 BW+AF+IMC tidge BW+AF+IMC 1BW+AF+IMC \$ † AF+IMC 2 † AF+IMC	69/ 95 (72-6%) 205/286 272/355 294/380 4/5 20/47 26/50 821/ 1123 (73-1%)	103 (69.9%) 2(109/160) 285/359 304/375 23/45 28/50 861/ 1156 (74.5%)	2:7 -11:4 -12:6 0:5 0:4 -1:3	58-9 129-1 135-5 0-3 8-5 11-6 343-8	2p = 0.4	→)•05 2
	I y alone * AF+IMC IBS1 BW+AF+IMC #BW+AF-IMC 15W+AF-IMC 2 † AF+IMC al *	69/ 95 (72-6%) 205/286 272/355 294/30 4/5 20/47 26/50 821/ 1123 (73-1%) 3794/ 6074	103 (69.9%) 22(109/160) 225/359 304/375 3/7 23/45 28/50 861/ 1156 (74.5%)	2:7 -11:4 -12:6 0:5 0:4 -1:3 -21:7	58-9 129-1 135-5 0-3 8-5 11-6 343-8	2p = 0.4	→)•05 2
(d) Mastectom (d) Mastectom (see NSABP B-03 (An Manchester 1 708 Kings/Cambr 7804 Soctish D 882 Tokyo CH P 880 Tokyo CH N (d) Subtor	Il y alone · AF+IMC BSI BW+AF+IMC BSI BW+AF+IMC IBW+AF+IMC ≥ t AF+IMC al * (a + b + c + d) *	69/ 95 (72-6%) 205/286 272/355 294/30 4/5 20/47 26/50 821/ 1123 (73-1%) 3794/ 6074	103 (69.9%) 2(109/160) 285/359 304/375 28/50 3/7 23/45 28/50 861/ 11566 (74-5%) 4004/ 6122	2:7 -11:4 -12:6 0:5 0:4 -1:3 -21:7	58-9 129-1 135-5 0-3 8-5 11-6 343-8	2p = 0.4	→)•05 2
CRC, ÜK (c) Subtota (c) Subtota (d) Mastectom NSABP B-03 70A: Manchester 1 70B: Kings/Cambr 70B: Kings/Cambr 82Z Tokyo CIH P 82Z Tokyo CIH P (d) Subtof (d) Subtof Total 99% or	l y alone → AF-IMC BSI BW+AF-IMC BSI BW+AF-IMC 15BV+AF-IMC 3 ↑ AF-IMC 2 ↑ AF-IMC 2 ↑ AF-IMC (a + b + c + d) * > 95% Cl	69/ 95 (72-6%) 205/286 272/355 294/380 4/5 204/7 28/50 821/ 1123 (73-1%) 3794/ 6074 (62-5%)	103 (69-9%) 26/369 304/375 37 23/45 28/50 861/ 1156 (74-5%) 4004/ 6122 (65-4%)	2.7 -11.4 -12.6 0.4 -1.3 -21.7 -163-1	58-9 129-1 135-5 0-3 8-5 11-6 343-8	2p = 0.4	→)•05 2
Here CRC, UK (c) Subtota (c)	y alone AF+IMC · AFBSI BW+AF+IMC BSI BW+AF+IMC ISW+AF+IMC ISW+AF+IMC 2 t AF+IMC t AF+IMC t AF+IMC t AF+IMC t AF+IMC t BW+AF+IMC t BW+AF+IMC	69/ 95 (72-6%) 205/286 272/355 294/380 4/5 20/47 28/50 821/ 1123 (73-1%) 3794/ 6074 (62-5%) (62-5%) xotals: χ_2^2 ;	103 (69-9%) 22(109/160) 225/359 304/375 37 23/45 28/50 861/ 1156 (74-5%) 4004/ 6122 (65-4%) = 1-8; p =	2:7 -11:4 -12:6 0:4 -1:3 -21:7 -163:1	58-9 129-1 135-5 0-3 8-5 11-6 343-8 1629-8	2p = 0.4	→ 0-05 2 0-02
(d) Mastectom sear NSABP B-0 Mastectom sear NSABP B-0 708 Kings/Cambr 708 King	l y alone → AF-IMC BSI BW+AF-IMC BSI BW+AF-IMC 15BV+AF-IMC 3 ↑ AF-IMC 2 ↑ AF-IMC 2 ↑ AF-IMC (a + b + c + d) * > 95% Cl	69/ 95 (72-6%) 205/286 272/355 294/380 4/0 20/47 28/50 821/ 1123 (73-1%) 3794/ 6074 (62-5%) (62-5%) cotals: χ^2_3 ;	103 (69-9%) 2(109/160) 285/359 304/375 37 23/45 28/50 861/ 1156 (74-5%) 4004/ 6122 (65-4%) = 1-8; p = = 52-2; p	2:7 -11.4 -12.6 0.5 0.4 -1.3 -21.7 -163.1 0.6 = 0.03	58-9 129-1 135-5 0-3 8-5 11-6 343-8 1629-8	2p = 0.4 2p = 0.4 0.94 (SE 0 2p = 0.2 0.90 (SE 0 2p = 0.000 2p = 0.000	→ 0-05 2 0-02

Webfigure 9a: 'More' surgery versus 'less' surgery, in women with node-negative disease (event rate ratios, one line per trial)

Ye and s	ear Code study name	Surgery D Radioth	ifference‡ herapy0	Allocated 'More'	Allocated 'Less'	Logrank O-E	Variance of O-E		annual event rates ore' : 'Less'
(a) II	MC removal								
63D	Internat. Co-op			18/3746	10/3967	3-5	6-8	_	
700	0	Na	RT	(0·5%/y) 0/418	(0·3%/y) 1/406	~ ~	~~		
730	Chicago U.		RT	(0-0%/y)	(0·2%/y)	-0-4	0-2		^
	(a) Subtotal			18/ 4164	11/ 4373	3-2	7.0		1.57 (SE 0.48
	5-year risl	k		4.7%	4.0%				2p = 0.2
<i>a</i>		-1	.		DT				
	PecM remov								
(6Q2	Berlin-Buch	Pe	RT	1/369 (0-3%/y)	4/449 (0·9%/y)	-1-2	1.2 —		
91R1	CAMS China	Pe		-/5486	(0·9%/y) -/5449	(no d	data)		
			optnl	(0·2%/y)	(0·3%/y)		,		
	(b) Subtotal	with dat	a §	1/ 369	4/ 449	-1-2	1.2 _		0.36 (SE 0.57
	5-year risł	‹		2•6%	7•1%				2p = 0·3
(c) A	C vs not								
67B1	Cardiff		ec)+Ax RT	11/724 (1·5%/y)	18/546 (3·3%/y)	-3-6	6.7		
67C1	Groote Schuur	Pe	c+Ax RT	3/206 (1.5%/y)	8/232 (3·4%/y)	-1-7	2-3 -		
71C1	NSABP B-04	Pe	c+Ax BT	35/3949 (0-9%/y)	94/3335 (2·8%/y)	-31-5	29-2		
72A	WSSA Glasgov			15/510 (2-9%/y)	12/565 (2·1%/y)	2.7	5.7		
•	(c) Subtotal			64/ 5389	132/ 4678	-34-1	44 ·0	\Diamond	0.46 (SE 0.10 2p < 0.00001
	5-year risł			11•9%		-			•
	lastectomy								
76B1	NSABP B-06 A		+Ax3 RT	54/4825 (1·1%/y)	152/3385 (4·5%/y)	-55-3	44-3		
	(d) Subtotal			54/ 4825	152/ 3385	-55-3	44-3	\Leftrightarrow	0.29 (SE 0.09
	5-year risl	k		10.9%					2p < 0.00001
	lastectomy	+ AC vs	BCS + A	C, both v					
82A	CRC, UK	BT	V+AF+IMC	2/263 (0-8%/y)	4/250 (1-6%/y)	-0-4	1.4 -		
3J2+3	Danish BCG 82	2TM BT		0/97	0/83 (0-0%/y)				
	(e) Subtotal			2/ 360	4/ 333	-0-4	1.4		0.74 (se 0.74
	5-year risl	k		5•7%	5•2%				2p = 0.7
_	99% or 🖘	95% CI					_		

Year Code Surg					irg. deaths	Batio of an	nual death rates
and study name R	ery Difference‡ adiotherapy≎	'More'	'Less'	0-E	of O-E		e' : 'Less'
(a) IMC removal vs r	not, neither w	ith RT					
63D Internat. Co-op.	IMC No RT	94/209	89/217	2-6	41.7		
73D Chicago U.	IMC No RT	(45-0%) 5/34 (14-7%)	(41-0%) 7/34 (20-6%)	-1-0	2.6 –		
(a) Subtotal		99/ 243 (40-7%)	96/ 251 (38-2%)	1.6	44-3		1·04 (se 0·15) 2p = 0·8
(b) PecM removal vs	not, both se	me BT c	or no BT				
76Q2 Berlin-Buch	Pec	20/49	18/56	3-4	8-6		
	No RT	(40-8%)	(32-1%)				
91R1 CAMS China	Pec RT optni	129/977 (13-2%)	138/978 (14-1%)	-5-0	64-6		
(b) Subtotal		149/ 1026 (14-5%)	156/ 1034 (15·1%)	-1.6	73-2	~	0.98 (SE 0.12) 2p = 0.8
(c) AC vs not							
67B1 Cardiff	(Pec)+Ax No RT	24/61 (39-3%)	35/61 (57-4%)	-4-8	13-6		
67C1 Groote Schuur	Pec+Ax	10/21	20/30	-2-8	6-1		
71C1 NSABP B-04	No RT Pec+Ax No RT	(47-6%) 155/389	(66-7%) 177/384	-9-3	76-1	—	-
72A WSSA Glasgow	Ax BW	(39-8%) 56/101 (55-4%)	(46-1%) 56/107 (52-3%)	5-6	24.1	—	• •
(c) Subtotal		245/ 572	288/ 582 (49-5%)	-11.3	119-9	~	0.91 (SE 0.09) 2p = 0.3
(d) Mastectomy + A		C neith	or with D	т			
76B1 NSABP B-06 N-	BT+Ax3 No RT	131/432 (30-3%)	157/432 (36-3%)	-9-6	69-4		•—
(d) Subtotal		131/ 432	157/ 432 (36-3%)	-9.6	69-4	V	0.87 (SE 0.11) 2p = 0.3
(e) Mastectomy + A	- wa BCE - A	C hoth	with DT				
82A CRC, UK	BT	19/49	15/51	1-3	7.9		
	BW+AF+IMC	(38-8%)	(29-4%)				
3J2+3 Danish BCG 82TM	BT BW+AF+IMC	2/10 (20-0%)	3/9 (33-3%)	0-1	0.9 —		*
∎ (e) Subtotal		21/ 59 (35-6%)	18/ 60 (30-0%)	1.3	8-8		1.17 (SE 0.36 2p = 0.6
🖶 99% or <> 95%	S CI				0	0.5	1.0 1.5 2.0

Any death

		Deaths		More' Su		Dati	f annual -	oth rote -	
Year Code and study name	Surgery Difference‡ Radiotherapy	Allocated 'More'	Allocated 'Less'	Logrank O-E	Variance of O-E		f annual de More' : 'Le		
(a) IMC removal	vs not, neither w	ith RT							
63D Internat. Co-op		133/209	142/217	-3-0	63-4	-	-	_	
73D Chicago U.	No RT IMC	(63-6%) 8/34	(65-4%) 11/34	-2-2	4.1				
73D Chicago U.	No RT	6/34 (23-5%)	(32-4%)	-2-2	4-1				
			153/					0.93 (SE 0·12
(a) Subtotal		141/ 243	251	-5-2	67.5			•	= 0.5
			(61-0%)					2p	= 0.9
(b) PecM remov	al vs not, both s	ame BT c	r no BT						
76Q2 Berlin-Buch	Pec	20/49	18/56	3-4	8.6	_			>
	No RT	(40-8%)	(32-1%)						
91R1 CAMS China	Pec	140/977	144/978	-2-8	68-8			_	
	RT optnl	(14-3%)	(14-7%)						
(b) Subtotal		160/	162/	0.6	77.4			_ 1.01 (se 0.11
_ 、/		1026	1034					2p	= 0-9
		(15-6%)	(15.7%)						
(c) AC vs not									
67B1 Cardiff	(Pec)+Ax	41/61	49/61	-7-2	19-8			-	
67C1 Groote Schuur	No RT Pec+Ax	(67-2%) 14/21	(80-3%) 26/30	-1-8	7.6		-		
	No RT	(66-7%)	(86-7%)	-1-0	7.0				
71C1 NSABP B-04	Pec+Ax	259/389	256/384	5-0	117-3		_		
	No RT	(66-6%)	(66-7%)						
72A WSSA Glasgov	v Ax BW	56/101 (55-4%)	56/107 (52-3%)	5-6	24-1			-	
		370/	387/					1.01 (SE 0.08
(c) Subtotal		572	582	1.5	168-9		-	•	= 0.9
		(64.7%)	(66-5%)					20	- 0-3
(d) Mastectomy	+ AC vs BCS + A	C, neith	er with R	т					
76B1 NSABP B-06 A		169/432	184/432	-8-8	84-8	-			
	No RT	(39-1%)	(42-6%)				_		
(d) Subtotal		169/	184/	-8-8	84-8			0.90 (se 0.10
		432	432		04.0			20	= 0-3
		(39-1%)	(42-6%)						
(e) Mastectomy	+ AC vs BCS + A	C, both	with RT						
82A CRC, UK	BT	19/49	15/51	1-3	7.9				>
	BW+AF+IMC		(29-4%)						
3J2+3 Danish BCG 82	TM BT BW+AF+IMC	2/10 (20-0%)	3/9 (33-3%)	0-1	0.9 —				
(-) C		21/	18/						
 (e) Subtotal 		59	60	1.3	8-8			-1.17 (se 0.36
		(35-6%)	(30.0%)					2p	= 0-6
- ■ - 99% or <⊃>	95% CI				_				
■ 00.0 GI <_>					0	0.5	1.0	1.5	2.0
									orse/

§ 1 trial with no data does not contribute to subtotals or to the overall total (allocated 'More' Surg.: 5486; allocated 'Less' Surg.: 5449) ‡ IMC = internal mammary chain, Rec - pectoral muscles, Xx = axilla, BT = breast tissue. Surgerés in brackets were not always different between treatment arms. © Similar addottenzy regimes given in DOTH surgers. BWV=breast(breast wall, AF=Aultimes, BMC)=Internal mammary chain.

Webfigure 9b: 'More' surgery versus 'less' surgery, in women with node-positive disease

(event rate ratios, one line per trial)

Ye	ar Code Su	rger	v Differencet	Allocated	nan-years Allocated	Logrank	Variance	Ratio		al event rates
and	study name	Rad	lotherapy0	'More'	'Less'	Ŏ-Е	of O-E		'More'	: 'Less'
(a) I	MC removal vs	s no	t, neither w	ith RT						
63D	Internat. Co-op.		IMC	46/2441	55/2377	-2-9	23-8	-		
720	Chicago U.		No RT IMC	(1·9%/y) 0/212	(2-3%/y) 0/201					
730	Chicago O.		No RT	(0-0%/y)	(0-0%/y)					
										0.88 (se 0.19)
	(a) Subtotal			46/ 2653	55/ 2578	-2-9	23.8	-	-	
	e									2p = 0·6
	5-year risk			19•1%	21•3%					
(b) F	PecM removal	vs r	not, both sa	me RT o	r no RT					
67C2	Groote Schuur		Pec	5/134	9/173	0.0	2-0			•
	Northwest UK		No RT Pec	(3·7%/y)	(5-2%/y)	-0-4	24-4			
69D	NORTHWEST UK		No RT	54/1859 (2·9%/y)	49/1843 (2-7%/v)	-0-4	24-4	-		
76Q2	Berlin-Buch		Pec	4/147	7/153	-0-1	2-0			>
			No RT	(2·7%/y)	(4-6%/y)					
91R1	CAMS China		Pec	-/5708	-/5607	(no i	data)			
			RT optnl	(0-4%/y)	(0-4%/y)					
	(b) Subtotal wi	ith d	ata 8	63/	65/	-0-5	28-4			<u>0</u> ·98 (se 0·19)
-	(=) ======			2140	2169	0.0	2014			2p = 0-9
	5-year risk			24•9%	25•3%					
(c) 4	AC vs not									
• •	Addenbrooke's	+	Pec+Ax	7/1148	15/1218	-3-3	5-4			
500	Augenbrookea		BW+AF+IMC	(0-6%/v)	(1.2%/v)	-0-0	04			
72A	WSSA Glasgow		Ax	3/69	2/53	-0-5	0-9 —			
			BW	(4·3%/y)	(3-8%/y)					
	(-) 0			10/	17/		• •			0.55 (SE 0.30)
•	(c) Subtotal			1217	1271	-3-8	6-3			2p = 0.1
	5-year risk			7•5%	13•5%					2p = 0.1
				A		-				
	lastectomy +	AU								
76B2	NSABP B-06 N+		BT+Ax3 No RT	52/2278 (2-3%/y)	133/1606 (8-3%/y)	-47-5	37-8	-		
			NORI	(2·3%/y)	(0-3%/y)					
	(d) Subtotal			52/	133/	-47-5	37-8	\Leftrightarrow		0·28 (SE 0·09)
	.,			2278	1606					2p < 0.00001
	5-year risk			19•0%	52•1%)				
(e) N	Aastectomy + A	AC	vs BCS + A	C, both v	vith RT					
82A	CRC, UK		вт	0/71	3/72	-1-3	0.7			>
			BW+AF+IMC		(4·2%/y)					
3J2+3	Danish BCG 82TM	1	BT	8/1068	10/996	-0-2	4-3		•	
			BW+AF+IMC	(0+7%/y)	(1-0%/y)					
	(e) Subtotal			8/	13/	-1-6	5-0			0.00
-	(-)			1139	1068		••			0.73 (SE 0.38)
	5-year risk			4•2%	8•0%					2p = 0.5
٠	99% or <-> 9	5% C	Я				0	0.5	. 1	•0 1.5 2.0

	adiotherapy0	'More'	'Less'	Ö-E	k Variance of O-E	Ratio of annual death rates 'More' : 'Less'
a) IMC removal vs r		ith BT				
3D Internat. Co-op.	IMC	208/259	216/274	1.5	91-2	
	No RT	(80.3%)	(78-8%)			T
3D Chicago U.	IMC	14/27	17/28	-2-2	6-6	
	No RT	(51.9%)	(60.7%)			
(a) Subtotal		222/	233/	-0.7	97.7	0.99 (se 0.10)
- (-)		286	302	• •	••••	2p = 0-9
		(77.6%)	(77.2%)			
o) PecM removal ve	s not, both sa	ume RT d	or no RT			
C2 Groote Schuur	Pec	15/22	18/25	0.9	6-0	
	No RT	(68-2%)	(72.0%)			
9D Northwest UK	Pec	136/278	142/256	-13-4	64-6	
Q2 Berlin-Buch	No RT Pec	(48·9%) 19/30	(55-5%) 15/28	2.9	6-4	
TOL DOMIN DUCK	No RT	(63-3%)	(53-6%)	2.0	0.4	
R1 CAMS China	Pec	260/1114	298/1112	-23-6	131-8	
	RT optnl	(23.3%)	(26-8%)			-
(1-) 01-1-1		430/	473/			0.85 (SE 0.06)
(b) Subtotal		1444	1421	-33-2	208-8	2p = 0.02
		(29.8%)	(33-3%)			20-02
c) AC vs not						
,	† Pec+Ax	74/112	78/121	2.2	32-8	-
OD Addenbrooke a	BW+AF+IMC	(66-1%)	(64-5%)	2.2	02-0	
2A WSSA Glasgow	Ax	13/17	12/16	1.0	3-1	· · · · · · · · · · · · · · · · · · ·
	BW	(76-5%)	(75-0%)			
(c) Subtotal		87/	90/	3.2	35-9	1.09 (SE 0.17)
(c) Subiotai		129	137	0.2	33.9	2p = 0.6
		(67-4%)	(65-7%)			
d) Mastectomy + A	C vs BCS + A	C. neith	er with R	т		
B2 NSABP B-06 N+	BT+Ax3	134/281	148/287	-3-5	65-1	
	No RT	(47.7%)	(51.6%)			-
		134/	148/			0.95 (se 0.12)
l (d) Subtotal		281	287	-3.5	65-1	2p = 0.7
			(51.6%)			2p = 0.7
e) Mastectomy + A		C hath				
2A CRC. UK	BT BT	11/22	13/23	0-0	5-1	
	BW+AF+IMC	(50-0%)	(56-5%)	0.0	9-1	
2+3 Danish BCG 82TM	BT	53/131	57/133	-2-3	25-1	
	BW+AF+IMC	(40-5%)	(42.9%)			
(e) Subtotal		64/	70/		20.4	0.93 (se 0.18)
		153	156	-2-3	30-1	2p = 0.7
		(41.8%)	(44-9%)			20 - 01

'More' Surg. better 'More' Surg. worse

Any doath

	ath	Deaths	Women	'More' S	urg. deaths	
Year Code study name	Surgery Differen Radiotherapy	nce‡ Allocated ☆ 'More'	Allocated 'Less'	Lograni O-E	Variance of O-E	Ratio of annual death rates 'More' : 'Less'
a) IMC removal	vs not, neith	er with RT				
63D Internat. Co-op.	IMC	227/259	239/274	-0-9	100-5	— # —
	No RT	(87-6%)	(87.2%)			
73D Chicago U.	IMC No RT	15/27 (55-6%)	18/28 (64-3%)	-1.7	6-9	
(a) Subtotal		242/ 286 (84-6%)	257/ 302 (85·1%)		107-4	0.98 (SE 0. 2p = 0.8
(b) PecM remova	l vs not. bot	h same RT o	or no RT			
37C2 Groote Schuur	Pec	19/22	22/25	1.9	7.7	-
	No RT	(86-4%)	(88-0%)	1.9		
69D Northwest UK	Pec	188/278	185/256	-8-3	86-4	
	No RT	(67-6%)	(72-3%)			-
76Q2 Berlin-Buch	Pec	19/30	15/28	2.9	6-4	
	No RT	(63-3%)	(53-6%)			
91R1 CAMS China	Pec	270/1114	307/1112	-22-8	136-4	
	RT optnl	(24-2%)	(27-6%)			_
(b) Subtotal		496/ 1444 (34-3%)	529/ 1421 (37·2%)	-26-3	236-9	0.89 (SE 0.0 2p = 0.09
(c) AC vs not						
58B Addenbrooke's	† Pec+Ax	107/112	108/121	3.1	46-5	
SOD HOUGHDIOORD S	BW+AF+		(89-3%)	0.1	40-0	-
72A WSSA Glasgow	Ax	13/17	12/16	1.0	3-1	
	BW	(76-5%)	(75-0%)			
		. ,	• •			1 00 (0
 (c) Subtotal 		120/ 129 (93-0%)	120/ 137 (87·6%)	4.0	49-6	<u>1</u> ·08 (SE 0· 2p = 0·6
(d) Mastectomy -	AC vs BCS	+ AC. neith	er with F	т		
76B2 NSABP B-06 N-		149/281	158/287	-5-0	70-4	_
	No RT	(53-0%)	(55-1%)			
(d) Subtotal		149/ 281 (53-0%)	158/ 287 (55-1%)	-5-0	70-4	0.93 (SE 0. 2p = 0.5
(e) Mastectomy +	AC vs BCS	+ AC, both	with RT			
82A CRC, UK	BT	11/22	13/23	0.0	5-1	
	BW+AF+	IMC (50-0%)	(56-5%)			
	ГМ ВТ	60/131	62/133	-1-2	28-0	_
3J2+3 Danish BCG 82	BW+AF+	IMC (45-8%)	(46-6%)			
3J2+3 Danish BCG 82		71/	75/	-1-3	33-0	0.96 (SE 0.
					33.0	2p = 0·8
3J2+3 Danish BCG 82 [°] ■ (e) Subtotal		153	156 (48-1%)			2µ = 0·8
3J2+3 Danish BCG 82 ■ (e) Subtotal ● 99% or →	95% Cl	153				2µ = 0.0

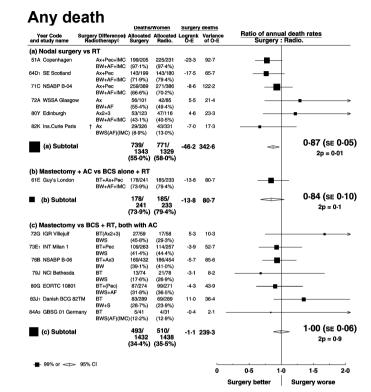
§ 1 trial with no data does not contribute to subtotals or to the overall total (allocated More' Surg: 5708; allocated Less' Surg: 5607) 1 in radical arm, mammary nodes optionally removed. In simple arm, accessible axiliary nodes optionally removed, but no en hocidisection. 2 MAC = internal mammary chain, Peo = pedoral muscle, Ax = axilia, BT = breast tissue. Surgeries in brackets were not always different between treatment arms. 5 Similar madotherapy regimens given in BOTH surgeries. BWI-breast/breast MAC = Marking-Sosa, IMC=internal mammary chain.

Webfigure 10a: Surgery versus 'less' surgery plus radiotherapy, in women with node-negative disease

(event rate ratios, one line per trial)

Isola	ted lo					e			Brea
Year Code S and study name	Surgery Difference Radiotherapy≎	-	Man-years Allocated Radio.		-		ual event rates / : Radio.		Year Code and study nan
(a) Nodal surgery	vs RT								(a) Nodal su
51A Copenhagen	Ax+Pec+IM BW+AF+IM		49/2527 (1-9%/y)	-3-9	19-4				51A Copenha
64D1 SE Scotland	Ax+Pec	26/2880	21/2204	0-5	11-3			>	64D1 SE Scotla
71C NSABP B-04	BW+AF+IM Ax+Pec	35/3949	(1-0%/y) 18/3896	8.7	13-0		-	→	71C NSABP E
72A WSSA Glasgow	BW+AF+IM Ax	C (0.9%/y) 15/510	(0-5%/y) 13/483	0-0	6-7				72A WSSA G
-	BW+AF	(2·9%/y)	(2·7%/y)						72A W33A G
80Y Edinburgh	Ax2+3 BW+AF+IM	8/1461 C (0.5%/y)	9/1442 (0-6%/y)	-0-4	4-0			\rightarrow	80Y Edinburg
82K Ins.Curie Paris	† Ax BWS(AF)(IN	34/2126	39/2045 (1·9%/y)	-1-6	17-5			-	82K Ins.Curie
(a) Subtotal		157/ 13492	149/ 12597	3.3	71.9	~		(SE 0.12) p = 0.7	(a) Subt
5-year ris	k	10•8%	9•6%				1 -	p = 0.1	
(b) Mastectomy +	AC vs BCS al	one + RT							(b) Mastecto
61E Guy's London	BT+Ax+Pec BW+AF+IM		81/2383 (3-4%/y)	-29-5	26-4				61E Guy's Lor
 (b) Subtotal 		35/ 3267	81/ 2383	-29-5	26-4	\Diamond		(SE 0·12) < 0·00001	🔳 (b) Subt
5-year ris	k	6•4%	25•3%				· ·		
(c) Mastectomy v	s BCS + RT, b	oth with A	C						(c) Mastecto
72G IGR Villejuif	BT(Ax2+3) BWS	4/867 (0·5%/y)	5/912	-0-2	2.1			>	72G IGR Villei
73E1 INT Milan 1	BT+Pec	5/4119	(0-5%/y) 27/3891	-11-4	7-9	e			73E1 INT Milan
76B NSABP B-06	BWS BT+Ax3	(0·1%/y) 45/4855	(0-7%/y) 79/4631	-16-4	28-9				73E1 INT MILAN
	BW	(0.9%/y)	(1.7%/y)	10 4	200	-			76B NSABP B
79J NCI Bethesda	BT BWS	0/858 (0-0%/y)	16/793 (2-0%/y)	-7.9	3.7 -				79J NCI Beth
80G EORTC 10801	BT+(Pec)	14/2633	(23/2577	-5-0	9-2				
83J1 Danish BCG 821	BWS+AF M BT	(0·5%/y) 19/2622	(0-9%/y) 15/2824	2.2	8-4				80G EORTC 1
8301 Danish BCG 821	BW+S	(0.7%/y)	(0-5%/y)	2.2	8-4			~	83J1 Danish B
84A3 GBSG 01 Germa	any BT BWS(AF)(IN	4/280	1/207 (0-5%/y)	1.0	1-1			>	84A3 GBSG 01
(c) Subtotal	DWG(AF)(IN	91/	166/	-37-8	61-3	\Leftrightarrow	0.54	(se 0·10)	040 0000
(0) 00010101		16234	15835	-07-0	01-0		2p -	< 0.00001	(c) Subt
5-year ris	ĸ	5•3%	8•6%						
🖶 99% or <	95% CI					0.5	1.0 1.5	2.0	- ■ - 99% or -
							1		- 99% 01 4
						Surgery better	Surgery w	orse	

Breast	cance	Pr m		alit	y Ty deaths	
Year Code and study name	Surgery Difference Radiotherapy					e Ratio of annual death rates Surgery : Radio.
(a) Nodal surge	ry vs RT					
51A Copenhagen	Ax+Pec+IMC		136/231	-13-6	54-1	
64D1 SE Scotland	BW+AF+IMC Ax+Pec BW+AF+IMC	90/199	(58-9%) 95/180 (52-8%)	-11-6	42-5	
71C NSABP B-04	Ax+Pec BW+AF+IMC	155/389	169/386 (43-8%)	-7.8	74-4	
72A WSSA Glasgo		56/101 (55-4%)	(43-87%) 42/85 (49-4%)	5.5	21-4	
80Y Edinburgh	Ax2+3 BW+AF+IMC	30/123	29/116 (25-0%)	-0-8	14-0	
82K Ins.Curie Paris	† Ax BWS(AF)(IM	29/326	43/331 (13-0%)	-7-0	17-3	
(a) Subtotal		470/ 1343 (35-0%)	514/ 1329 (38·7%)	-35-3	223-6	0.85 (SE 0.06) 2p = 0.02
(b) Mastectomy	+ AC vs BCS ald	one + RT				
61E Guy's London	BT+Ax+Pec BW+AF+IMC	122/241 (50-6%)	142/233 (60-9%)	-13-8	58-8	
(b) Subtotal		122/ 241 (50-6%)	142/ 233 (60·9%)	-13-8	58-8	0.79 (SE 0.12) 2p = 0.07
(c) Mastectomy	vs BCS + RT, bo	th with A	C			
72G IGR Villejuif	BT(Ax2+3) BWS	25/59 (42-4%)	17/58 (29-3%)	4.4	9-8	•>
73E1 INT Milan 1	BT+Pec BWS	62/263 (23-6%)	72/257 (28-0%)	-5-0	32-3	
76B NSABP B-06	BT+Ax3 BW	131/432	141/454 (31·1%)	-1-1	65-2	
79J NCI Bethesda	BT BWS	11/74 (14-9%)	19/78 (24-4%)	-3-2	7.2	
80G EORTC 10801	BT+(Pec) BWS+AF	74/274 (27.0%)	86/271 (31-7%)	-6-3	38-4	
83J1 Danish BCG 8	2TM BT BW+S	66/289 (22-8%)	58/289 (20-1%)	6-8	29-6	
84A3 GBSG 01 Gerr	nany BT BWS(AF)(IM	3/41 C) (7-3%)	0/31 (0·0%)	1.1	0-7	
(c) Subtotal		372/ 1432 (26·0%)	393/ 1438 (27·3%)	-3-2	183-1	0.98 (SE 0.07) 2p = 0.8
- ₩ - 99% or <=>	95% CI				0	0.5 1.0 1.5 2.0
						Surgery better Surgery worse



† Surgery comparison was conservative surgery with axillary clearance versus conservative surgery alone.

+ IMC = internal mammary chain, Pec = pectoral muscle, Ax = axilla, BT = breast tissue. Surgeries in brackets were not always different between treatment arms

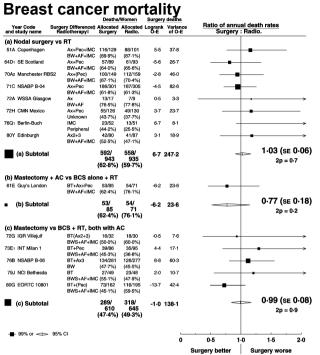
Women receiving more surgery were either given no radiotherapy or the less radical radiotherapy regimen. BW=breast/chest wall, S=scar (as site of RT boost), AF=Axilla/Fossa, IMC=Internal mammary chain. Site(s) in brackets were not always treated

† Surgery comparison was conservative surgery with axillary clearance versus conservative surgery alone

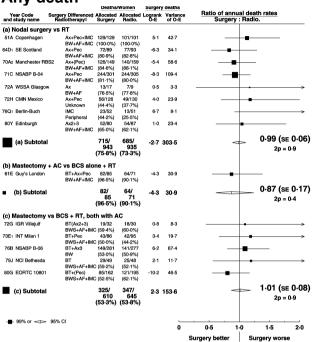
† Surgery comparison was conservative surgery with axillary clearance versus conservative surgery alone

Webfigure 10b: Surgery versus 'less' surgery plus radiotherapy, in women with node-positive disease (event rate ratios, one line per trial)

Isolated local recurrence Ratio of annual event rates Surgery : Radio. Year Code Surgery Difference‡ Allocated Allocated Logrank Variance and study name Radiotherapy≎ Surgery Radio. O-E of O-E (a) Nodal surgery vs RT 51A Copenhagen Ax+Pec+IMC 89/411 5-3 65/393 15.0 BW+AF+IMC (21.7%/v) (16.5%/v) 64D1 SE Scotland Ax+Pec 24/943 17/878 BW+AF+IMC (2-5%/y) (1-9%/y) 2-9 9-8 5-7 19-9 70A₂ Manchester RBS2 Ax+(Pec) 48/997 41/1113 BW+AF+IMC (4-8%/y) (3-7%/y) 42/2025 71C NSABP B-04 Ax+Pec 0-5 20-8 45/2268 BW+AE+IMC (2.0%/v) (2.1%/v) 0-5 79A MISSA Glasse 2/60 1/41 0.0 (4-3%/y) (2-4%/y) BW+AF 3-8 72H CMN Mexico Ax+Pec 19/867 12/955 7-3 (2.2%/v) (1.3%/// Inknown 76Q1 Berlin-Buck 2/357 2/431 0-4 0.7 Peripheral (0-6%/v) (0-5%/v) 5-1 6.5 80V Edinburgh Av2+3 18/6/6 10/835 BW+AF+IMC (2.8%/y) (1.2%/y) 248/ 6558 190/ 6671 (a) Subtotal 24.1 81.0 1.35 (SE 0.13) 2p = 0.007 5-year risk 27•6% 21•8% (b) Mastectomy + AC vs BCS alone + RT BT+Ax+Pec 17/873 31/519 BW+AF+IMC (1.9%/y) (6.0%/y) 61E Guy's Londor 10.5 0.38 (SE 0.19) 31/ 519 17/ (b) Subtotal -10-5 10-8 -873 2p = 0-001 15•8% 35•5% 5-year risk (c) Mastectomy vs BCS + RT, both with AC 72G IGR Villeiui BT(Ax2+3) 1/357 5/372 -1-6 BWS+AF+IMC(0-3%/v) (1-3%/v) -0-3 73E1 INT Milan BT+Per 3/1102 4/1382 3WS+AF+IMC (0-3%/y) (0-3%/y) 9-2 76B NSABP B-06 BT+Ax3 36/2322 18/2314 13-0 (1.6%/y) (0-8%/y) 7/409 (1-7%/y) 79J NCI Bethesd 0/40 -3-7 WS+AF+IMC (0.0%/y) 80G EORTC 10801 BT+(Pec) 7/1222 12/1361 -1-9 4.6 BWS+AF+IMC (0.6%/v) (0-9%/v 47/ 5404 46/ 5838 (c) Subtotal 1.8 22.2 1.08 (SE 0.22) 2n = 0.77•9% 4•7% 5-year risk - 99% or <>> 95% Cl 0.5 1.0 1.5 2.0 Surgery worse Surgery bette



Any death



1 IMC = internal mammary chain, Pec = pectoral muscle. Ax = axilla. BT = breast tissue. Surgeries in brackets were not always different between treatment arms

\$ IMC = internal mammary chain, Pec = pectoral muscle, Ax = axilla, BT = breast tissue. Surgeries in brackets were not always different between treatment arms

± IMC = internal mammary chain. Pec = pectoral muscle. Ax = axilla. BT = breast tissue. Surgeries in brackets were not always different between treatment arms + mod anternal mammaly clean, to be pototal modely, Ac a cone, DT = oreas assoc. Sugeries in values are not anterparticle and the second a