Supplementary Files

Study Characteristics

Where specified, 80.3% of patients had ER or PR positive, 10% had HER2 positive and 12.5% had triple negative disease. 29.9% of patients with a reported tumour grade had grade 3 carcinoma, 93.6% of patients received radiotherapy and 25% received some form of re-excision. Studies identified were from North or South America (n=26), Asia (n=11), Australasia (n=4), Europe (n=21) and the UK (n=6). One study was a retrospective analysis of two randomised controlled trials[15], whilst 67 represented observational cohort studies.

Prevalence of positive and close margins by geographical region

UK studies had the highest positive margin rate (TOI) (529/3102, 17.1%), followed by North and South America (1103/10664, 10.3%), Asia (301/4311, 7.0%), the rest of Europe (1351/13829, 9.8%) and Australia/New Zealand (59/2606, 2.3%). UK studies also had the highest rate of a positive or very close/close margin (327/990, 33.0%), followed by Asia (2586/8954, 28.9%), North or South America (5800/37192, 15.5%), Australia/New Zealand (490/3238, 15.1%) and the rest of Europe (2202/30590, 7.2%).

Results of Planned subgroup analysis

Radiotherapy and DR

Of 8 studies reporting on DR, one study included a population of patients where less than 95% received radiotherapy (63% of patients receiving radiotherapy)(19).When more than 95% of patients received radiotherapy(7 studies), positive margins (tumour on ink) were associated with increased DR (HR and 95%CI: 2.07(1.55-2.76), p<0.001, I2 =51, egger p value:0.16). Positive or close margins were associated with increased DR (HR and 95%CI:1.32(1.08-1.62), p=0.0057, I2 =21, egger p value:0.77).

Study Publication and DR

In the 5 studies published after 2010 where the majority of patients received systemic adjuvant therapy, positive margins(tumour on ink) were associated with DR (HR and 95%CI: 2.41(1.81-3.21), p<0.001, I2 =31, egger p value :0.86). Four studies found patients with a positive or close margin were associated with DR (HR and 95%CI:1.44(1.22-1.71), p<0.001, I2 =0%, egger p value :0.74).

Lymph node negative patients (N0) and DR

Node negative (N0) rates varied from 56.6%-90.7% across studies reporting on margins and DR. Meta-regression techniques confirmed that variation in node negative rates did not contribute to meta-analysis heterogeneity for both positive versus negative margin (p=0.5694) and positive and close versus negative margin analyses with respect to DR (p=0.222).

Adjuvant Chemotherapy and DR

Rates of adjuvant chemotherapy use varied from 15-75% in the included studies reporting on DR. Meta-regression techniques confirmed that variation in adjuvant chemotherapy rates did not contribute to meta-analysis heterogeneity for both positive versus negative margins (p=0.467) and positive and close versus negative margin analyses with respect to DR (p=0.320).

Supplementary Table 1– characteristics of all 33 included studies reporting on margin status and local recurrence

Study	*P/C*	*TOI*	*Total*	*%P/C*	*Number(%) Radiotherapy+*	*Number (%) aCT+*	*Factors adjusted in multivariable models*	*Adequate adjustment**
Barbieri 2011	35	NS	387	9	387(100)	116	T stage	N
Behm 2013	206	43	2300	9	1457(63.3)	1112(48.3)	Age, Radiotherapy, grade, nodal involvement, ER/PR status, hormone therapy	Y
Bhatti 2014	137	NS	603	22.7	603(100)	410	T,N stage	N
Biglia 2014	75	NS	1339	5.6	1339(100)	NS	NS	N
Bodilsen 2016	39	NS	1519	2.6	1519(100)	616(40.6)	Age, Histology, N Stage, Vascular invasion, Re-excision, Chemotherapy, Boost radiotherapy	N
Bosma 2016	1155	621	8485	13.6	8485(100)	1858(22)	Age, T stage, N Stage, Histology, grade, chemotherapy, radiotherapy	Y
Braunstein 2016	405	405	2158	18.7	2140	1049	Unadjusted	N
Carter 2016	361	NS	4693	7.7	3703(78.9)	3154	Age, N stage, Grade, LVI, molecular phenotype, Radiotherapyt	Y
Ewertz 2008	192		3647	5.3	3506(96.1)	1250(34.2)	Age, T Stage, N Stage, Radiotherapy	N
Goldstein 2003	269	269	602	44.7	602(100)	95(15.8)	Age, T stage	N
Hennigs 2016	486	NS	2657	18.3	2350(88.4)	975	Unadjusted	N
Holleczek 2019	188	188	3786	4.9	3786(100)	70% of node positive	Age, T stage, N Stage, Grade, Molecular Phenotype	Y
Horiguchi 2006	51	NS	289	17.6	NS	NR	Unadjusted	N
Jobsen 2014	472	472	3963	11.9	3963(100)	1601	Age, chemotherapy	N
Kahlert 2018	105	105	1081	9.7	1081(100)	486(45)	Age, Grade, multifocality, LVI, re-excision	N
Kreike 2008	95	78	580	16.4	580(100)	154(15)	Age, LVI	N
Liau 2010	107	NS	563	19	509(90.4)	114(20)	unadjusted	N
Livi 2007	303	303	3834	7.9	3834(100)	920(24)	Age, T stage, N Stage, Chemotherapy	N
Lupe 2011	222	62	2202	10.1	2202(100)	1915(85)	Stage, Grade, CT	Y
Maishman 2017	239	239	1395	17.1	1339(96)	1055(75.6)	Age, T stage, N Stage, Histology, Boost dose radiotherapy, focality	Y
Mcbain 2003	279	279	1544	18.1	1544(100)	1249(58)	Age, Overall Stage	N
Mitsumori 2009	358	NS	1410	25.4	1410(100)	NR	Age, T stage, N stage, RT, Molecular phenotype	Y
Petersen 1999	220	124	738	29.8	738(100)	308	Unadjusted	N
Pilewskie 2014	71	NS	535	13.3	525(98.1)	452	T stage, Chemotherapy	N
Sadek 2013	279	NS	1476	18.9	1476(100)	1256(85)	Age, Nodal status, grade, boost RT, CT	Y
Smith 2014	451	NS	5848	7.7	5848(100)	2995	Age, T stage, Grade, histology, ER status	N
Smitt 2003	55	NS	397	13.9	397(100)	282	Radiotherapy	N
Tang 2019	247	NS	1045	23.6	1045(100)	NR	ER status	N
Tyler 2018	1622	NS	10863	14.9	10863(100)	3950(36.3)	Age, Grade, Vascular invasion, N stage, Radiotherapy, histology	Y
Varghese 2008	11	11	163	6.7	79(48.5)	0	Unadjusted	N
Voogd 2001	165	165	633	26.1	633(100)	272(43)	Age, T stage, N stage, Histology, Grade, Vascular Invasion	N
Yoon 2018	208	208	3403	6.1	3403(100)	2019	Age, T stage, N stage, Histology, grade, chemotherapy	Y
Yoshida 2009	708	NS	2110	33.6	2110(100)	591	Age, T stage, N stage, LVI, Molecular pheotype, Endocrine therapy, Chemotherapy	Y

Supplementary Table 2– characteristics of all 68 included studies reporting on margin status and either local recurrence, distant recurrence or overall survival

Study	*DR*	*TOI*	*P/C*	*Total*	*%P/C*	*Margin definitions*	*Country*	*Follow up (months)*	*Included years*	*Number(percent) receiving RT*	*Number LR with positive margin*	*Number LR with negative margin*	*Number DR with positive margin*	*Number DR with negative margin*
Spivack 1994	N	44	44	258	17.1	0mm	USA	48	1982-1990	258(100)	44	214	NS	NS
Burke 1995	N	16	16	306	5.2	0mm	Australia	50.4	1982-1989	306(100)	2	6	NS	NS
Renton 1996	N		117	209	56	5mm	UK	60	1981-1990	209(100)	28	15	NS	NS
Pierce 1997	Y	33	33	398	8.3	0mm	USA	52.8	1984-1995	398(100)	3	12	2	30
Obedian 1999	N	55	102	380	26.8	0mm,2mm	USA	156	1979-1988	380(100)	6	6	NS	NS
Petersen 1999	Y	124	220	738	29.8	0mm,2mm	USA	96	1977-1992	738(100)	28	9	33	22
Touboul 1999	N	13	34	451	7.5	0mm,2mmm	France	120	1976-1993	451(100)	2	52	NS	NS
Park 2000	N		282	529	53.3	1mm	USA	96	1968-1987	529(100)	282	204	NS	NS
Kokubo 2000	Y	93	233	908	25.7	0mm,5mm	Japan	52	1987-1988	231(25.4)	11	9	NS	NS
Voogd 2001	Y	165	165	633	26.1	0mm	Europe	118	1980-1986	633(100)	23	35	80	126
Mirza 2002	Y	36	36	758	4.7	0mm	USA	108	1970-1994	758(100)	2	44	5	32
Neuschatz 2002	N	105	204	494	41.3	0mm,2mm	USA	144	1982-1994	494(100)	22	5	NS	NS
McBain 2003	N	279	279	1544	18.1	0mm	UK	60	1989-1992	1544(100)	279	1265	NS	NS
Goldstein 2003	Y	269	269	602	44.7	0mm	USA	104.4	1980-1996	602(100)	34	3	NS	NS
Smitt 2003	N		55	397	13.9	2mm	USA	60	1972-1996	397(100)	36	10	NS	NS
Karasawa 2003	Y		102	355	28.7	2mm	Japan	51.6	1987-2001	348(98.0)	4	7	3	15
Santiago 2004	N	104	184	639	28.8	0mm, 2mm	USA	180	1977-1990	639(100)	28	7	NS	NS
Leong 2004	Y		184	639	28.8	2mm	Australia	80	1979-1994	452(70.7)	39	10	NS	NS
Bellon 2005	Y	51	98	221	44.3	0mm, 1mm	USA	135	1984-1992	221(100)	NS	NS	35	27
Freedman 2005	N		294	1262	23.3	2mm	USA	180	1970-1998	1262(100)	25	47	NS	NS
Karasawa 2005	N	358	684	940	0	0mm,2mm	Japan	120	1986-2000	940(100)	39	16	NS	NS
Horiguchi 2006	Y		51	289	17.6	5mm	Japan	60	1980-2001	NS	NS	NS		NS

Kunos 2006	N		119	341	34.9	2mm	USA	56	1996-2002	341(100)	4	110	NS	NS	
Kasumi 2006	N		791	2449	32.3	5mm	Japan	78	1986-2002	987(40.3)	21	78	NS	NS	
Livi 2006	N		86	2093	4.1	2mm,5mm	Italy	62.4	2000-2008	2093(100)	11	30	NS	NS	
Livi 2007	N	284	284	2874	9.9	0mm	Italy	62.4	1980-2001	2093(72.8)	19	85	NS	NS	
Kreike 2008	Y	78	95	580	16.4	0mm,1mm	Holland	159.6	1979-1988	580(100)	44	41	NS	NS	
Besana-Ciani 2008	Y	46	46	461	10	0mm	Italy	132	1988-1992	461(100)	13	50	28		344
Ewertz 2008	Y		192	3647	5.3	5mm	Denmark	180	1989-1998	3506(96.1)	20	226	40		566
Varghese 2008	N	11	11	163	6.7	0mm	UK	102	1990-2004	79(48.5)	1	9	NS	NS	
Mitsumori 2009	N		358	1410	25.4	5mm	Japan	60	2004-2005	1410(100)	139	302	NS	NS	
Yoshida 2009	Y		708	2110	33.6	5mm	Japan	64.7	1987-2007	2110(100)	56	45	Check	NS	
Perez 2010	N		338	1228	27.5	3mm	USA	79.2	1970-1997	1228(100)	20	40	NS	NS	
Whipp 2010	N		103	218	47.2	1mm,2mm	UK	60	1997-2000	218(100)	3	0	NS	NS	
Liau 2010	Y		107	563	19	2mm	UK	58	1999-2004	509(90.4)	38	56	NS	NS	
Groot 2011	N		201	692	29	2mm	Canada	86	1991-2000	NS	19	52	NS	NS	
Lupe 2011	Y	62	222	2202	10.1	0mm, 2mm	Canada	52	2001-2003	2202(100)	11	23	NS	NS	
Barbieri 2011	N		35	387	9	5mm	Italy	59	2000-2006	387(100)	16	4	NS	NS	
Demirci 2012	N	11	38	1036	3.7	0mm,2mm	USA	117.6	1991-2000	1036(100)	NS	NS	NS	NS	
Adams 2013	N	58	62	521	11.9	0mm,1mm	USA	57.3	2001-2005	355(68.1)	12	6	NS	NS	
Cannon 2013	N	16	16	277	5.8	0mm	USA	61	2000-2006	277(100)	1	12	NS	NS	
Russo 2013	Y		177	906	19.5	2mm	USA	87.5	1998-2006	906(100)	1	12	NS	NS	
Behm 2013	N	43	206	2300	9	0mm,2mm	Australia	94.8	1997-2007	1457(63.3)	40	48	46		181
Sadek 2013	N		279	1476	18.9	2mm	USA	103.2	1992-2009	1476(100)	NS	NS	NS	NS	
Smith 2014	N		451	5848	7.7	2mm	Canada	116	1989-2006	5848(100)	16	156	NS	NS	
Bhatti 2014	N		137	603	22.7	2mm	Pakistan	47.2	1997-2009	603(100)	16	18	NS	NS	
Biglia 2014	Y		75	1339	5.6	2mm	Italy	47.5	2000-2009	1339(100)	6	37	7		139
Pilewskie 2014	Y		71	535	13.3	2mm	USA	84	1999-2009	525(98.13)	3	7	NS	NS	
Jobsen 2014	N	472	472	3963	11.9	0mm	Netherlands	105	1984-2010	3963(100)	36	148	NS	NS	
Bernardi 2014	Y		226	1192	19	2mm	Italy	82	2002-2011	532(44.6)	6	88	NS	NS	

Takahashi 2016	Y		113	306	36.9	5mm	Japan	144	1990-2002	306(100)	3	3	21		27
Dixon 2016	N		218	1239	17.6	1mm	Scotland	76.8	2000-2005	1239(100)	7	33	NS	NS	
Braunstein 2016	N	135	405	2140	18.9	0mm,2mm	USA	106	1998-2007	2140(100)	NS	NS	NS	NS	
Bodilsen 2016*	Y		39	1519	2.6	1mm	Denmark	63.6	2000-2009	1519(100)	3	122	4		122
Bodilsen 2016*	N		232	11900	1.9	2mm	Denmark	58.8	2000-2009	11900(100)	15	344	NS	NS	
Hennigs 2016	N		486	2657	18.3	1mm	Germany	60	2003-2011	2350(88.4)	24	43	NS	NS	
Carter 2016	N		361	4693	7.7	2mm	Texas	40.8	2007-2014	3703(78.9)	NS	NS	NS	NS	
Maishman 2017	Y	239	239	1395	17.1	0mm,1mm, 2mm	UK	120	2000-2008	1339(95.9)	NS	NS	NS	NS	
Kim 2017	N		93	524	17.7	2mm	Korea	84	1999-2010	407(77.68)	29	54	NS	NS	
Kahlert 2018	N	105	105	1081	9.7	0mm	Germany	124	1990-2006	1081(100)	17	78	NS	NS	
Yoon 2018	N	208	208	3403	6.1	0mm	Korea	88	2000-2008	3403(100)	10	89	NS	NS	
Guinot 2018	N		196	248	0	2mm	Spain	127	1996-2011	248(100)	28	1	21		4
Tyler 2018	Y		1622	10863	14.9	2mm	Canada	96	2002-2011	10863(100)	50	205	111		564
Clement 2018	Y		100	299	33.4	2mm,5mm	Australia	84	2007-2011	238(79.6)	6	5	NS	NS	
Hammer 2019	Y		31	2193	1.4	1mm	Austria	114	1984-1999	2193(100)	3	125	7		310
Tang 2019	N		247	1045	23.6	1mm	England	89	1997-2007	1045(100)	21	36	NS	NS	
Holleczek 2019	Y	188	188	3786	5	0mm	Germany	110	1999-2009	3786(100)	NS	NS	40		302

Abbreviations: DR: Distant recurrence data provided, TOI: Number of patients with tumour at ink, P/C: Number of patients with tumour at ink or close (within a defined margin distance), %P/C: The percentage of the total cohort with patients with tumour at ink or within a defined margin distance. *Two papers were published by Bodilsen in 2016. Data from both of these two studies did not contribute to any one analysis.

Supplementary Table 3 – Assessment of bias utilising the risk of bias in non-randomised studies tool (ROBINS)

Study	1- bias	2- selection	3- classification	4- deviation	5- missing data	6- outcome measurement	7- selection of results	Overall
Adams 2013	Moderate	Moderate	Low	Moderate	Serious - Significant concerns re missing data and ascertainment	Low	Low	Serious
Barbieri 2011	Serious- minimal adjustment for confounders	Low	Moderate	Not stated	Low	Moderate	Moderate	Serious
Behm 2013	Low	Low	Low	Low	Low	Low	Low	Low
Bellon 2005	Moderate	Low	Low	Moderate	Unknown	Low	Low	Moderate
Bernardi 2014	Moderate	Low	Low	Low	Moderate- some missing info	Low	Low	Moderate
Besana-Ciani 2008	Serious- no adjustment for confounders	Low	Low	Low	Low	Moderate	Moderate	Serious
Bhatti 2014	Low	Low	Moderate	Moderate	Low	Moderate	Low	Moderate
Biglia 2014	Low	Low	Low	Moderate	Low	Low	Low	Moderate
Bodilsen 2016	Low	Low	Low	Low	Low	Moderate	Low	Moderate
Bodilsen 2016	Low	Low	Low	Moderate	Moderate	Low	Low	Moderate
Braunstein 2016	Low	Low	Low	Low	Low	Low	Low	Low
Burke 1995	Serious- no adjustment for confounders	Low	Moderate	Moderate	Low	Low/Moderate	Low	Low
Cannon 2013	Low	Low	Low	Low	Low	Low	Low	Serious

Carter 2016	Low	Low	Low	Low	Low	Low	Low	Low
Clement 2018	Moderate	Moderate	Serious - confoundiing introduced by differenital treatment of patients with positive margins	Moderate	Low	Low	Low	Serious
Demirci 2012	Low	Low	Low	Low	Low	Low	Low	Low
Dixon 2016	Moderate	Low	Moderate	Low	Low	Low	Low	Moderate
Ewertz 2008	Low	Low	Moderate	Moderate/Low	Low	Low	Low	Moderate
Freedman 2005	Serious - no multivariable	Low	Moderate	Serious - treatment differed significantly for those with postive margins (extra RT given)	Unknown	Low	Low	Serious
Goldstein 2003	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Groot 2011	Low	Low	Low	Low	Low	Low	Low	Low
Guinot 2018	Low	Low	Moderate	Low	Low	Low	Low	Low
Hammer 2019	Serious- no adjustment for confounders	Low	Low	Low	Low	Low	Low	Serious
Hennigs 2016	Serious- minimal adjustment for confounders	Low	Low	Moderate	Moderate	Low	Low	Moderate

Holleczek 2019	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Horiguchi 2006	Low	Low	Moderate	Moderate	Low	Moderate	Low	Moderate
Jobsen 2014	Moderate	Low	Low	Moderate	Low	Low	Low	Moderate
Kahlert 2018	Low	Low	Low	Low	Low	Low	Low	Low
Karasawa 2003	Serious- no multivariate	Low	Low	Moderate	Low	Low	Moderate	Serious
Karasawa 2005	Moderate	Low	Low	Low	Low	Low	Moderate	Moderate
Kasumi 2006	Low	Low	Low	Moderate	Low	Low	Low	Low
Kim 2017	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Kokubo 2000	Low	Low	Low	Moderate	Low	Low	Low	Low
Kreike 2008	Moderate	Low	Moderate	Low	Low	Low	Moderate	Moderate
Kunos 2006	Low	Low	Low	Low	Low	Low	Low	Low
Leong 2004	Low	Low	Low	Moderate	Moderate	Moderate	Low	Moderate
Liau 2010	Serious - no adjustment for confounders	Low	Low	Low	Moderate	Low	Low	Serious
Livi 2013	Low	Low	Low	Low	Low	Low	Low	Low

Livi 2007	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Lupe 2011	Moderate	Low	Low	Low	Low	Moderate	Low	Moderate
Maishman 2017	Low	Low	Low	Low	Low	Low	Low	Low
McBain 2003	Low	Low	Low	Low	Moderate	Low		Low
Mirza 2002	Moderate	Low	Moderate	Low	Low	Low	Low	Moderate
Mitsumori 2009	Moderate	Low	Low	Unknown	Low	Low	Low	Moderate
Neuschatz 2002	Low	Low	Low	Moderate	Low	Low	Low	Moderate
Obedian 1999	Moderate	Low	Serious - large number of patients with margin data missing	Low	Low	Low	Low	Serious
Park 2000	Low	Moderate	Low	Low	Moderate	Low	Low	Moderate
Perez 2010	Serious - no multivariable	Low	Low	Low	Low	Moderate	Low	Low
Petersen 1999	Serious- no adjustment for confounders	Low	Critical- 27.7% missing margin data	Moderate	Serious/critical- missing data used as part of analysis inappropriately	Low	Low	Critical
Pierce 1997	Low	Low	Moderate	Moderate	Moderate	Low	Low	Moderate

Pilewskie 2014	Critical - excluded 10 patients developing recurrence in 1 year	Low	Moderate	Unknown	Low	Low	Moderate	Critical
Renton 1996	Moderate	Low	Serious - limited detail on pathological examination	Low	Moderate	Moderate	Low	Serious
Russo 2013	Low	Moderate	Low	Low	Low	Low	Low	Low
Sadek 2013	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Santiago 2004	Low	Low	Low	Low	Serious- 32% missing margin data	Low	Low	Serious
Smith 2014	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate
Smitt 2003	Low	Low	Low	Moderate	Serious- 20% missing margin data	Low	Low	Moderate
Spivack 1994	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Takahashi 2016	Low	Low	Low	Low	Low	Low	Low	Low
Tang 2019	Low	Low	Low	Moderate	Low	Low	Low	Moderate
Touboul 1999	Moderate	Low	Serious - large number of patients with margin data missing	Moderate	Moderate	Low	Low	Moderate
Tyler 2018	Low	Low	Low	Low	Low	Low	Low	Low
Varghese 2008	Moderate	Low	Low	Moderate	Low	Low	Moderate	Serious
Voogd 2001	Low	Low	Low	Low	Low	Low	Low	Low
Whipp 2010	Serious - no multivariable	Low	Low	Low	Low	Low	Low	Low

Yoon 2018	Low	Low	Low	Low	Low	Low	Low	Low
Yoshida 2009	Low	Low	Low	Low	Low	Low	Low	Low

Supplementary Table 4 – Sample database searching strategy utilising OVID search of medline as example

	Medline Search Term	Number of Results
1	exp Breast Neoplasms/	310059
2	breast conserving surgery.mp.	5831
3	lumpectomy.mp. or Mastectomy, Segmental/	10947
4	exp Neoplasm Recurrence, Local/ or local recurrence.mp.	145480
5	distant recurrence.mp.	3342
6	overall survival.mp.	189772
7	exp Disease-Free Survival/ or exp Survival/ or exp Progression-Free Survival/	87794
8	2 or 3	13691
9	exp "Margins of Excision"/	3201
10	margin.mp.	65050
11	4 or 5 or 6 or 7	356144
12	9 or 10	66332
13	1 and 8 and 11 and 12	678

Supplementary Table 5 – PRISMA Checklist

	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title page, 1,5
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	√
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	6,7
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	7
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	7
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Supp 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	8
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	8, Supp table 4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	8
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	8/9
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	9
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	9
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	9
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	9

	Item #	Checklist item	Location where item is reported
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	9
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	9
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	9
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	9
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	9
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	11
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	PRISMA diagram (figure 1)
Study characteristics	17	Cite each included study and present its characteristics.	Table 1/2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplementary table 1
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	11-15
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	11-15
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	11-15
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	11-15
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	11-15
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	11-15
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	11-15
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	16
	23b	Discuss any limitations of the evidence included in the review.	17

	Item #	Checklist item	Location where item is reported
	23c	Discuss any limitations of the review processes used.	17
	23d	Discuss implications of the results for practice, policy, and future research.	17/18
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	7
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	7
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	7
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Title page
Competing interests	26	Declare any competing interests of review authors.	Title page
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Title page

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Supplementary figure 1– Forest plots of margin involvement and overall survival (a) tumour on ink versus tumour not at ink (b) tumour on ink or tumour at less than 2mm from margin versus margins wider than 2mm. Abbreviations: OS: Overall survival, RE: Random effects, df: Degrees of freedom

Supplementary figure 2 – Funnel plots of margin involvement and distant recurrence. a) tumour on ink versus tumour not at ink (b) tumour on ink or tumour at less than 1mm defined versus wide margins >1mm (c) tumour on ink and <2mm margin versus wide margin >2mms (d) Tumour between 0.1 and 1mm from ink versus margins wider tha€mm (e) tumour between 0.1 and 2 mm from ink compared to wider margins >2mm (f) tumour between 1.1 and 2mm from ink margin compared to margins greater than 2mm from ink.

Supplementary –figure 3 - Funnel plots of margin involvement and local recurrence – a) tumour on ink versus tumour not at ink (b) tumour on ink or tumour at less than 1mm defined versus wide margins >1mm (c) tumour on ink and <2mm margin versus wide margin >2mms (d) Tumour between 0.1 and 1mm from ink versus margins wider €n 2mm (e) tumour between 0.1 and 2mm from ink compared to wider margins >2mm (f) tumour between 1.1 and 2mm from ink margin compared to margins greater than 2mm from ink

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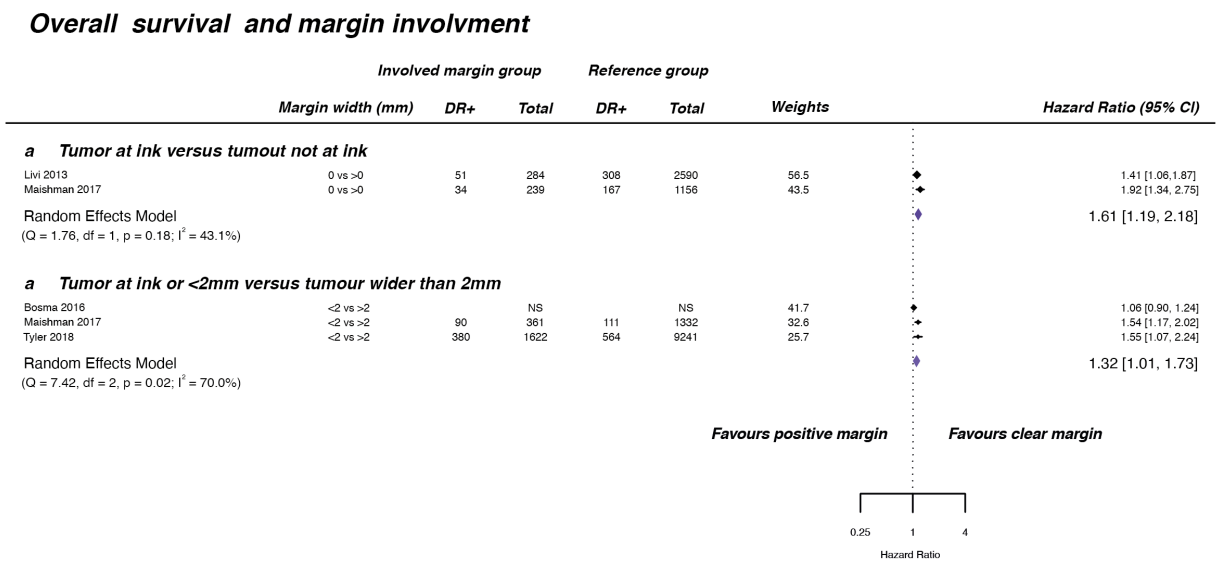
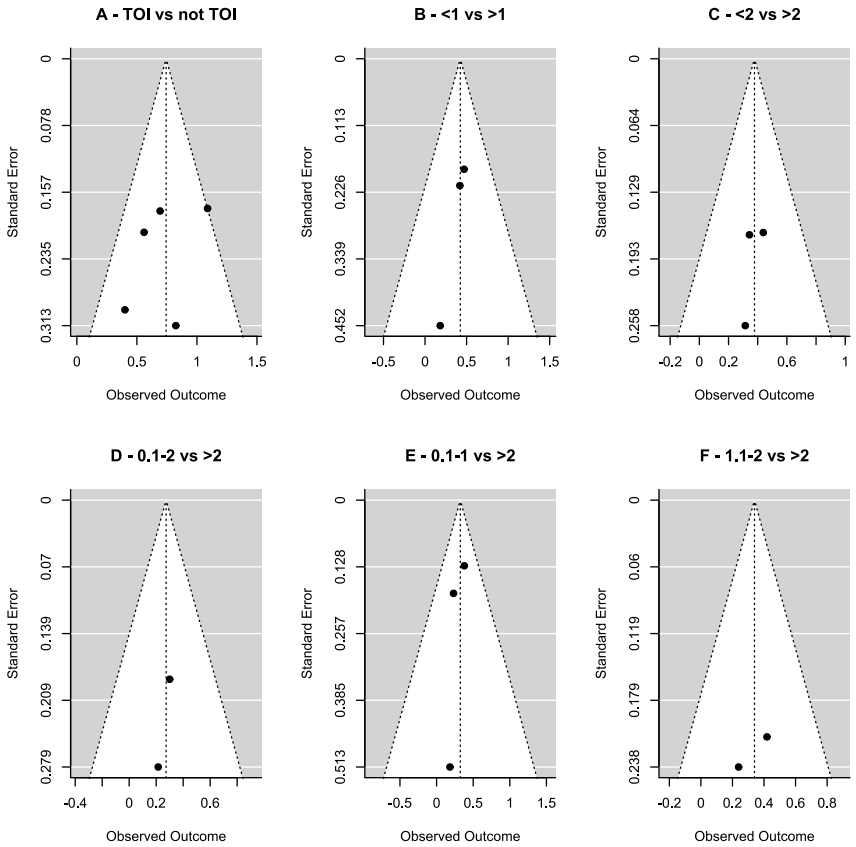
Supplementary Figure 1: Overall Breast Cancer Survival according to Margin Width.

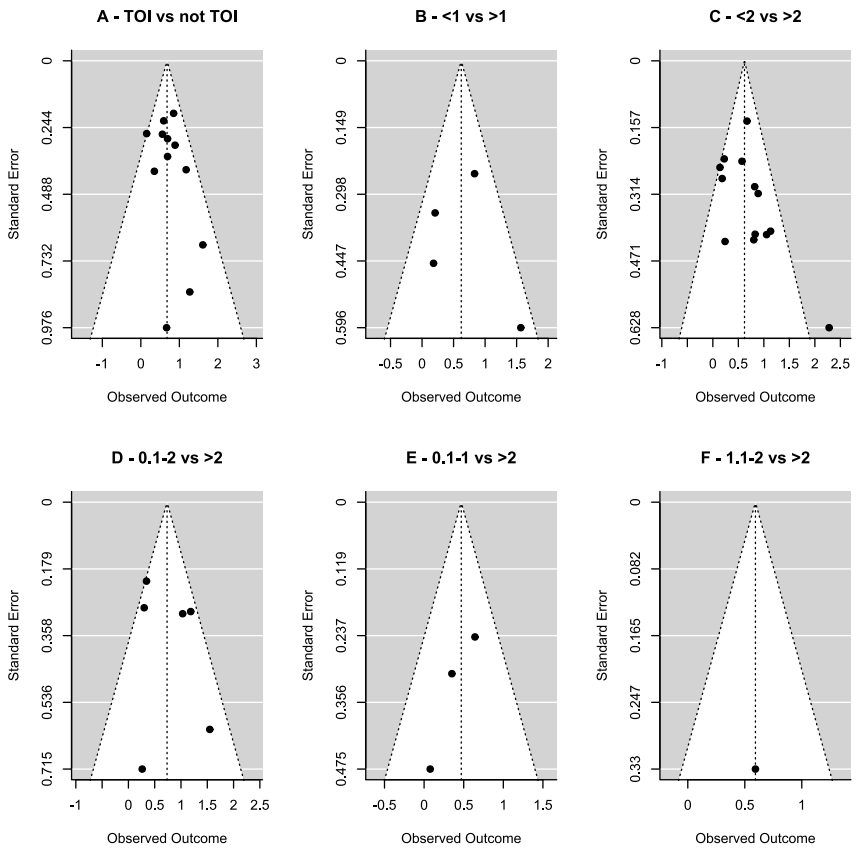


Both models showed wider margins improved overall breast cancer survival.

Supplementary Figure 2 – Funnel plots of studies reporting distant recurrence outcomes



Supplementary Figure 3 – Funnel plots of studies reporting local recurrence outcomes



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