# BCS versus mastectomy

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Survival

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Introduction

- Breast conserving surgery (BCS) was introduced in the 1980ties in RCT comparing the procedure with mastectomy
- Long term follow-up has confirmed an equal survival
  - Veronesi et al. NEJM 2002; 347: 1227-32
  - Fisher et al. NEJM; 347: 567-75
  - Blichert-Toft et al. Acta Oncol 2008; 47: 672-81
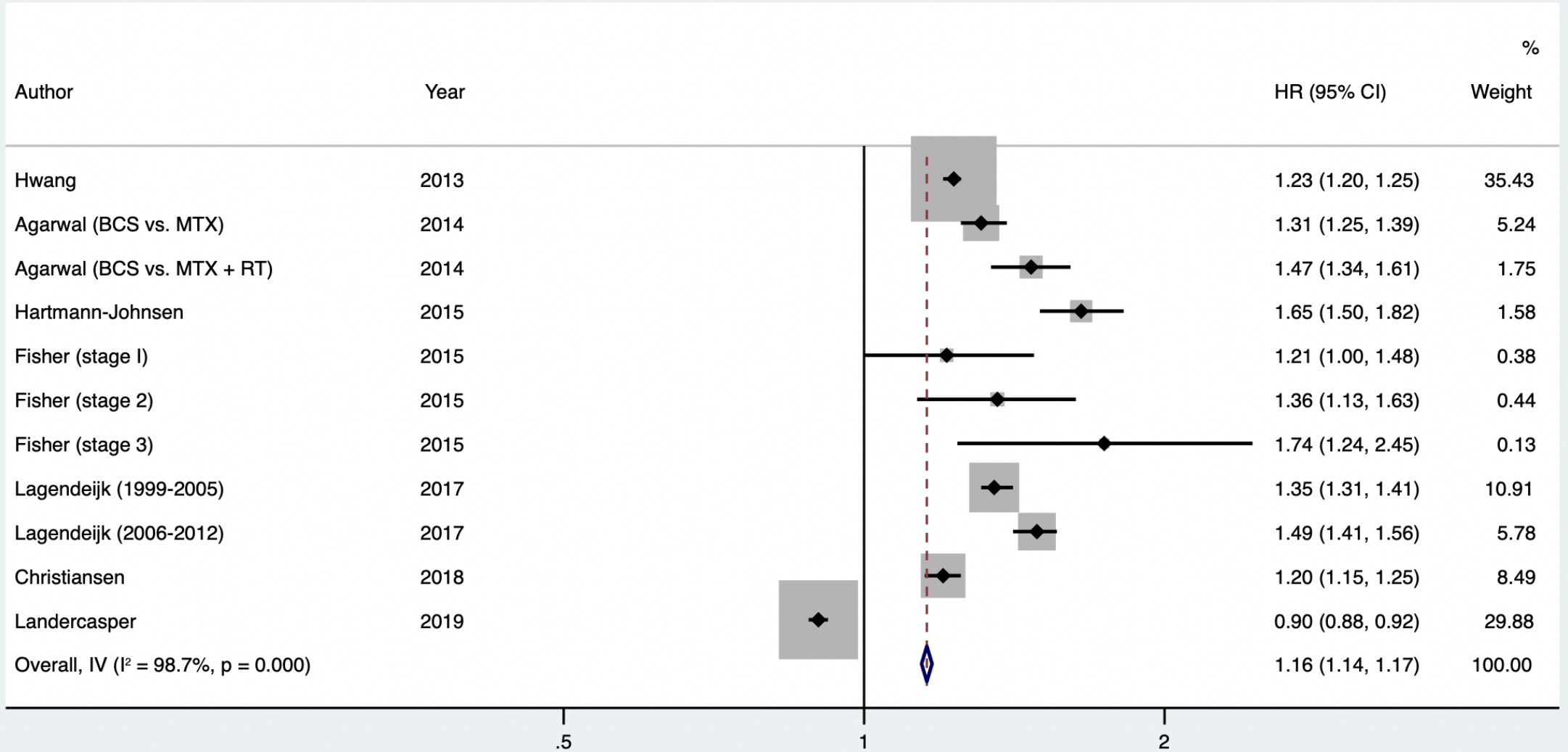
Changes in surgical treatment over time in Denmark

Change in surgical strategy over time

Mastectomy   BCS final   BCS + mast.
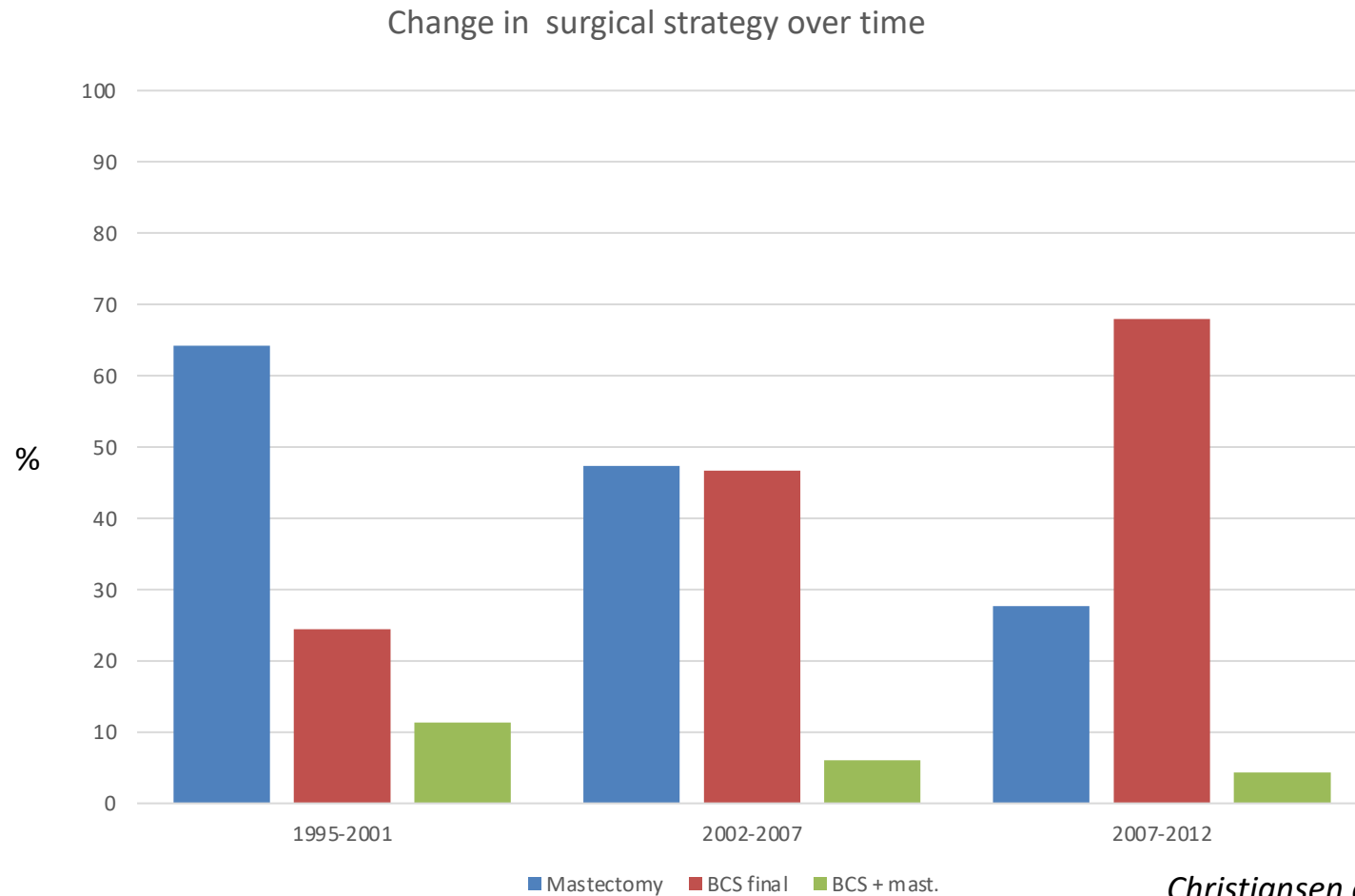
Christiansen et al. Acta Oncol 2018; 57: 19-25
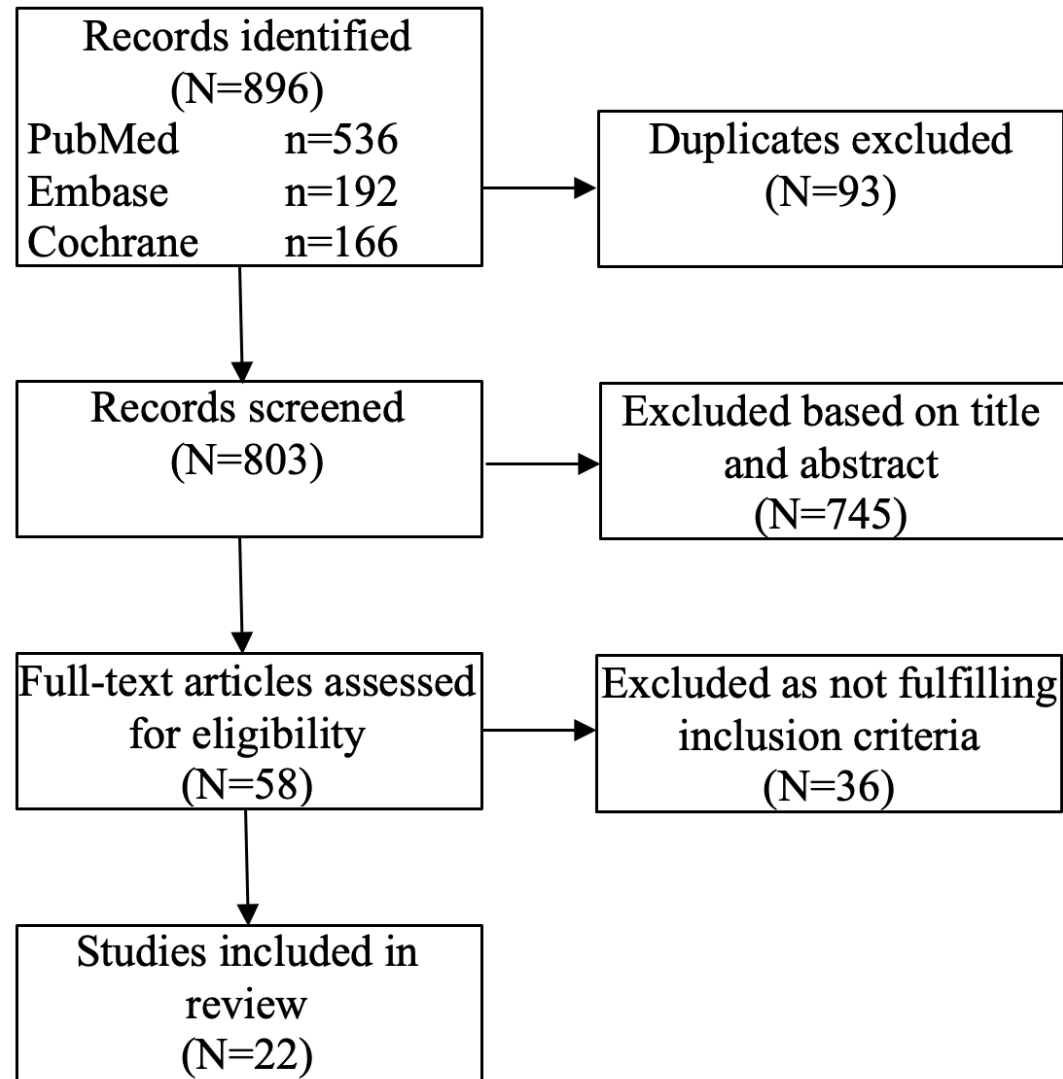
22 population-based studies

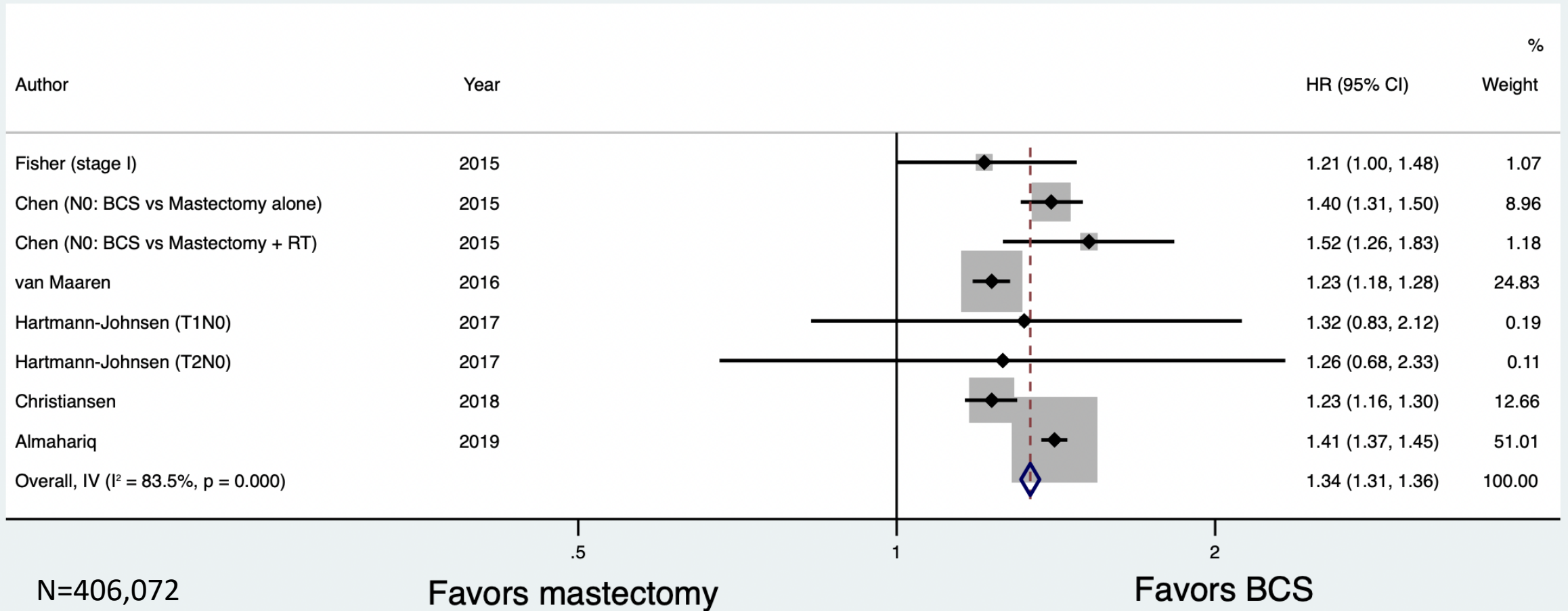| Population	N	Publications
SEER, USA	180,997	Mahmood et al. 2012; Agarwal et al. 2013; Ye et al 2015; Bleicher et al. 2016; Chen, Wang et al. 2017; Mogal et al. 2017; Li et al. 2019
NCDB, USA	1,279,841	Chen, Liu et al. 2015; Lazow 2019; Mazor 2019; Landercasper 2019; Almahariq 2020
California Cancer Registry, USA	112,514	Hwang et al. 2013
Alberta Cancer Registry, Canada	14,939	Fisher et al. 2015
Cancer Registry, Norway	19,403	Johnsen et al. 2015; Johnsen et al. 2017
Breast Cancer Screening Database, Norway	9,547	Hofwind et al. 2015
Netherlands Cancer Registry	169,970	van Maren et al. 2017; van Maren et al. 2017; Lagendeijk et al. 2017
DBCG, Denmark	58,331	Christiansen et al. 2018

Unrestricted population-based studies

Author	Year	HR (95% CI)	% Weight
Hwang	2013	1.23 (1.20, 1.25)	35.43
Agarwal (BCS vs. MTX)	2014	1.31 (1.25, 1.39)	5.24
Agarwal (BCS vs. MTX + RT)	2014	1.47 (1.34, 1.61)	1.75
Hartmann-Johnsen	2015	1.65 (1.50, 1.82)	1.58
Fisher (stage I)	2015	1.21 (1.00, 1.48)	0.38
Fisher (stage 2)	2015	1.36 (1.13, 1.63)	0.44
Fisher (stage 3)	2015	1.74 (1.24, 2.45)	0.13
Lagendeijk (1999-2005)	2017	1.35 (1.31, 1.41)	10.91
Lagendeijk (2006-2012)	2017	1.49 (1.41, 1.56)	5.78
Christiansen	2018	1.20 (1.15, 1.25)	8.49
Landercasper	2019	0.90 (0.88, 0.92)	29.88
Overall, IV (I^2 = 98.7%, p = 0.000)		1.16 (1.14, 1.17)	100.00

N=1,287,364

Favors mastectomy   Favors BCS

T1-2N0

Author	Year	HR (95% CI)	% Weight
Fisher (stage I)	2015	1.21 (1.00, 1.48)	1.07
Chen (N0: BCS vs Mastectomy alone)	2015	1.40 (1.31, 1.50)	8.96
Chen (N0: BCS vs Mastectomy + RT)	2015	1.52 (1.26, 1.83)	1.18
van Maaren	2016	1.23 (1.18, 1.28)	24.83
Hartmann-Johnsen (T1N0)	2017	1.32 (0.83, 2.12)	0.19
Hartmann-Johnsen (T2N0)	2017	1.26 (0.68, 2.33)	0.11
Christiansen	2018	1.23 (1.16, 1.30)	12.66
Almahariq	2019	1.41 (1.37, 1.45)	51.01
Overall, IV (I^2 = 83.5%, p = 0.000)		1.34 (1.31, 1.36)	100.00

.5   1   2

Favors mastectomy   Favors BCS

N=406,072

T1-3N1-2

Author	Year	HR (95% CI)	% Weight
Chen N1: (BCS vs. MTX alone)	2015	1.44 (1.31, 1.58)	12.02
Chen (N1: BCS vs. MTX + RT)	2015	1.33 (1.17, 1.51)	6.48
Chen (N2-3: BCS vs. MTX alone)	2015	1.64 (1.42, 1.88)	5.36
Chen (N2-3: BCS vs. MTX + RT)	2015	1.12 (1.00, 1.26)	7.90
van Maaren (T1N1)	2016	1.23 (1.11, 1.37)	9.53
van Maaren (T2N1)	2016	1.25 (1.14, 1.39)	10.73
van Maaren (T1-2N2)	2016	1.14 (1.01, 1.30)	6.62
Hartmann-Johnsen (T1N1)	2017	2.91 (1.30, 6.48)	0.16
Hartmann-Johnsen (T2N1)	2017	1.40 (0.69, 2.86)	0.21
Christiansen (N1)	2018	1.23 (1.15, 1.31)	24.87
Christiansen (N2)	2018	1.06 (0.97, 1.19)	10.10
Christiansen (N3)	2018	1.13 (0.99, 1.29)	6.02
Overall, IV (I^2 = 76.3%, p = 0.000)		1.24 (1.20, 1.28)	100.00

.125   1   8

Favors mastectomy   Favors BCS

N=84,582

In summary

Population	N	Hazard ratio (95% CI)
Unrestricted	1,287,364	1.16 (1.14-1.17)
T1-2N0	406,072	1.34 (1.31-1.36)
T1-3N1-2	84,582	1.24 (1.20-1.28)
Age ≤ 50	115,767	1.16 (1.11-1.21)
Age > 50	221,403	1.28 (1.24-1.32)
TNBC	31,033	1.47 (1.36-1.59)

Interaction between surgery, lymph node status and radiation therapy

	Mastectomy (N)	BCS (N)	Overall mortality		SMR	
			RR	95% CI	RR	95% CI
Node negative[§]	11,469	16,658	1.46	1.38-1.54	1.28	1.22-1.36
Node positive[#]: no RT to chest wall and nodes*	3,285	836	1.32	1.18-1.48	1.27	1.14-1.42
Node positive: RT to chest wall and nodes	6,556	5,248	1.35	1.25-1.45	1.28	1.19-1.38

RR = relative risk; SMR = standard mortality rate.

[§] Including micrometastases; [#] Only macrometastases; * Residual breast irradiated after BCS.

Christiansen et al. Acta Oncol 2018; 57: 19-25

JAMA Surgery | **Original Investigation**

Survival After Breast Conservation vs Mastectomy Adjusted for Comorbidity and Socioeconomic Status
A Swedish National 6-Year Follow-up of 48 986 Women

Jana de Boniface, PhD; Robert Szulkin, PhD; Anna L. V. Johansson, PhD

CONCLUSIONS AND RELEVANCE Despite adjustment for previously unmeasured confounders, BCS+RT yielded better survival than Mx irrespective of RT. If both interventions are valid options, mastectomy should not be regarded as equal to breast conservation.

Original Study

A Reappraisal of the Comparative Effectiveness of Lumpectomy Versus Mastectomy on Breast Cancer Survival: A Propensity Score—Matched Update From the National Cancer Data Base (NCDB)

Jeffrey Landercasper,[1,2] Luis D. Ramirez,[2] Andrew J. Borgert,[2] Humera F. Ahmad,[2] Benjamin M. Parsons,[1] Leah L. Dietrich,[1] Jared H. Linebarger[1]

Table 2 Comparative Effectiveness of Lumpectomy Versus Mastectomy (Reference) on 10- year Overall Survival in Stage I-III Patients by Univariate, Multivariate, and Propensity Score—Matched Analyses

| Model | Surgery | No. of Patients | No. of Deaths | Survival Rate[a] | | Univariate (n = 845,136) | | Multivariate[b] (n = 845,136) | | Propensity Score Matched (n = 248,278) | |
				5-Year (%)	10-Year (%)	Hazard Ratio (95% CI)	P	Hazard Ratio (95% CI)	P	Hazard Ratio (95% CI)	P
All patients	Lumpectomy	464,052	51,677	90.7	77.5	0.62 (0.61-0.62)	<.001	1.11 (1.09-1.13)	<.001	1.02 (1.00-1.04)	.002
	Mastectomy	381,084	64,747	84.5	68.3	1 (Ref)		1 (Ref)		1 (Ref)	
Hormone receptor positive[c]	Lumpectomy	382,081	38,227	91.9	78.2	0.64 (0.63-0.65)	<.001	1.13 (1.11-1.15)	<.001	1.05 (1.03-1.07)	<.001
	Mastectomy	296,255	43,923	87.0	69.6	1 (Ref)		1 (Ref)		1 (Ref)	
Hormone receptor negative[d]	Lumpectomy	73,057	11,944	85.0	74.2	0.59 (0.58-0.60)	<.001	1.06 (1.03-1.09)	<.001	1.00 (0.96-1.03)	.65
	Mastectomy	74,345	18,586	75.2	63.0	1 (Ref)		1 (Ref)		1 (Ref)	

| Table 3	Comparative Effectiveness of Lumpectomy Versus Mastectomy (Reference) on 10- year Overall Survival by Stage and Hormone Receptor Status in Stage I-III Patients After Propensity Score Matching					
Patient Cohort	**Lumpectomy 10-Year OS (%)**	**Mastectomy 10-Year OS (%)**	**Hazard Ratio**	**CI**		***P***
Stage I-III patients, any ER/PR status						
Stage I	67.5	71.4	1.27	1.23	1.31	<.001
Stage II	71.1	69.2	0.98	0.95	1.01	.21
Stage III	59.5	52.7	0.83	0.80	0.86	<.001
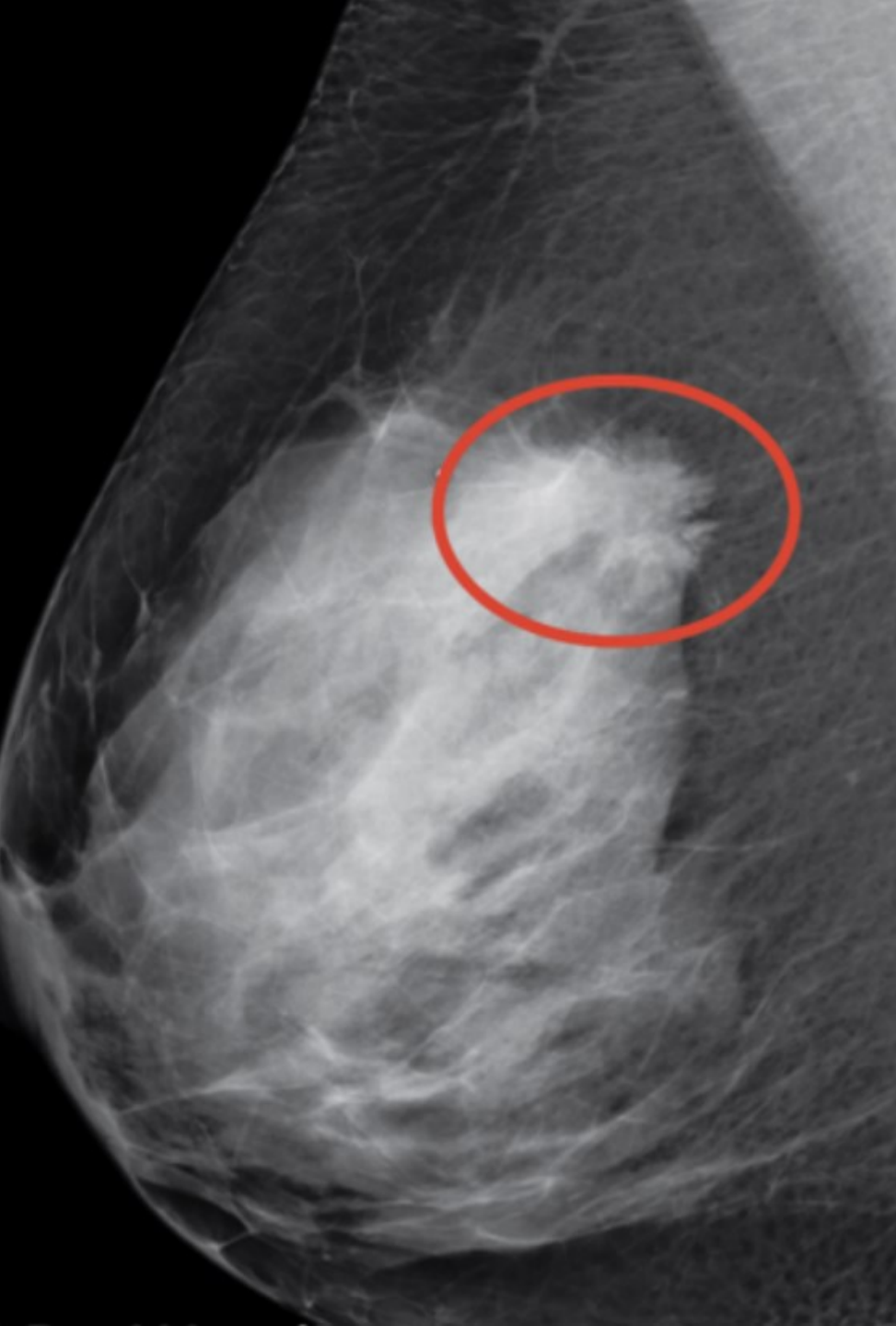
Why is survival better after BCS?

- **Abscopal effect**
  - In breast conserving surgery small tumor foci are left behind
  - Radiation therapy eradicates tumor cells
  - Debris from destroyed tumor cells activates the immune system
  - Circulating tumor cells and micrometastases are attacked by the activated immune system

Reynders et al.

The abscopal effect of local radiotherapy: Using immunotherapy to make a rare event clinically relevant
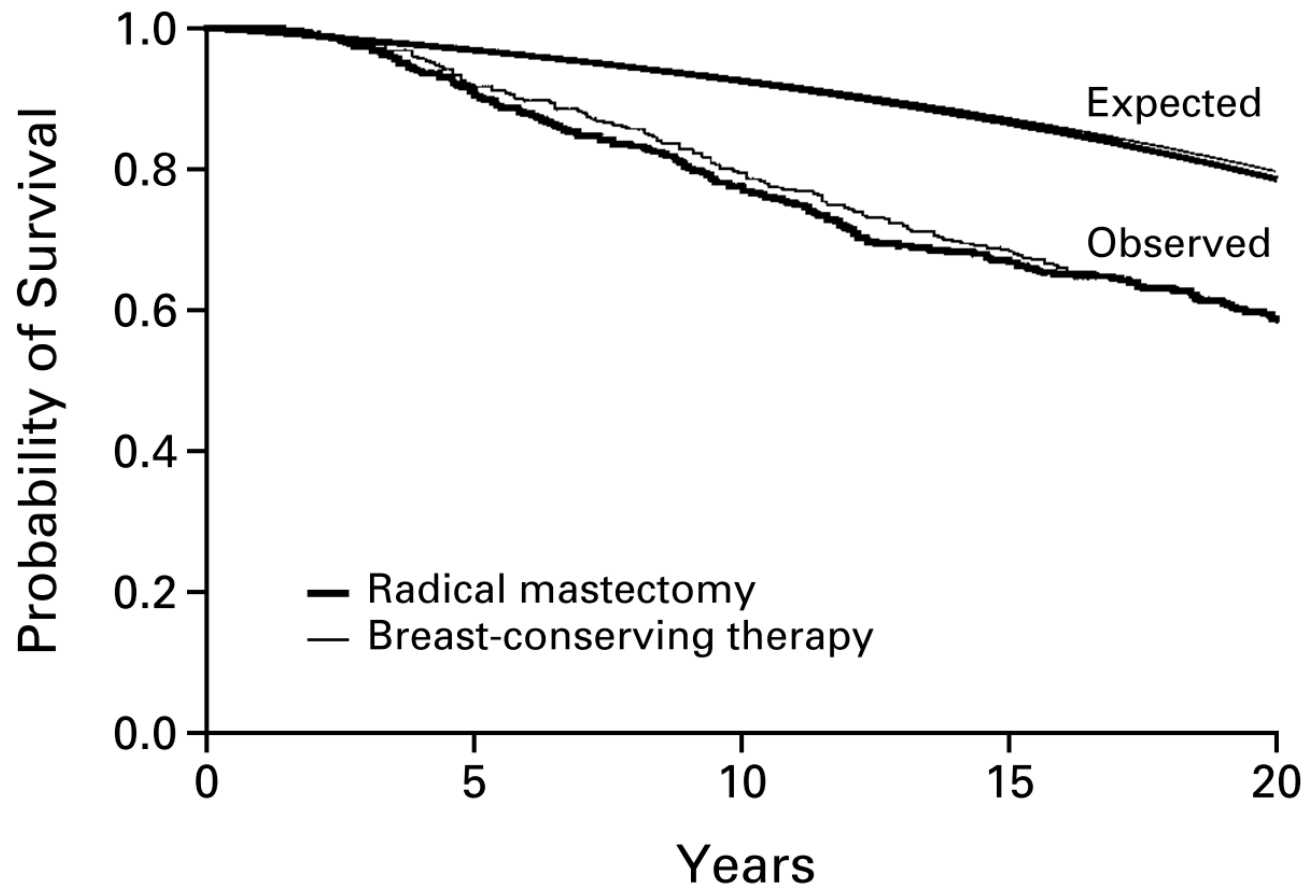
Cancer Treatment Reviews 2015; 41: 503-10
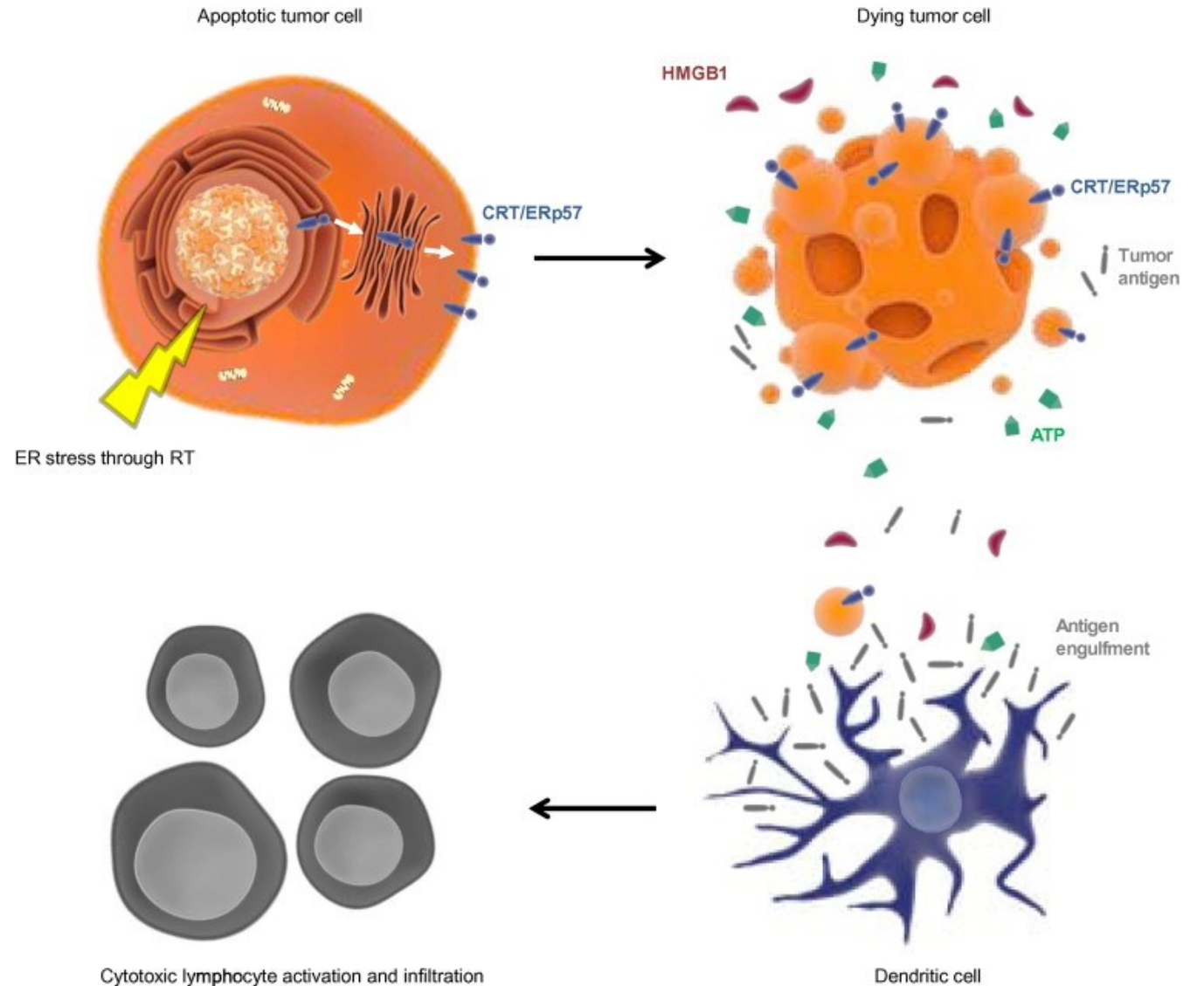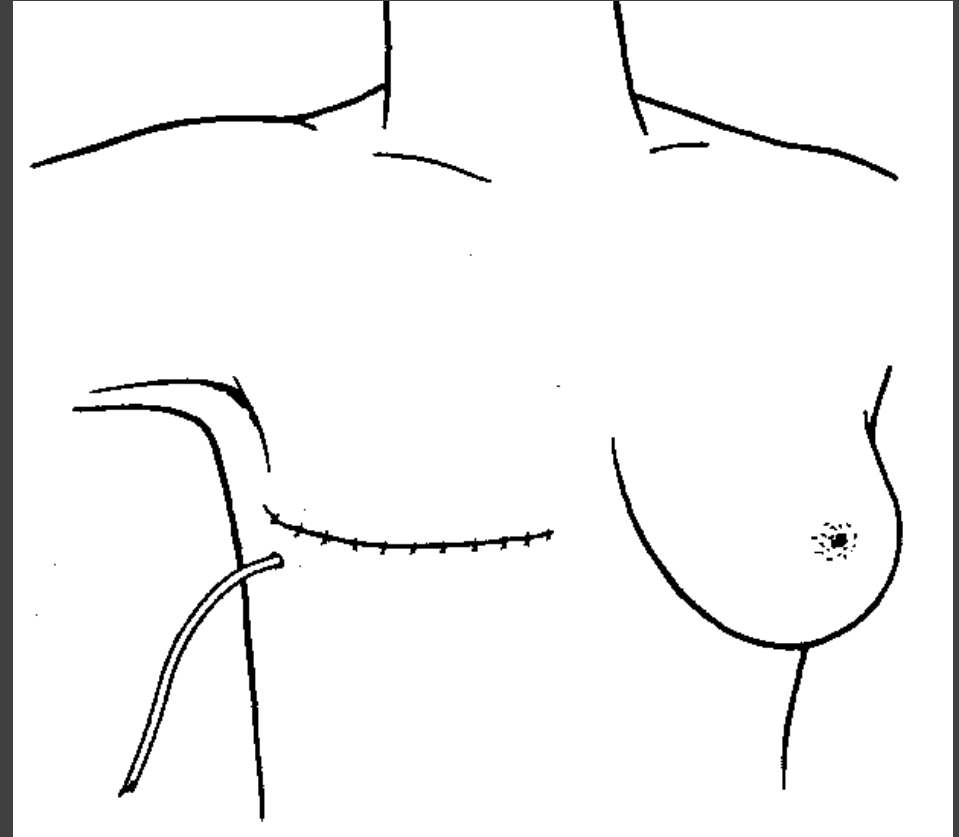
Surgical trauma

Mastectomy vs. BCS:

1. Greater surgical trauma

2. More pronounced suppression of the immune system

3. Less suppression of tumor cell growth (in loco, circulating, micrometastases)

Local recurrence
- Mastectomy 8 (2.3%)
- BCS 30 (8.5%)

Articles

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

Early Breast Cancer Trialists' Collaborative Group (EBCTCG)*

Overall, about one breast cancer death was avoided by year 15 for every four recurrences avoided by year 10

Veronesi et al. NEJM 2002: 347: 1227-32

Conclusions

- Breast conserving surgery is followed by a better survival than mastectomy in breast cancer

- BCS, rather than mastectomy, should be preferred in early breast cancer (T1-2N0-1M0), if a radical lumpectomy can be performed