
BETYDNINGEN AF FRIE RESEKTIONSGRÆNSE VED BRYSTBEVARENDE OPERATIONER

Anne Bodilsen

Thresholds for therapies: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2009

A. Goldhirsch^{1,2*}, J. N. Ingle³, R. D. Gelber⁴, A. S. Coates⁵, B. Thürlimann⁶, H.-J. Senn⁷
& Panel members[†]

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Meta-analysis of the impact of surgical margins on local recurrence in women with early-stage invasive breast cancer treated with breast-conserving therapy ☆

Nehmat Houssami ^{a,*}, Petra Macaskill ^a, M. Luke Marinovich ^a, J. Michael Dixon ^b,
Les Irwig ^a, Meagan E. Brennan ^a, Lawrence J. Solin ^c

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^b Breakthrough Research Unit Edinburgh, Western General Hospital, Edinburgh, Scotland, United Kingdom

^c Department of Radiation Oncology, Albert Einstein Medical Center, Philadelphia, PA, USA

- 21 studier (n: 48-3899)
- 14,571 patienter

European Journal of Cancer 46 (2010) 319-3232

ORIGINAL ARTICLE – BREAST ONCOLOGY

The Association of Surgical Margins and Local Recurrence in Women with Early-Stage Invasive Breast Cancer Treated with Breast-Conserving Therapy: A Meta-Analysis

Nehmat Houssami, MD, PhD¹, Petra Macaskill, PhD¹, M. Luke Marinovich, MPH¹, and Monica Morrow, MD²

- 33 studier (n: 79-3899)
- I alt 28,162 patienter
- Alle modtager strålebehandling, 96% også boost

METAANALYSENS KONKLUSION

” Adoption of wider margins, relative to narrower widths, for declaring negative margins is unlikely to have a substantial additional benefit for long-term local control”

Houssami et al. Ann Surg Oncol 2014;21:717-30

DBCG STUDIE - INKLUSIONS KRITERIER

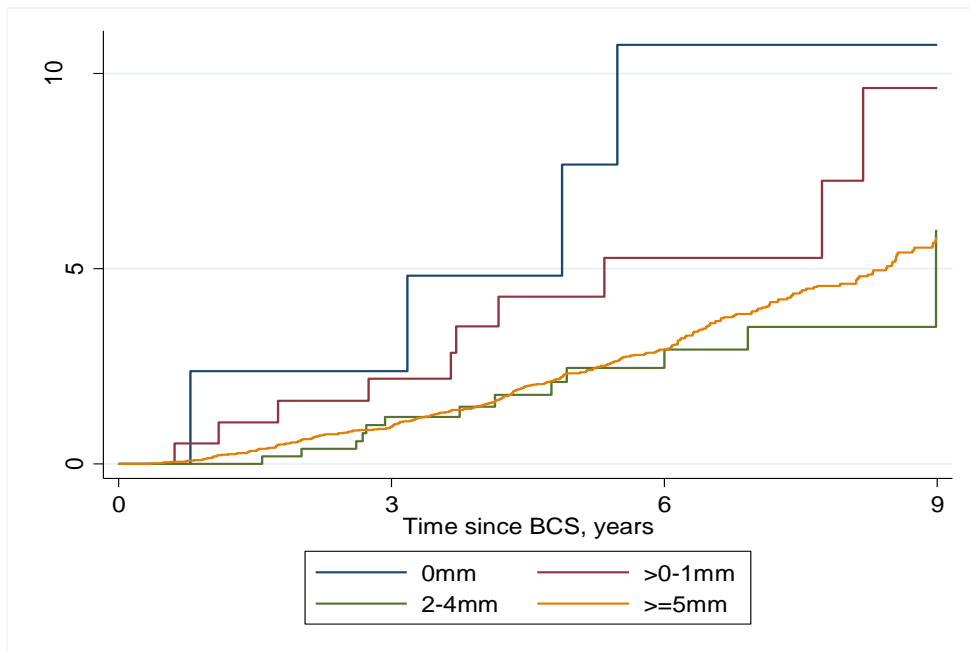
- 2000-2009
- Kvinder
- Alder: 18-75
- Brystbevarende behandling
- Invasiv cancer
- Unilateral
- Ingen tidligere cancersygdomme
- Behandlet i henhold til DBCG guidelines
- I alt 11,900 patienter

BETYDNINGEN AF MARGINS STØRRELSE

Margin i mm	Antal patienter
0 mm	43
>0-<1mm	72
1mm	117
2mm	196
3mm	185
4mm	163
5mm	732
>5-10mm	4375
>10mm	6017

BETYDNINGEN AF MARGINS STØRRELSE

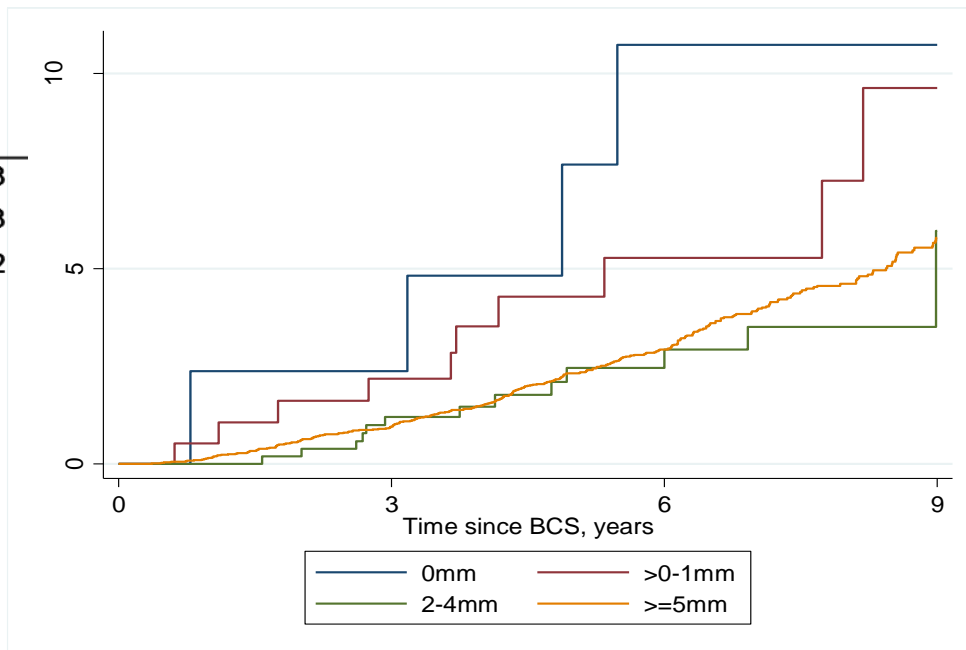
Overall risiko
for IBTR:
5 år: 2.4%
9 år: 5.9%



Cumulative incidence of IBTR by margin width in 11,900 women

BETYDNINGEN AF MARGINS STØRRELSE

	HR	95% CI
0 mm	2.51	1.02-6.23
> 0-1mm	1.54	0.81-2.93
2-4 mm	0.95	0.56-1.62
≥ 5 mm	1	



Cumulative incidence of IBTR by margin width in 11,900 women

BETYDNINGEN AF MARGINS STØRRELSE

	HR	95% CI	p value
Age			<0.001
≤40	5.08	2.75-9.38	
41-49	3.16	1.78-5.58	
50-64	1.20	0.89-1.61	
65-74	1		
Histology/grade			0.06
Ductal NST, grade I-II	1		
Ductal NST, grade III	1.34	1.00-1.80	
Special subtypes	0.87	0.63-1.18	
Unknown	1.66	0.80-3.45	
Lymph node status			0.008
Negative	1		
1-3 positive	1.18	0.92-1.52	
4-9 positive	1.61	1.05-2.47	
>10 positive	2.47	1.35-4.54	

	HR	95% CI	p value
Re-excisions			0.003
No	1		
Yes	1.53	1.16-2.02	
Chemotherapy			<0.001
No	1		
Yes	0.45	0.33-0.61	
Boost			0.08
No	1		
Yes	0.58	0.36-0.93	
Unknown	1.09	0.38-3.09	
ER status/treatment			<0.001
ER negative	1		
ER pos, no endocrine	0.43	0.31-0.60	
ER pos, endocrine	0.35	0.25-0.49	

Adjusted risk of IBTR as first event

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Adjusted risk of IBTR as first event

SÅ HVAD VED VI.....

- øget risiko for IBTR ved positiv margin
- ingen forbedring af lokal kontrol med bredere margin, MEN....
- fortsat begrænset viden om helt smalle marginer ($>0-1$ mm)

BETYDNING AF MARGIN FOR FJERNMETASTASER

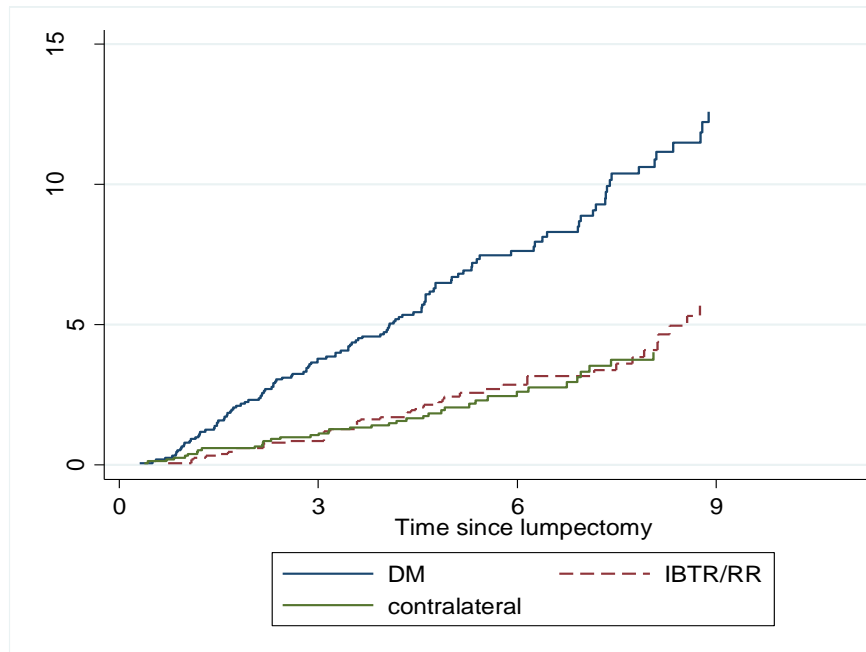


BETYDNING AF MARGIN FOR FJERNMETASTASER

	DBCG	Patobank	Journal	Total
IBTR+RR	47	6	4	57
DM	94	2	30	126
Total	141	8	34	183

BETYDNING AF MARGIN FOR FJERNMETASTASER

Risiko ved 5 vs 9 år:
IBTR/RR: 2.4% vs 5.7%
DM: 6.5% vs 12.6%
Contralateral: 2.0% vs 4.0%



Cumulative risk of DM, loco-regional recurrence, and contralateral

BETYDNING AF MARGIN FOR FJERNMETASTASER

	HR	95% CI	p-value
Final margin			0.53
0 mm	2.37	0.23-17.33	
>0-1mm	1.27	0.46-3.57	
2-4mm	1.52	0.77-3.02	
>=5mm	1		
Tumour size			<0.001
<=20 mm	1		
>20 mm	2.29	1.57-3.32	
Lymph node status			<0.001
Negative	1		
Positive	2.01	1.34-3.01	
Vascular invasion			0.016
No	1		
Yes	1.70	1.10-2.63	

Adjusted risk of DM as first event

BETYDNING AF MARGIN FOR FJERNMETASTASER

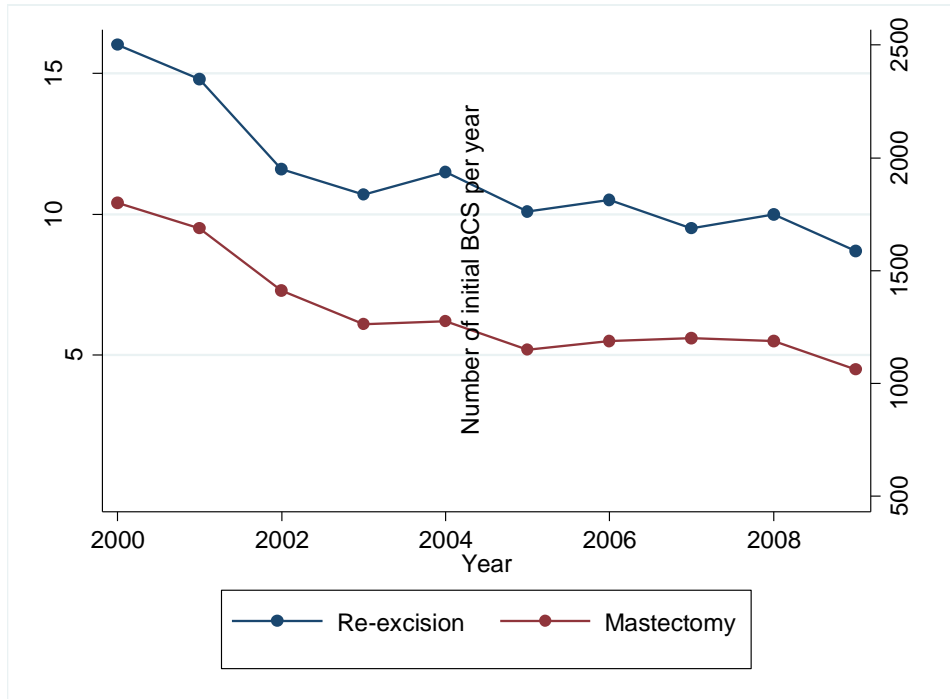
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Lymph node status			<0.001
Negative	1		
Positive	2.01	1.34-3.01	
Vascular invasion			0.016
No	1		
Yes	1.70	1.10-2.63	

Adjusted risk of DM as first event

RE-RESEKTION

- inkluderede alle med primær brystbevarende operation
- i alt 12,656

RE-RESEKTION



Development in use of repeat surgery over time

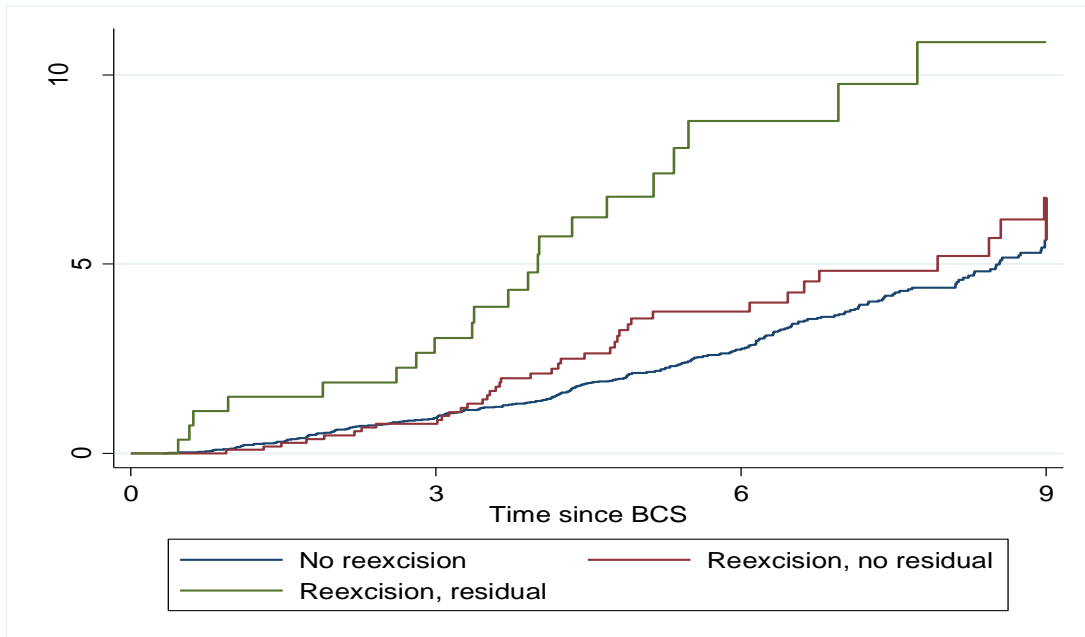
RE-RESEKTION

20% havde resttumour ved re-resektion

23% invasivt carcinom

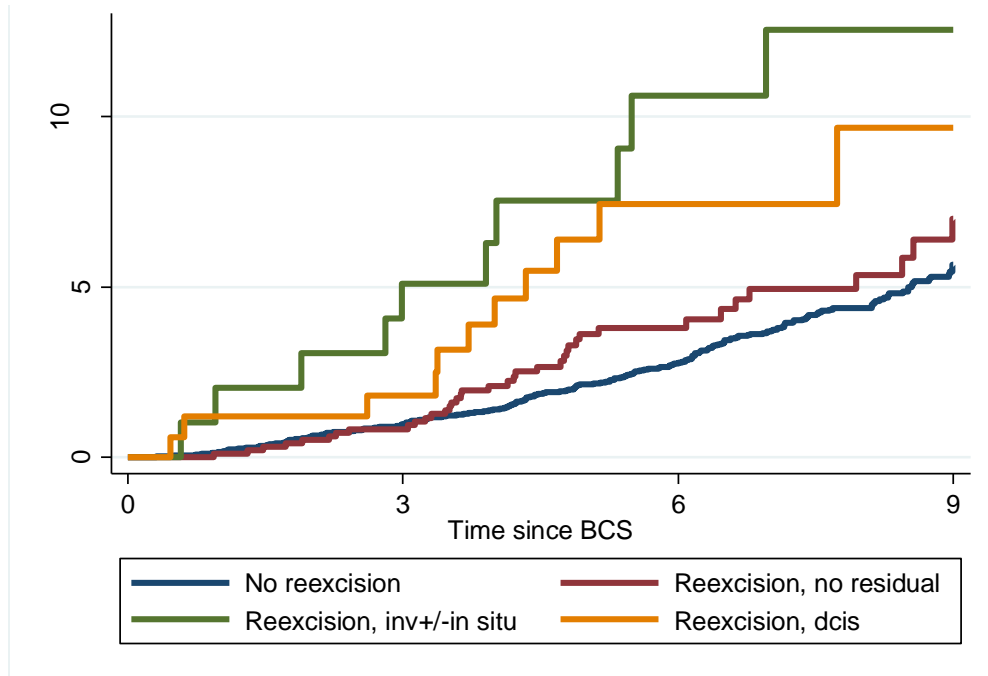
- 63% DCIS
- 14% DCIS+invasivt carcinom

RE-RESEKTION



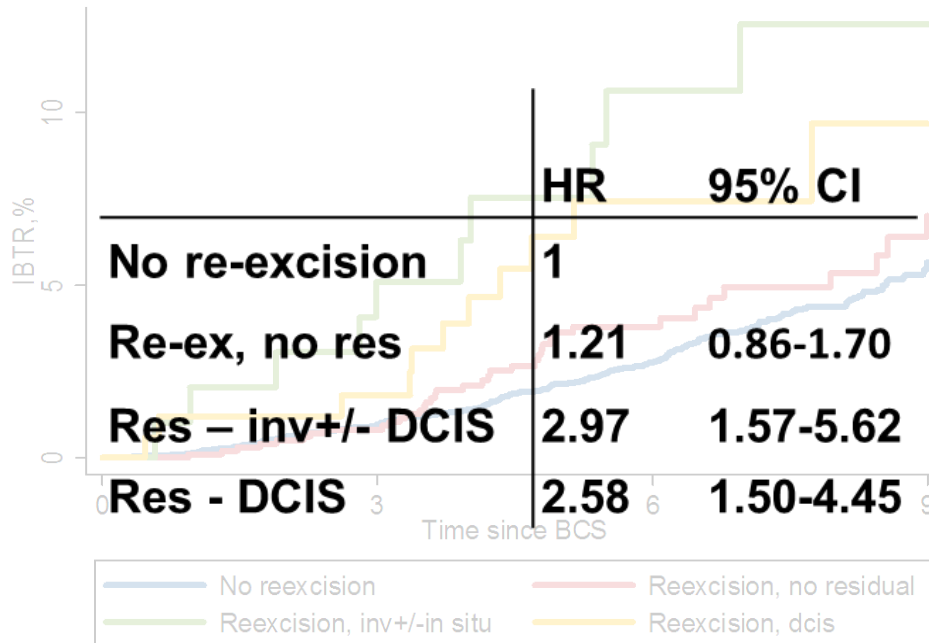
Cumulative incidence of IBTR after final BCS by surgery and residual finding

RE-RESEKTION



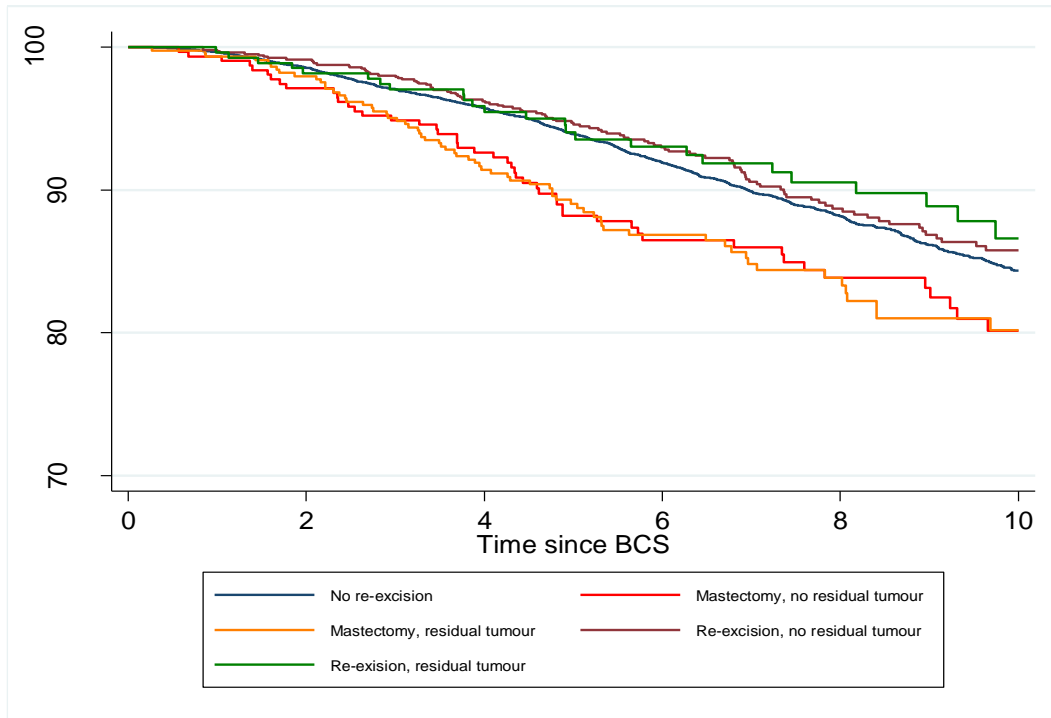
Cumulative incidence of IBTR after final BCS by surgery and residual finding

RE-RESEKTION



Cumulative incidence of IBTR after final BCS by surgery and residual finding

RE-RESEKTION



Overall survival by surgical procedure and residual finding

RE-RESEKTION

- 11% re-reseseres, 6% fortsætter til mastektomi. Faldende over tid
- Øget risiko for lokalt recidiv associeret med resttumor ved re-resektion
- Overlevelse er ikke påvirket

KONKLUSION

- Fordoblet risiko for lokalt recidiv ved positiv margin
- Ingen forbedring i lokal kontrol med bredere margin
- Formentligt samme billede for fjerne metastaser
- Resttumor øger risiko for recidiv og selvom der er negative marginer til slut

Spørgsmål/kommentarer

BOOST

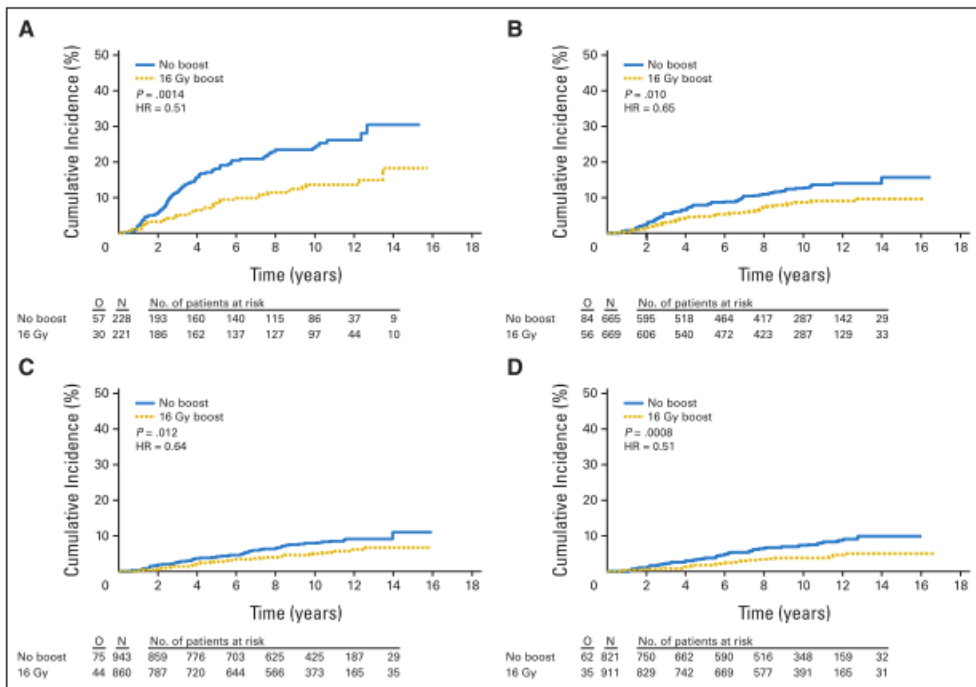


Fig 3. Cumulative incidence of ipsilateral breast cancer recurrence according to age. Age (A) ≤ 40 , (B) 41 to 50, (C) 51 to 60, and (D) > 60 years. HR, hazard ratio; Q, occurrences; N, number of patients at risk.

Bartelink et al. JCO 2007;25:3259-65

BOOST

- SSO/ASTRO guidelines anbefaler ikke brug af boost på baggrund af margin status
- Boost vs no boost trial – kun negativ margin randomiseret. Forskellig dosis til positiv margin – men ingen forskel
- Andre studier med lignende resultater
- Ikke muligt at undersøge i DBCG data

MARGIN HOS PATIENTER MED ANDRE DÅRLIGE PROGNOSTIKA

”Margins wider than no ink on tumour are not indicated based on biologic subtype”

”There is no evidence that increased margin width nullifies the increased risk of IBTR in young patients”

”There is no evidence of an association between increased risk of IBTR [and DCIS outside invasive tumour] when margins are negative”

Moran et al. Ann Surg Oncol 2014;88:553-64

MARGIN HOS PATIENTER MED ANDRE DÅRLIGE PROGNOSTIKA

”Margins wider than no ink on tumour are not indicated based on biologic subtype”

Ann Surg Oncol (2014) 21:1209–1214
DOI 10.1245/s10434-013-3416-5

Annals of

SURGICAL ONCOLOGY

OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – BREAST ONCOLOGY

Effect of Margin Width on Local Recurrence in Triple-Negative Breast Cancer Patients Treated with Breast-Conserving Therapy

Melissa Pilewskie, MD¹, Alice Ho, MD², Emily Orell, BS¹, Michelle Stempel, MPH¹, Yu Chen, BS³, Anne Eaton, MS⁴, Sujata Patil, PhD⁴, and Monica Morrow, MD¹

MARGIN HOS PATIENTER MED ANDRE DÅRLIGE PROGNOSTIKA

”There is no evidence that increased margin width nullifies the increased risk of IBTR in young patients”

Hollansk studie – med patienter ≤ 40 år:

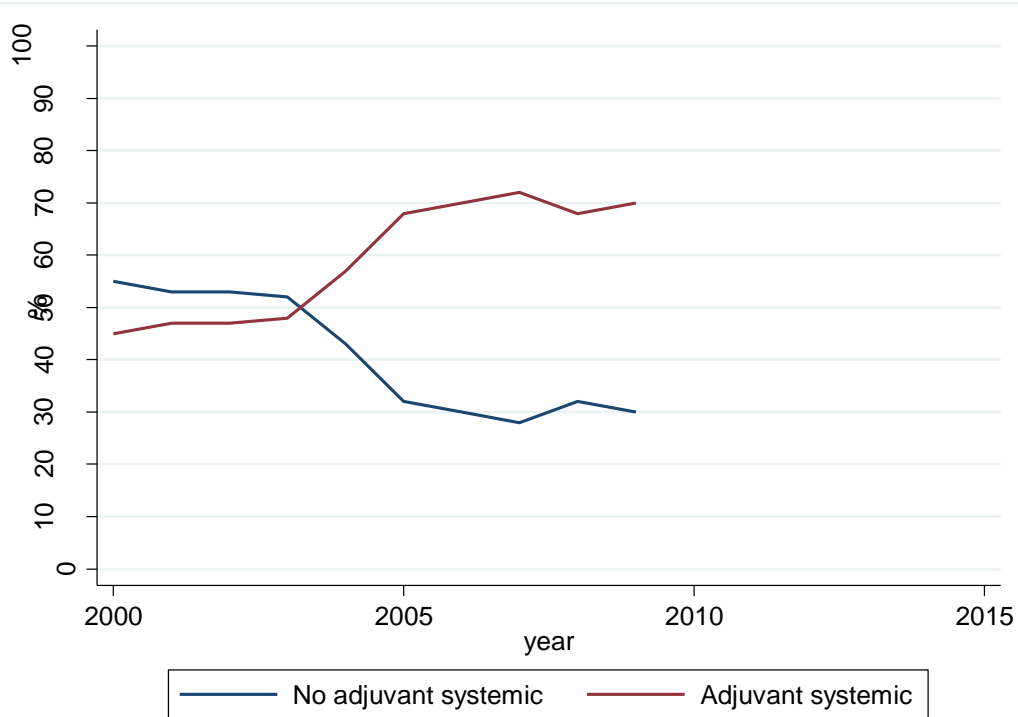
- 5 års risiko for lokalt recidiv positiv (on ink) vs negativ (not on ink)
margin: 36.9% vs 8.4%

Jobsen et al. Int J Radiat Oncol 2003;57:724-31

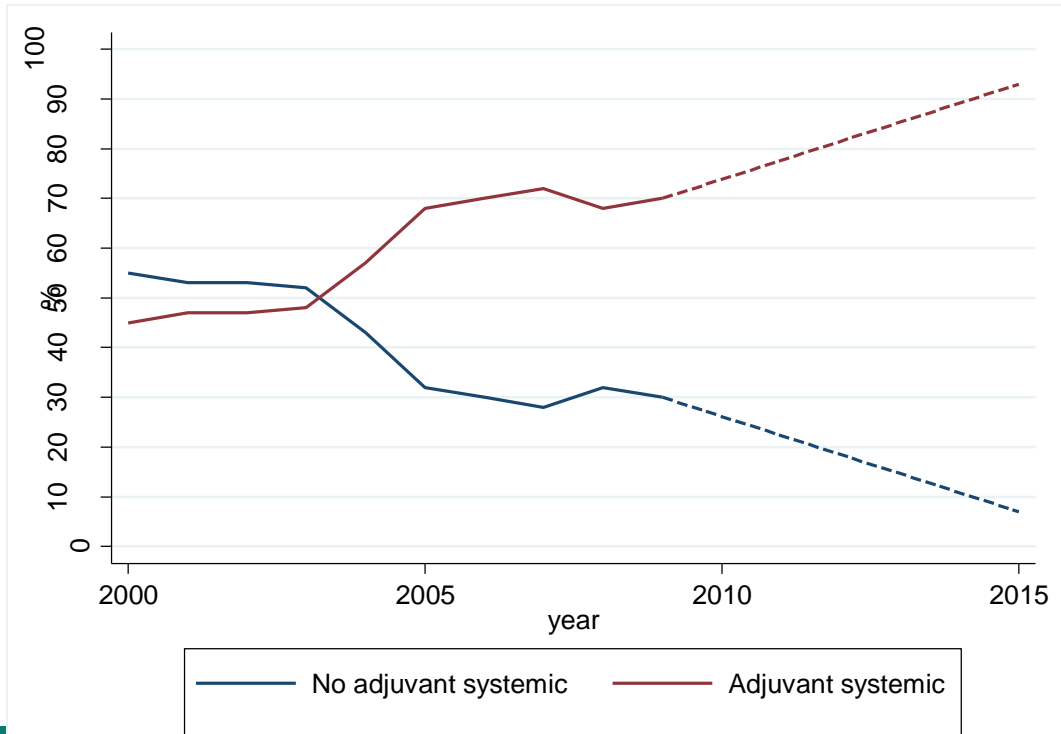
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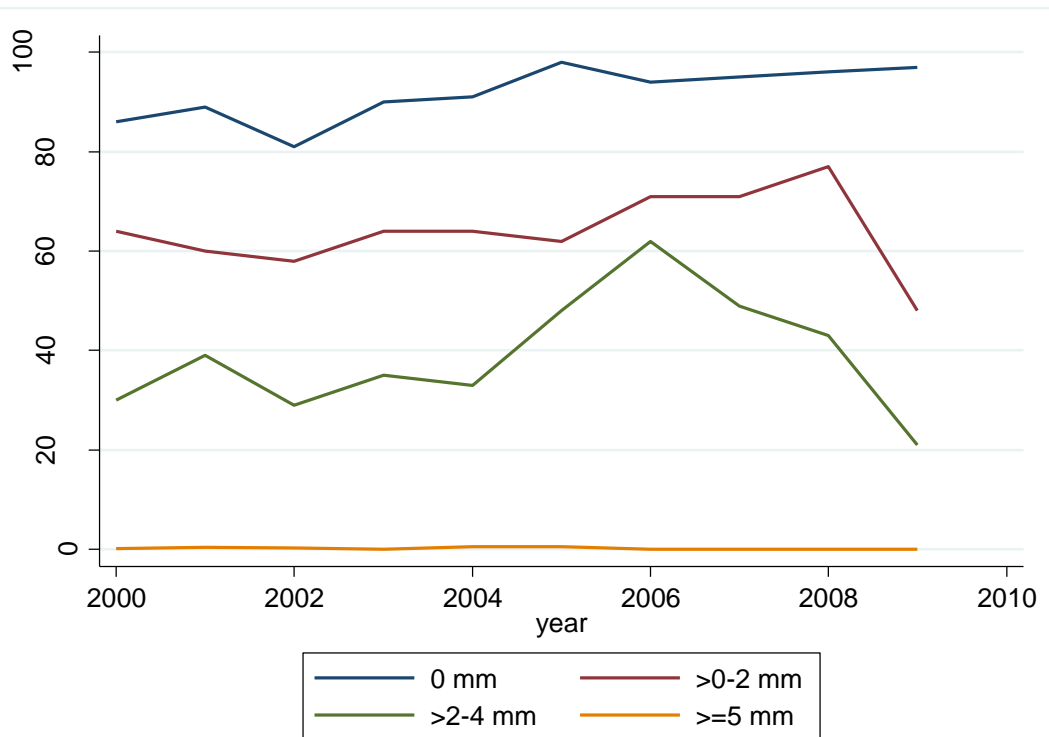
DEVELOPMENT IN THE USE OF ADJUVANT SYSTEMIC THERAPY



DEVELOPMENT IN THE USE OF ADJUVANT SYSTEMIC THERAPY



CANDIDATES OF RE-EXCISION



Percentage receiving re-excision by margin group

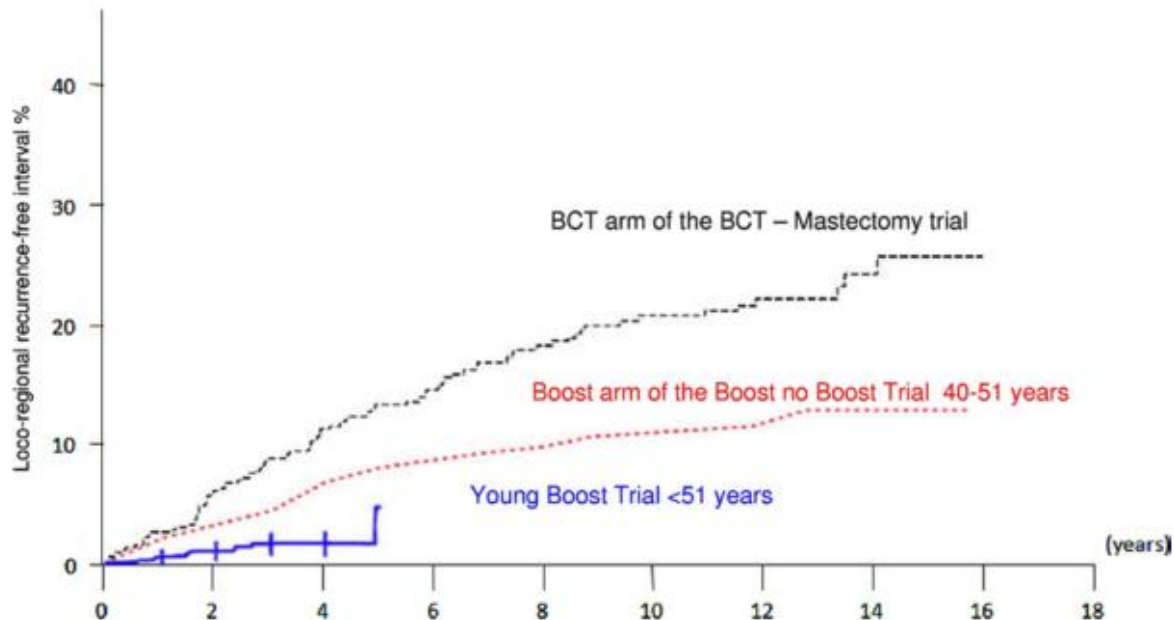
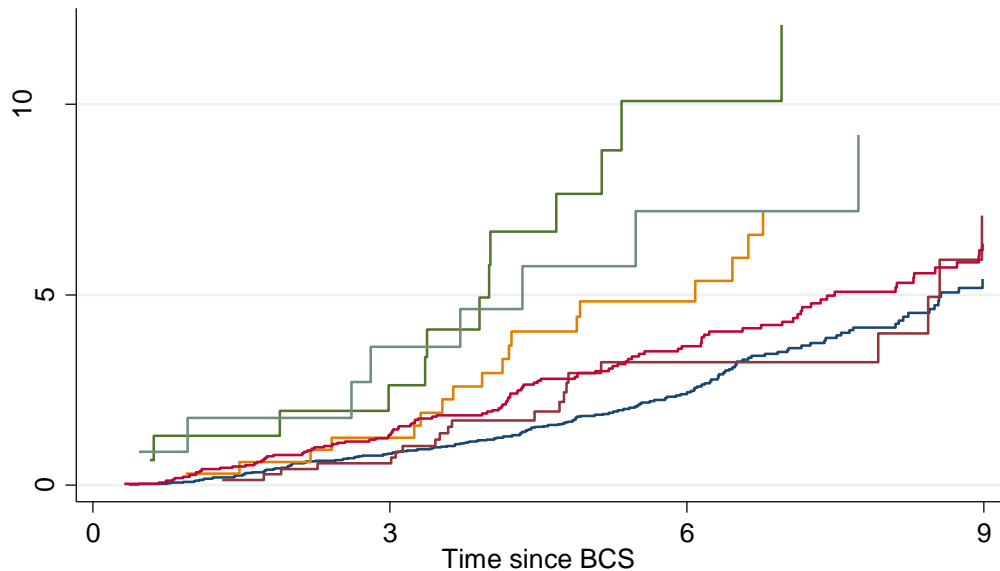
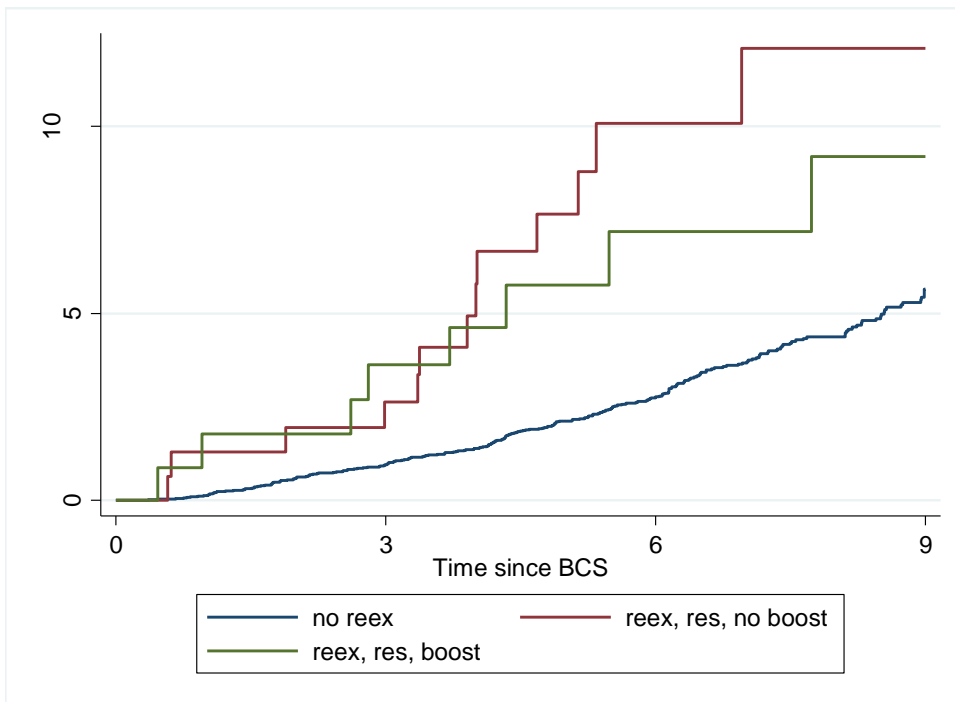


Figure 4 The local recurrence rate in the consecutive EORTC 10801, EORTC 22881-10882, and the Young Boost trials.¹⁴

RE-RESEKTION OG BOOST



RE-RESEKTION OG BOOST



Risk of IBTR after BCT by residual finding and receipt of boost