The SENOMAC trial: an early glimpse and where do we go from here?

10th Aarhus Workshop in Breast Surgery

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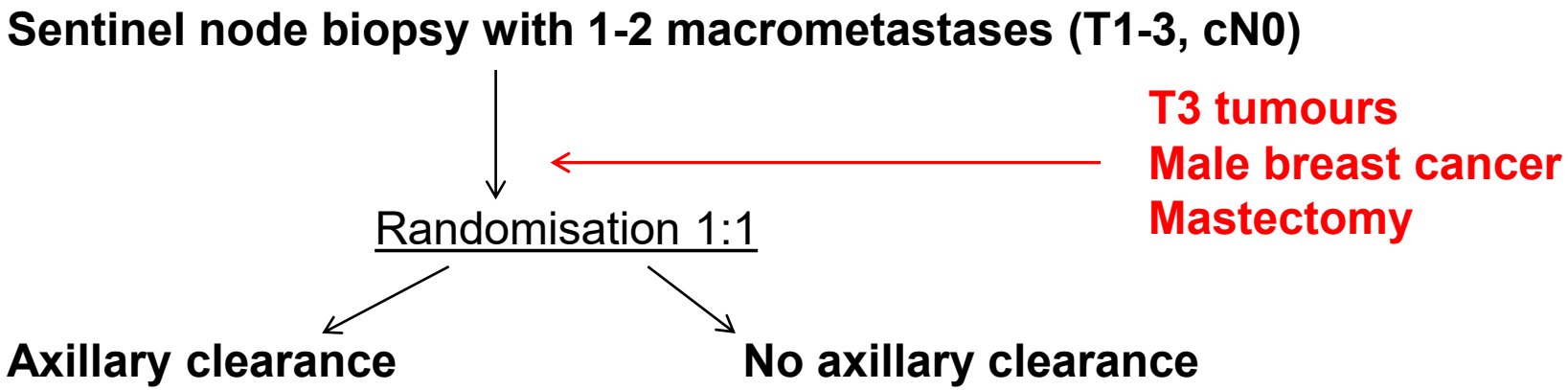
The SENOMAC trial

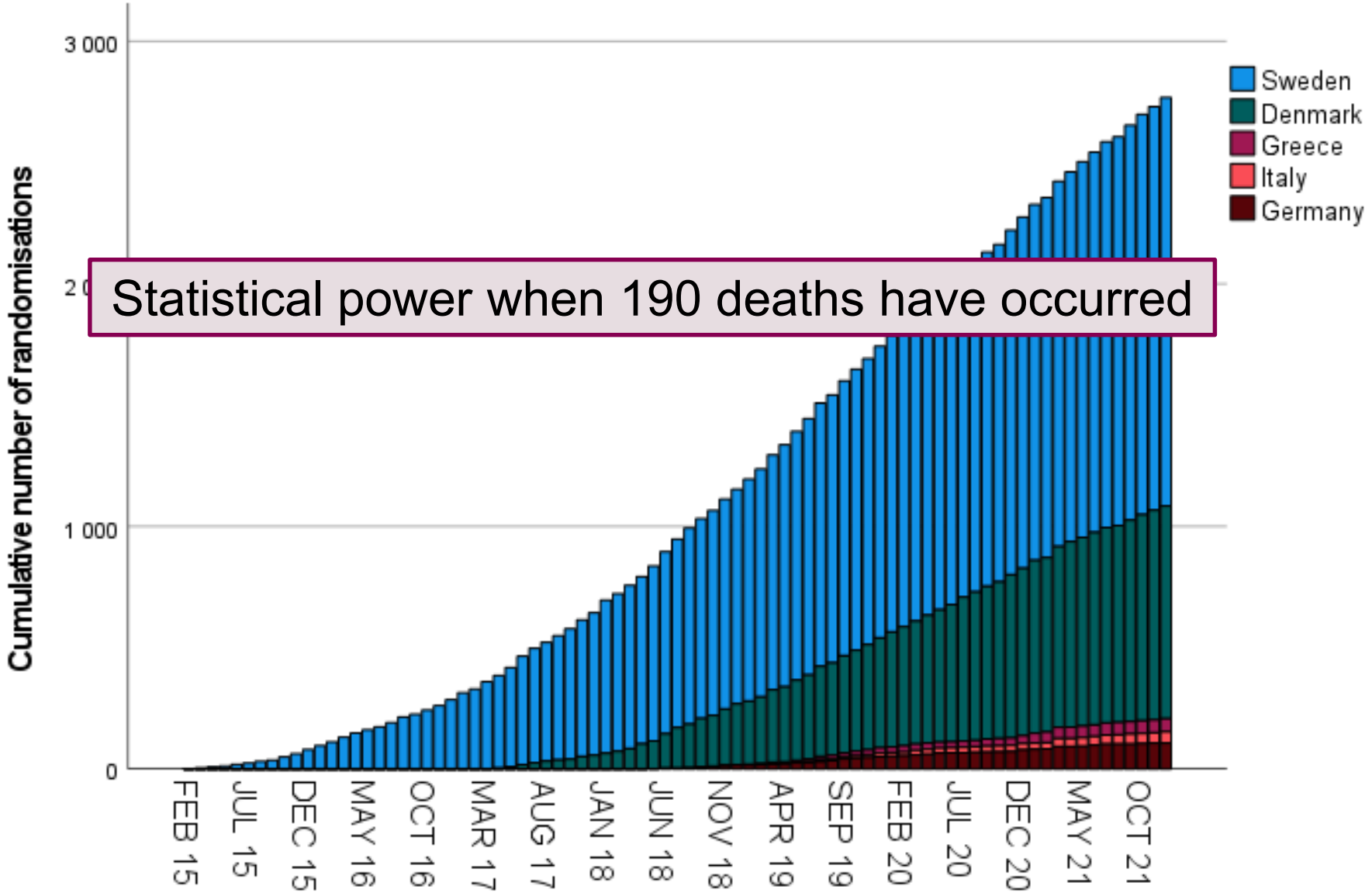
Omission of axillary clearance in breast cancer patients with sentinel node **macrometastasis**: A randomized trial.



NCT 02240472 (www.clinicaltrials.gov)

Aim: non-inferiority regarding overall survival (N=3000)

Randomised patients N=2768



Statistical power when 190 deaths have occurred

Top ten sites

1.	Rigshospitalet	288
2.	Capio St. Göran	193
3.	South General Hospital	163
4.	Aarhus	143
5.	Skåne (Malmö/Lund)	133
6.	Karolinska	124
7.	Linköping	114
8.	Gothenburg	113
9.	Viborg	110
10.	Aalborg	101

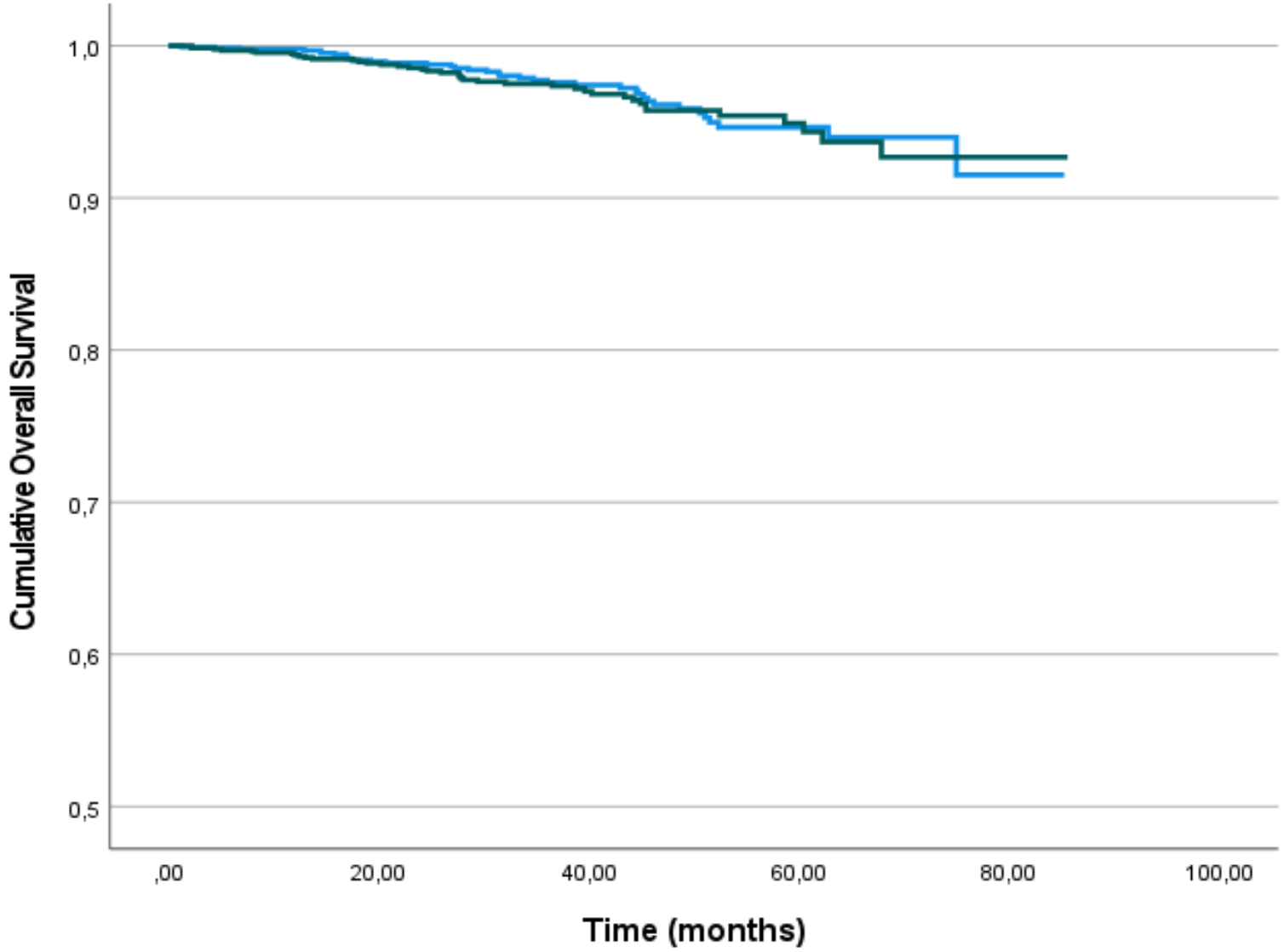
ITT population (N=2491)

- Median age 61 years (maximum age 94)
- NST (invasive ductal histology) 76%, invasive lobular 20%
- Mastectomy 36% (N=897)
- Median tumour size 20 mm (max. 155 mm)
- ER negativity 6.4%

- Median number of excised SLN 2 (1-11)
- 22.5% extranodal extension
- Proportion of cases with positive non-SLNs 33.2%
  → pN1 87%, pN2 10%, pN3 3%

Follow-up

- Median follow-up 33 months (1.3-84.4 months)
- 72 deaths, 31 due to breast cancer
- 5-year overall survival 94.6% versus 94.9% (p=0.677)
  → AMAROS: 93.3 versus 92.5%
  → ACOSOG Z0011: 91.8 versus 92.5%
- 5 regional recurrences (4 monitored)
  → 1 axilla only
  → 1 axilla and infraclavicular
  → 1 supra-/infraclavicular only
  → 1 intramammary


Cumulative Overall Survival
1,0
0,9
0,8
0,7
0,6
0,5
,00
20,00
40,00
60,00
80,00
100,00
Time (months)

Where do we go from here: Clinical implementation of trial results

- ACOSOG Z0011
- AMAROS
- OTOASOR
- IBCSG 23-01

- **Underrepresentation of**
  - → Macrometastases
  - → Mastectomy patients
  - → Tumours larger than 5 cm
  - → ER negativity
  - → Extranodal extension
  - → Lobular carcinoma

The ”post-Z0011 era”

Received: 10 December 2020 | Revised: 2 March 2021 | Accepted: 3 March 2021

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The Breast Journal WILEY

SHORT COMMUNICATION

Extrapolation of ACOSOG Z0011 trial results—A survey of breast cancer providers

Anna Weiss MD[1,2,3] | Victoria Cooley MS[4] | Zahraa Al-Hilli MD[5] | Karla Ballman PhD[3,4] | Nancy Poorvu PhD[6] | Bruce Haffty MD, MS[7] | Kelly K. Hunt MD[3,8] | Heidi Nelson MD[3] | Sarah L. Blair MD[3,9] | Judy Boughey MD[3,10]

Mastectomy—1+ SLN	
No further axillary treatment	5 (8%)
ALND	14 (23%)
PMRT	12 (20%)
ALND +PMRT	-
Multi-disciplinary discussion, decision on a case-by-case basis	27 (45%)
Other	2 (3%)
Unknown	34

Mastectomy—2+ SLNs	
No further axillary treatment	2 (3%)
ALND	12 (19%)
PMRT	10 (16%)
ALND +PMRT	3 (5%)
Multi-disciplinary discussion, decision on a case-by-case basis	34 (55%)
Other	1 (2%)
Unknown	32

External validity 2016-2017: Swedish SENOMAC vs national register

- ++ middle age groups
- ++ breast conservation
- Smaller tumours
- ++ ER positivity
- ++ proportion of only one macromet
- No differences in HER2, grade, histological type, multifocality

Breast Cancer Research and Treatment
https://doi.org/10.1007/s10549-020-05537-1

CLINICAL TRIAL

The generalisability of randomised clinical trials: an interim external validity analysis of the ongoing SENOMAC trial in sentinel lymph node-positive breast cancer

Clinical implementation of trial results

- ACOSOG Z0011
- AMAROS
- OTOASOR
- IBCSG 23-01

- **Underrepresentation of**
  - → Macrometastases
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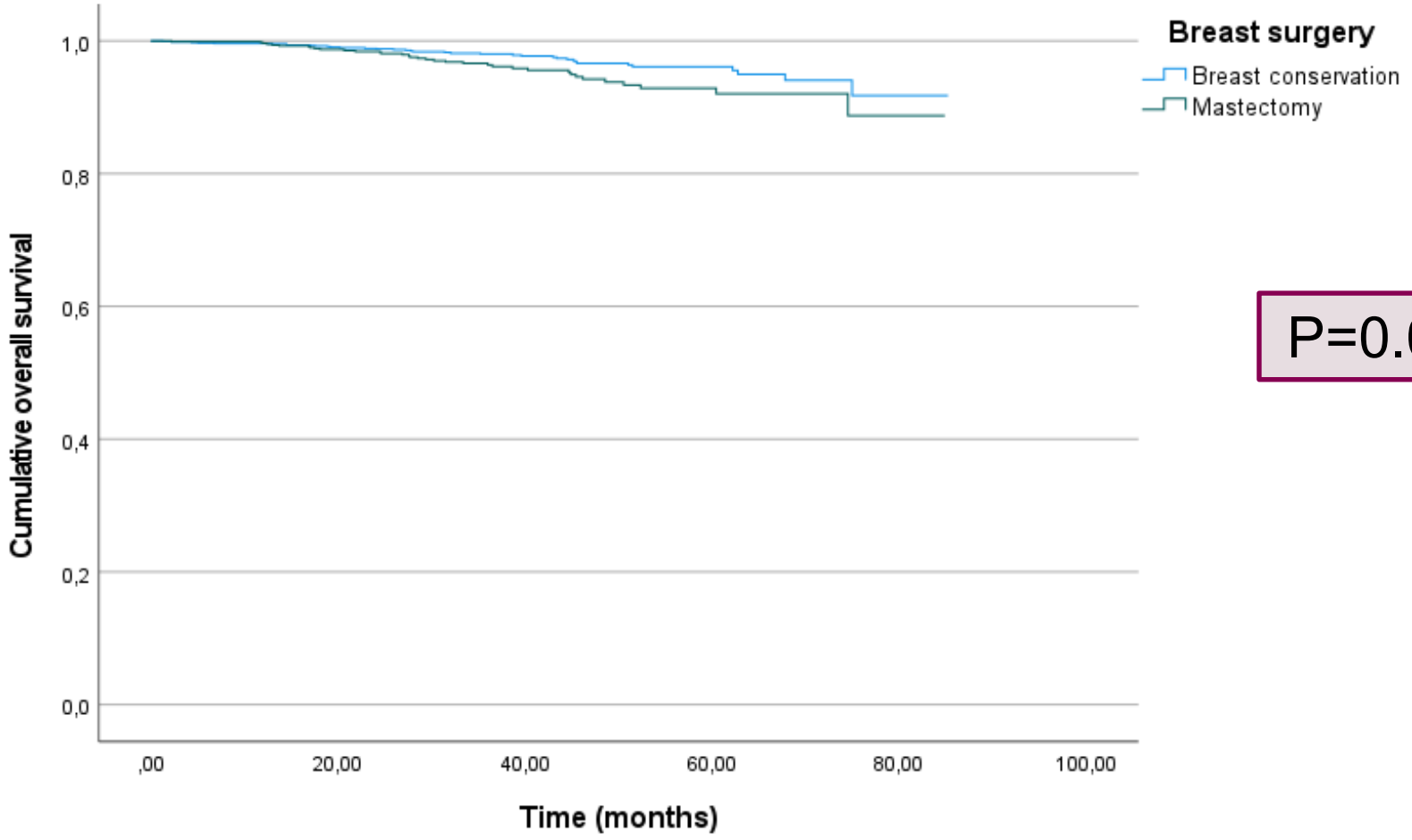
Breast conservation versus mastectomy



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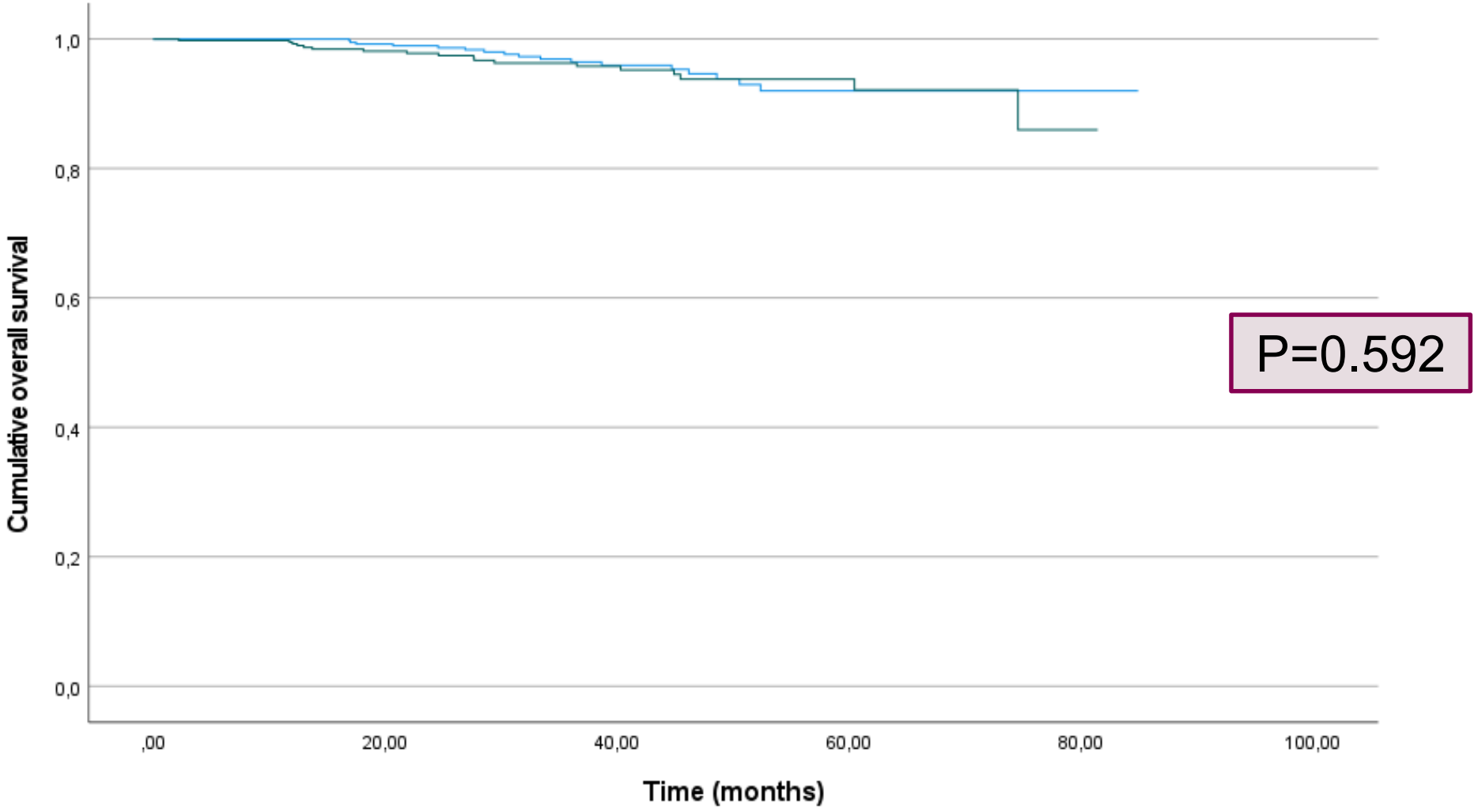
Mastectomy only



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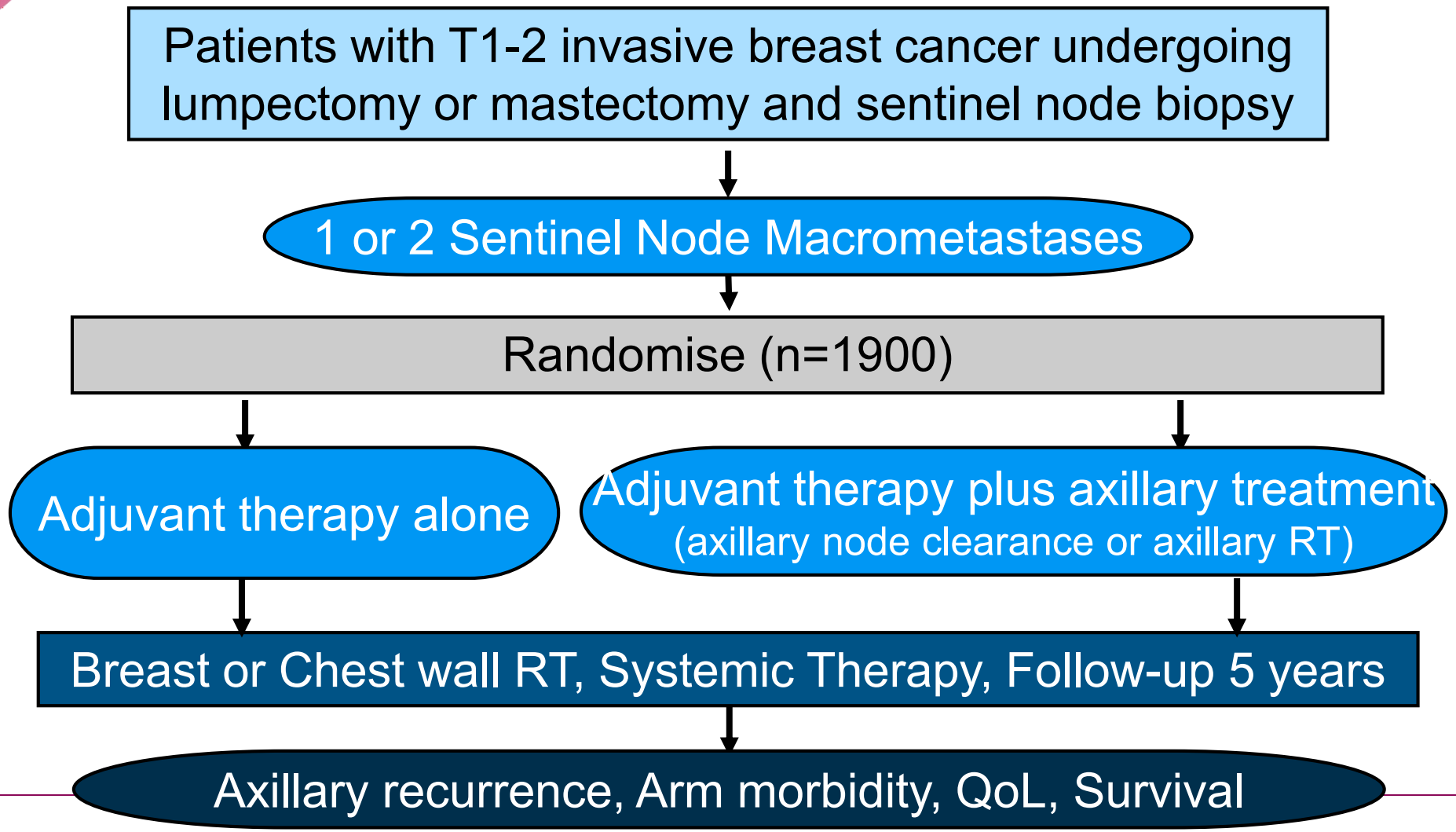

Patients with T1-2 invasive breast cancer undergoing lumpectomy or mastectomy and sentinel node biopsy
1 or 2 Sentinel Node Macrometastases
Randomise (n=1900)
Adjuvant therapy alone
Adjuvant therapy plus axillary treatment
(axillary node clearance or axillary RT)
Breast or Chest wall RT, Systemic Therapy, Follow-up 5 years
Axillary recurrence, Arm morbidity, QoL, Survival

Lobular carcinoma

- More commonly higher nodal stages
- More commonly luminal A
- More commonly larger tumour size
- More common in older adults

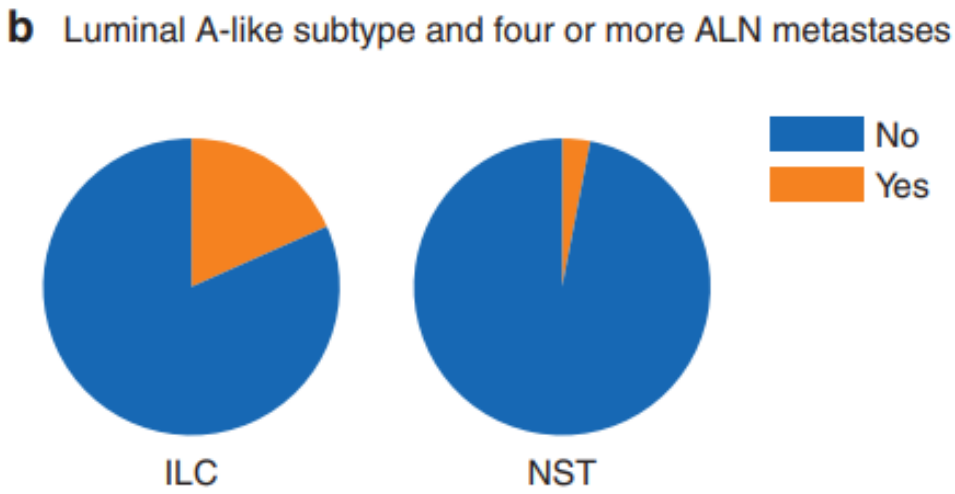
≥ 4 axillary mets in 31% of lobular cancer *versus* 14.9% of NST

OXFORD

BJS, 2021, **108**, 1465–1473
DOI: 10.1093/bjs/znab327
Advance Access Publication Date: 12 October 2021
Original Article

St Gallen 2019 guidelines understage the axilla in lobular breast cancer: a population-based study

U. Narbe [1,2], P.-O. Bendahl[1], M. Fernö[1], C. Ingvar [3,4], L. Dihge [3,5] and L. Rydén[3,4,*]



Nodal stage by histology (ALND)

	NST (ductal)	ILC (lobular)
pN1	89.2%	80.3%
pN2	8.7%	13.1%
pN3	2.1%	6.6%

Where do we go from here?

- Mastectomy patients
  → Worse survival regardless of randomisation group
  → Probably nothing to be compensated by more surgery
- Lobular carcinoma
  → Higher risk of higher nodal burden
  → Understaging & potential undertreatment

Swedish national guidelines 2022:
No axillary clearance in 1-2 SLN macrometastases
No further differentiation regarding type of surgery, histology etc

Where do we go from here?

- Mastectomy patients
  → Worse survival regardless of randomisation group
  → Probably nothing to be compensated by more surgery
- Lobular carcinoma
  → Higher risk of higher nodal burden

- Tailoring surgery by tumour type?
- Predictive nomograms/testing?
- Radiotherapy de-escalation?

Keep making a difference for patients' quality of life

Tack!

SVENSKA SÄLLSKAPET FÖR MEDICINSK FORSKNING

Cancerfonden

Vetenskapsrådet

BRÖSTCANCER FÖRBUNDET

Stockholms läns landsting

Stiftelsen Olle Engkvist Byggmästare

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