Mammo-50

Mammographic surveillance in early breast cancer patients aged 50 years or over: results of the Mammo-50 non-inferiority trial of annual versus less frequent mammography

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On behalf of the Mammo-50 Investigators

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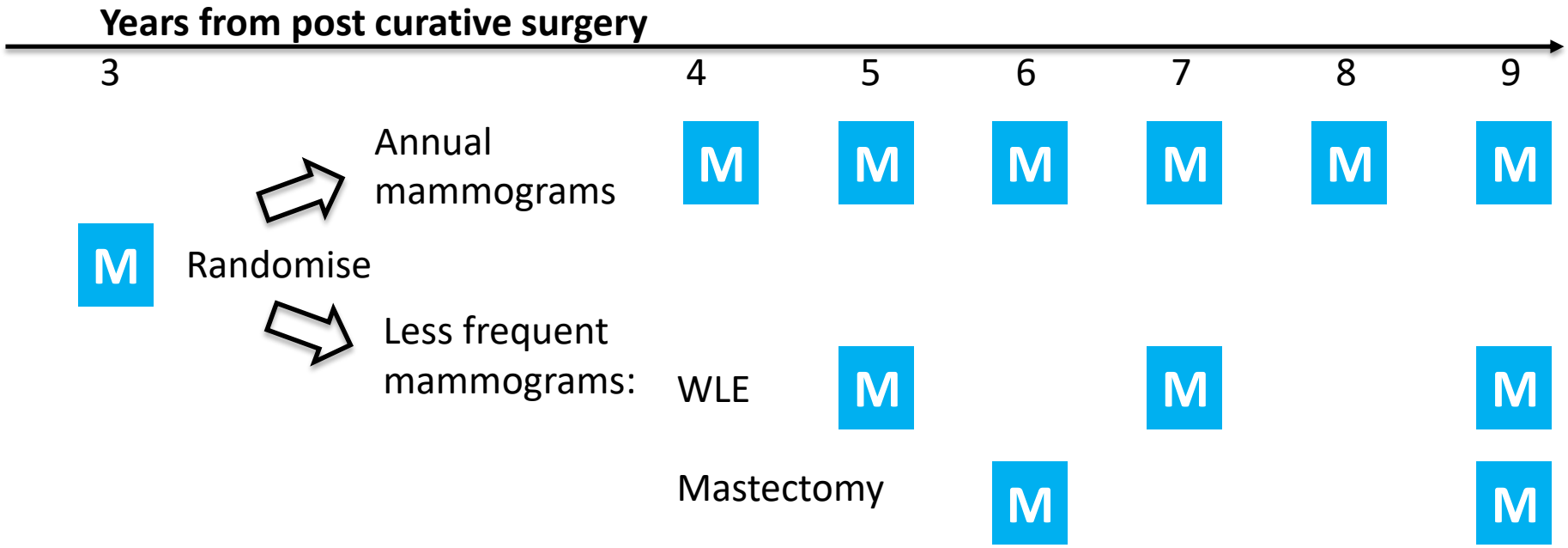
Background

- Current guidelines in USA[1] and Europe[2] recommend annual surveillance mammograms for an unspecified period after treatment for early breast cancer
- Current UK guidelines recommend annual surveillance mammograms up to 5 years, then reverts to 3 yearly screening, without specified risk stratification[3]
- Annual mammograms are a significant cost burden to the healthcare system and causes anxiety to patients[4;5]
- Further evidence needed to determine the optimum frequency and duration of mammographic surveillance - commissioned call from UK NIHR funding body

[1] Runowicz CD et al Clin Oncol 2016 34 611-35 ASCO Guideline; [2] Cardoso F et al Ann Oncol 2019 1194-220 ESMO Guideline; [3] Early and locally advanced breast cancer. NICE guideline [NG101] www.nice.org.uk; [4] Gurevich M et al. Psychosom Med. 2004 Jan-Feb;66(1):104-12; [5] Hafslund B et al. J Clin Nurs. 2012 Nov;21(21-22):3223-34

Mammo-50 Study design

- **Eligibility:** Female patients aged >50, previous treatment with curative intent for invasive or non-invasive breast cancer and who are 3 years post curative surgery



Mammo-50 trial

- Primary outcomes: breast cancer specific survival (BCSS) & cost effectiveness
- Secondary outcomes: recurrence free interval & overall survival
- QoI sub-study (Distress thermometer[1], Assessment of Survivor Concern[2], WEMWBS[3], FACT-B+4[4] collected annually)

- 5000 women to detect a 3% absolute non-inferiority (NI) margin for BCSS; 2.5% one-sided alpha; 85% power
- Primary analysis carried out on intention-to-treat basis
- Sensitivity analysis for per protocol population

[1]Brennnan et al. Psycho-oncology 2012 Dec: 21(12); [2]Gotay et al. Health and Quality of Life Outcomes 2007: 5:15; [3]Tennant et al. Health and Quality of Life Outcomes 2007:5(1), 63; [4]Webster et al. Health and Quality of Life Outcomes 2003; 1(1).

Recruitment

- 5235 women randomised between April 2014 - September 2018

Characteristic	Annual	Less frequent	Total
Total	**2618**	**2617**	**5235**
Age in years			
<60	625 (26%)	705 (27%)	1377 (26%)
60-70	**1184 (45%)**	**1118 (43%)**	**2302 (44%)**
71+	762 (29%)	794 (30%)	1556 (30%)
Surgery Type			
WLE	**2103 (80%)**	**2099 (80%)**	**4202 (80%)**
Mastectomy	515 (20%)	518 (20%)	1033 (20%)
Disease Type			
DCIS	335 (13%)	331 (13%)	666 (13%)
Invasive	**2283 (87%)**	**2288 (87%)**	**4569 (87%)**

Invasive tumour characteristics (n=4569)

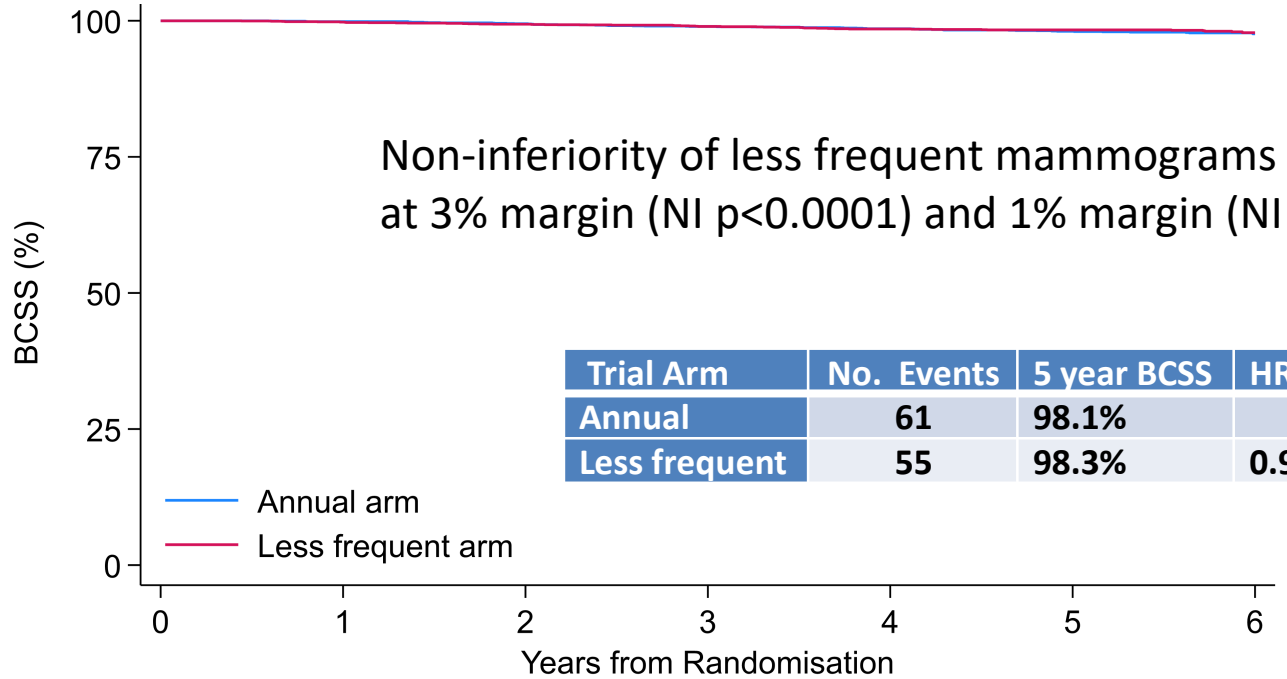
Characteristic	Annual	Less frequent	Total
Invasive tumour size (mm)			
<=20mm	**1545 (69%)**	**1560 (69%)**	**3105 (69%)**
>20mm	698 (31%)	696 (31%)	1394 (31%)
Histological Grade			
1	500 (22%)	473 (21%)	973 (21%)
2	**1222 (54%)**	**1172 (51%)**	**2394 (53%)**
3	543 (24%)	626 (28%)	1169 (26%)
Lymph node status			
Node negative	**1718 (76%)**	**1656 (73%)**	**3374 (75%)**
1-3 nodes	455 (20%)	511 (22%)	966 (21%)
4+ nodes	89 (4%)	104 (5%)	193 (4%)
Receptor status			
HER2 positive	255 (11%)	269 (12%)	524 (12%)
ER/PgR positive, HER2 negative	**1846 (83%)**	**1824 (82%)**	**3670 (82%)**
Triple negative	134 (6%)	144 (6%)	278 (6%)

Events

- Median follow-up 5.7 years (IQR 5.0-6.0 yrs); 8.7 years post curative surgery

- 343 (7%) women have died
  - 116 breast cancer; 93 other cancer; 134 other causes
- 345 (7%) invasive breast cancer recurrence
  - 103 loco-regional recurrences; 102 new breast primaries; 192 distant recurrences
- 252 (5%) new non breast malignancy (mainly skin, lung, colorectal & gynae)

Breast Cancer Specific Survival (BCSS)

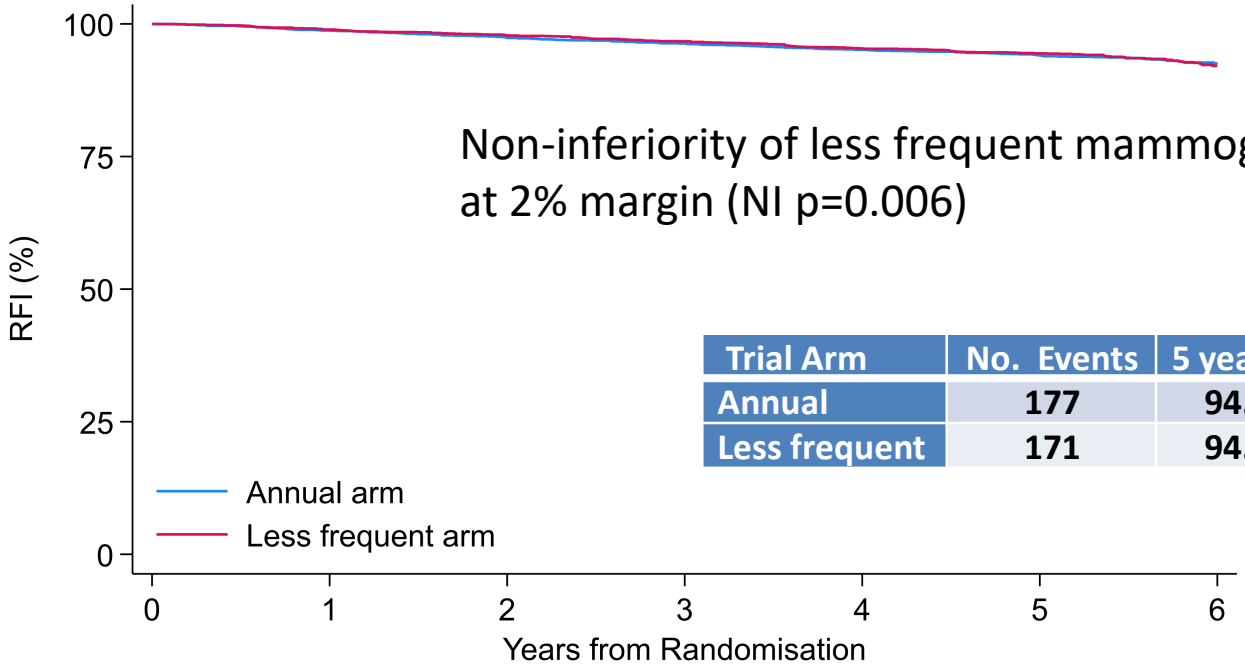


Non-inferiority of less frequent mammograms demonstrated at 3% margin (NI p<0.0001) and 1% margin (NI p=0.003)

Trial Arm	No. Events	5 year BCSS	HR (95% CI)
Annual	61	98.1%	
Less frequent	55	98.3%	0.92 (0.64-1.32)

Number at risk							
Annual arm	2618	2591	2554	2500	2426	1906	538
Less frequent arm	2617	2514	2456	2398	2307	1837	471

Recurrence free interval (RFI)

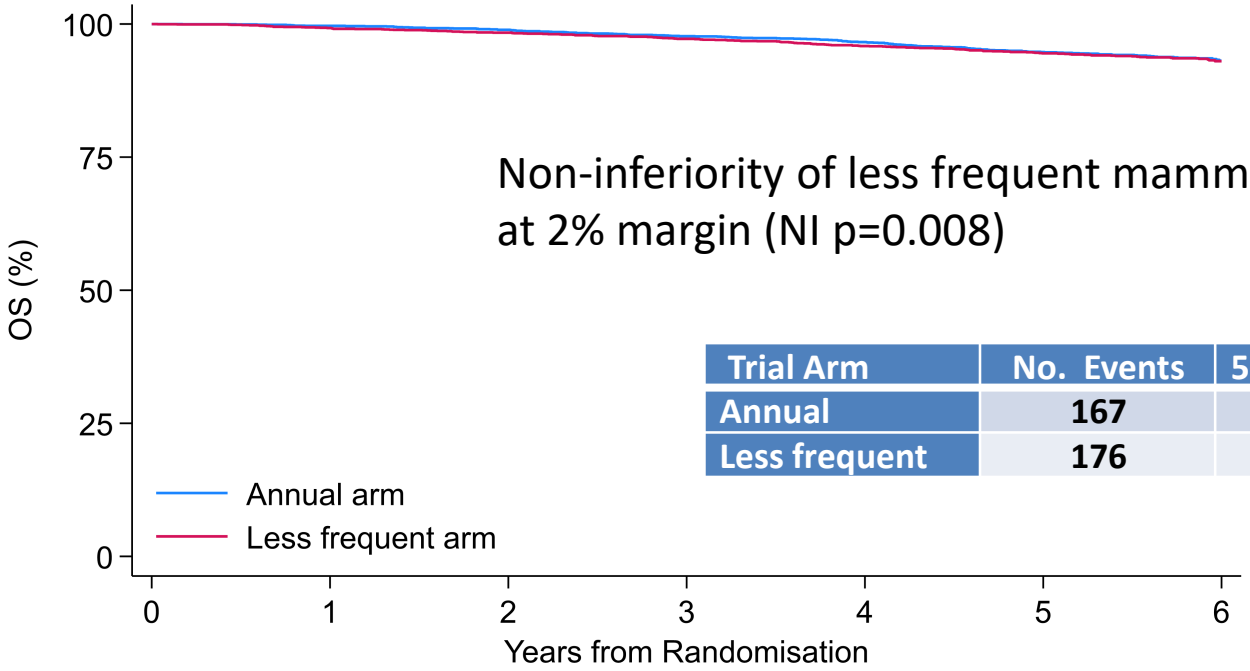


Non-inferiority of less frequent mammograms demonstrated at 2% margin (NI p=0.006)

Trial Arm	No. Events	5 year RFI	HR (95% CI)
Annual	177	94.1%	
Less frequent	171	94.5%	1.00 (0.81-1.24)

Number at risk							
Annual arm	2618	2563	2502	2439	2346	1835	515
Less frequent arm	2617	2494	2425	2353	2244	1779	442

Overall survival (OS)



Non-inferiority of less frequent mammograms demonstrated at 2% margin (NI p=0.008)

Trial Arm	No. Events	5 year OS	HR (95% CI)
Annual	167	94.7%	
Less frequent	176	94.5%	1.08 (0.87-1.33)

Number at risk

Annual arm	2618	2591	2554	2500	2426	1906	538
Less frequent arm	2617	2514	2456	2398	2307	1837	471

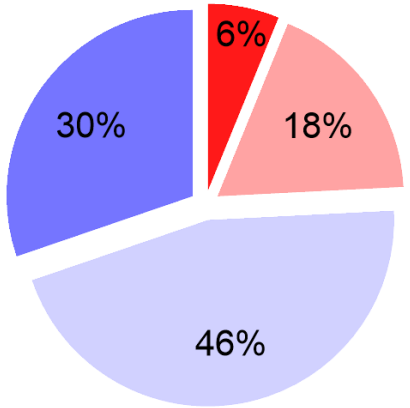
Mammograms

- 15967 mammograms performed on the annual arm and 8662 on the less frequent arm
- 83% women on the annual arm complied with their allocated schedule; 69% women on the less frequent arm

	Annual N=2618	Less frequent N=2617	Total N=5235
Complied	2170 (83%)	1817 (69%)	3987 (76%)
Missed mammograms	314 (12%)	138 (5%)	452 (9%)
Additional mammograms	13 (1%)	374 (15%)	387 (7%)
Withdrawal from trial allocation	121 (4%)	288 (11%)	409 (8%)

- COVID-19 pandemic affected compliance - 160/452 (35%) women missed mammograms
- **Conclusions remained unchanged after sensitivity analysis of complied population**

QoL: Distress thermometer pre-randomisation

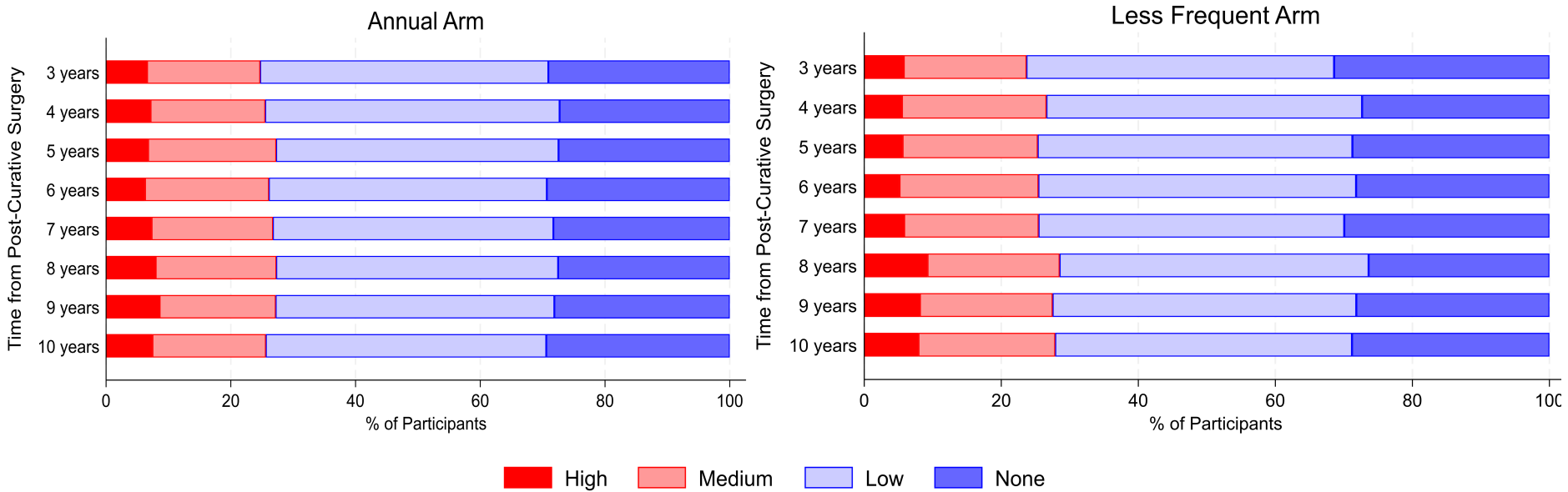


Level of distress	N (%)
None	1171 (30%)
Low	1764 (46%)
Medium	698 (18%)
High	239 (6%)

Reason for high levels of distress	N (%)
Fatigue, exhaustion or extreme tiredness	166 (58%)
Sleep problems and/or nightmares	155 (54%)
Worry, fear or anxiety	143 (50%)
Hot flushes	118 (41%)
Memory or concentration	111 (39%)
Pain	109 (38%)
Sadness or depression	101 (35%)

QoL: Levels of distress over time

- Levels of distress similar over time and across trial arms



Conclusions

- Mammo-50 demonstrated that for patients aged 50 years or older and 3 years post diagnosis, less frequent mammograms were non-inferior to annual mammograms
- There is a need to have a mechanism for easy access back into the system for symptom management and ongoing support
- Mammo-50 provides evidence for changing clinical practice

Mammo-50 Acknowledgements

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PPI:	**Sophie Gasson, Lesley Turner ICPV**
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HE:	**Claire Hulme, Peter Hall, Beth Shinkins**
Nursing:	**Sue Hartup, Annie Young**
Pathology	**Sarah Pinder**
Surgeons:	**Riccardo Audisio, Alistair Thompson**
Qualitative:	**Eila Watson**

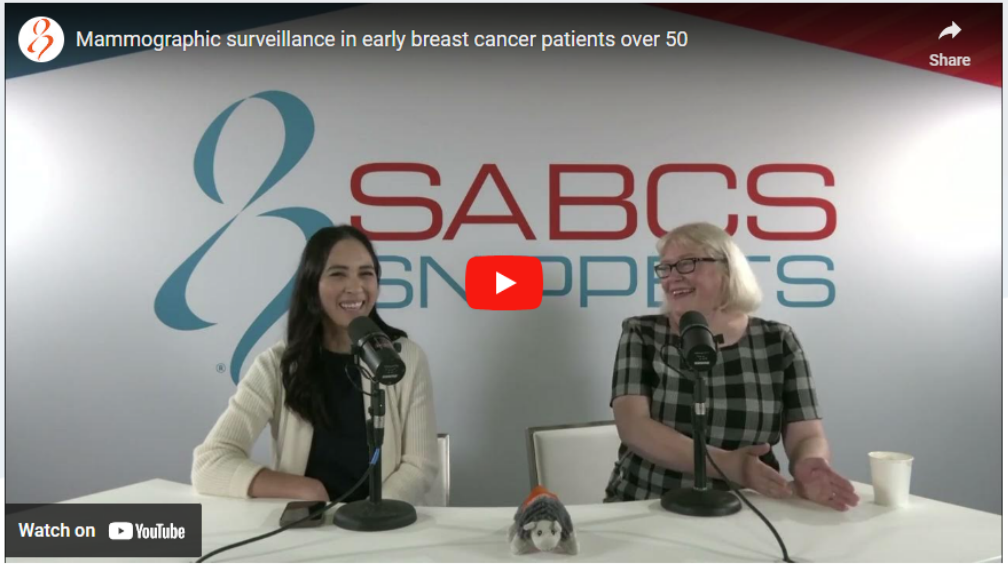
Thank you to all the 115 UK recruiting centres & the Mammo-50 Trial team

Special thanks to all the women who took part in Mammo-50

SABCS Snippets: Mammographic surveillance in early breast cancer patients over 50

December 8, 2023 // Estimated Read Time: 1 minute

Janet Dunn, PhD, head of cancer trials at Warwick Clinical Trials at Warwick Medical School, and Carissia Calvo-Strube, MD, FACS, assistant professor of breast surgical oncology at Mays Cancer Center at UT Health San Antonio, discuss the results of the Mammo-50 non-inferiority trial of annual versus less frequent mammography.



10 requests for slides:

- USA x3
- Canada
- UK x4
- Australia x2

Next steps

- NIHR HTA synopsis due 14th July
- Main trial paper, HE paper, Patient outcome paper
- Provisional date for PPI focus group 12th June for results

- Longer term follow-up (20 years in protocol) – ONS flagging
- Sites have access to Electronic Forms for ongoing data entry

Thank you for listening