Supplementary File 1: Search Strategy for Searches of Bibliographic Databases

Source	Date Searched and Results	Search Terms		
Bibliographic Databases				
Ovid MEDLINE(R) ALL <1946 to September 11, 2023>	Sept. 11, 2023 **Results:** 5404	1	exp Breast Neoplasms/	344338
		2	((breast* or mamma or mammar*) adj3 (cancer* or carcinoid* or carcinoma* or carcinogen* or adenocarcinoma* or adeno-carcinoma* or malignan* or neoplasia* or neoplasm* or sarcoma* or tumour* or tumor*)).tw,kw,kf.	428676
		3	exp Carcinoma, Intraductal, Noninfiltrating/	11265
		4	intraductal carcinoma*.tw,kw,kf.	1208
		5	(ductal carcinoma in situ or DCIS).tw,kw,kf.	9264
		6	or/1-5 [BREAST CANCER]	493511
		7	exp Breast Neoplasms/di, pc	53011
		8	exp Mass Screening/	144262
		9	screen*.tw,kw,kf.	986688
		10	Early Detection of Cancer/	38058
		11	((early or earlier or earliest) adj3 (detect* or diagnos* or identif* or recogni*)).tw,kw,kf.	338321
		12	exp Breast Neoplasms/dg [diagnostic imaging]	28933
		13	exp Mammography/	33407
		14	(mammograph* or mammogram*).tw,kw,kf.	37099
		15	exp Magnetic Resonance Imaging/	536120
		16	(fMRI or fMRIs or MRI or MRIs or NMRI or NMRIs or MR imaging or NMR imaging or magnetic resonance imag* or magnetic resonance tomograph* or MR tomograph*).tw,kw,kf.	549844
		17	(chemical shift imaging or proton spin tomograph* or zeugmatograph*).tw,kw,kf.	1182
		18	(ultrasound* or ultrason* or echograph* or echotomograph* or echo-tomograph* or sonograph*).tw,kw,kf.	504018
		19	(echomammogra* or echo-mammogra*).tw,kw,kf.	11

		20	Imaging, Three-Dimensional/	81554
		21	((3D or "3-D") adj3 imag*).tw,kw,kf.	28853
		22	(("3" or three) adj dimension* adj3 imag*).tw,kw,kf.	21223
		23	tomosynthes*.tw,kw,kf.	2337
		24	or/7-23 [SCREENING]	2566333
		25	6 and 24 [BREAST CANCER SCREENING]	123501
		26	exp Infant/ not (exp Adult/ and exp Infant/)	924634
		27	exp Child/ not (exp Adult/ and exp Child/)	1397736
		28	Adolescent/ not (exp Adult/ and Adolescent/)	688872
		29	or/26-28	2150464
		30	25 not 29 [CHILD-ONLY REMOVED]	122849
		31	exp Animals/ not (exp Animals/ and Humans/)	5154279
		32	30 not 31 [ANIMAL-ONLY REMOVED]	121340
		33	(comment or editorial or news or newspaper article).pt.	1696172
		34	(letter not (letter and randomized controlled trial)).pt.	1222049
		35	32 not (33 or 34) [OPINION PIECES REMOVED]	113654
		36	(Case Reports not (Case Reports and Randomized Controlled Triail)).pt.	2356020
		37	(case adj (series or study or st udies or report or reports)).ti.	415116
		38	35 not (36 or 37) [CASE STUDIES/SERIES REMOVED]	103599
		39	limit 38 to yr="2014-current"	46655
		40	controlled clinical trial.pt.	95422
		41	Controlled Clinical Trial/ or Controlled Clin ical Trials as Topic/	95422
		42	(control* adj2 trial).tw,kw,kf.	214944
		43	Non-Randomized Controlled Trials as Topic/	1064
		44	(nonrandom* or non-random* or quasi-random* or quasi-experiment*).tw,kw,kf.	74493
		45	(nRCT or non-RCT).tw,kw,kf.	531
		46	Controlled Before-After Studies/	733
		47	(control* adj3 ("before and after" or "before after")).tw,kw,kf.	5349
		48	Interrupted Time Series Analysis/	1898
		49	time series.tw,kw,kf.	46844

		50	(pre- adj5 post-).tw,kw,kf.	132314
		51	((pretest adj5 posttest) or (pre-test adj5 post-test)).tw,kw,kf.	11920
		52	Historically Controlled Study/	230
		53	(control* adj2 study).tw,kw,kf.	212912
		54	Control Groups/	2022
		55	(control* adj2 group?).tw,kw,kf.	630931
		56	trial.ti.	292436
		57	or/40-56	1396866
		58	39 and 57 [nRCTs]	3356
		59	exp Cohort Studies/	2518661
		60	cohort?.tw,kw,kf.	876733
		61	Retrospective Studies/	1143098
		62	(longitudinal or prospective or retrospective).tw,kw,kf.	1711760
		63	((followup or follow-up) adj (study or studies)).tw,kw,kf.	59422
		64	Observational study.pt.	145987
		65	(observation$2 adj (study or studies)).tw,kw,kf.	168360
		66	((population or population-based) adj (study or studies or analys#s)).tw,kw,kf.	28009
		67	((multidimensional or multi-dimensional) adj (study or studies)).tw,kw,kf.	152
		68	Comparative Study.pt.	1913019
		69	((comparative or comparison) adj (study or studies)).tw,kw,kf.	135803
		70	exp Case-Control Studies/	1442707
		71	((case-control* or case-based or case-comparison or case-compeer or case-referrent or case-referent) adj3 (study or studies)).tw,kw,kf.	143028
		72	Multicenter Study.pt.	337684
		73	((multicenter or multi-center or multicentre or multi-centre) adj (study or studies)).tw,kw,kf.	56295
		74	or/59-73	5468150
		75	39 and 74 [OBSERVATIONAL STUDIES]	16738
		76	58 or 75 [nRCTs, OBSERVATIONAL STUDIES, 2014-PRESENT]	18158
		77	exp Mass Screening/ae [Adverse Effects]	933
		78	exp Mass Screening/mo [Mortality]	85

		79	Early Detection of Cancer/ae [Adverse Effects]	365
		80	Early Detection of Cancer/mo [Mortality]	100
		81	exp Mass Screening/ae [Adverse Effects]	933
		82	exp Mammography/mo [Mortality]	26
		83	exp Diagnostic Errors/	122646
		84	exp Neoplasms, Radiation-Induced/	19514
		85	Mortality/	49503
		86	((avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*) adj5 (death* or fatal* or morbidit* or mortalit*)).tw,kw,kf.	290502
		87	((avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*) adj5 (advanced stage? or (advanc* adj3 cancer?) or biopsy or biopsies or chemotherap* or chemo-therap* or disfigur* or exacerbat* or incidental finding? or progress* stage? or progression* or late? stage? or stage? III or stage? 3 or stage? IV or stage? 4)).tw,kw,kf.	100916
		88	((avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*) adj5 (adverse* or harm* or impair* or injur* or invasiv* or side-effect* or sideeffect* or undesirabl* or un-desirabl*)).tw,kw,kf.	283440
		89	((avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*) adj5 (alarm* or anxiet* or anxious* or distress* or emotion* or feeling* or psycholog* or uncertain* or un-certain*)).tw,kw,kf.	93054
		90	(misdiagnos* or mis-diagnos* or misdetect* or mis-detect* or misidentif* or mis-identif*).tw,kw,kf.	51229
		91	(miss$3 adj3 (detect* or diagnos* or identif*)).tw,kw,kf.	13521
		92	((undetected or un-detected or ("not" adj3 detect*) or undiagnos* or un-diagnos* or ("not" adj3 diagnos*) or unidentif* or un-identif* or ("not" adj3 identif*)) adj3 (cancer* or carcinoid* or carcinoma* or carcinogen* or adenocarcinoma* or adeno-carcinoma* or lump or lumps or malignan* or neoplasia* or neoplasm* or sarcoma* or tumour* or tumor*)).tw,kw,kf.	8298
		93	(overdiagnos* or over diagnos*).tw,kw,kf.	6926
		94	(false adj (negative* or positive*)).tw,kw,kf.	90499
		95	((error* or false$2 or wrong$3) adj3 (alarm* or detect* or diagnos*)).tw,kw,kf.	29089
		96	exp Medical Overuse/	15050
		97	overtreat*.tw,kw,kf.	6752
		98	((medical or health service? or procedur* or therap* or treatment*) adj3 (overuse? or overusing or overutilis* or overutiliz*)).tw,kw,kf.	941

		99	((inappropriate* or unnecessar*) adj3 (followup or follow-up or health care or healthcare or procedur* or therap* or treatment*)).tw,kw,kf.	16716
		100	(inappropriate* or unnecessar* or safe or adverse or adversely or undesirabl* or un-desirabl* or unintend* or un-intend* or unintent* or un-intent* or unsafe* or un-safe* or unwanted or un-wanted or harm* or injurious* or risk or risks or side-effect* or sideeffect* or reaction* or complication*).ti,kw,kf.	1438760
		101	((adverse* or undesirabl* or un-desirabl* or unintend* or un-intend* or unintent* or un-intent* or unwanted or un-wanted or harm* or toxic or injurious* or serious* or fatal) adj5 (affect or affected or affecting or affects or consequence* or effect* or react or reacts or reacted or reacting or reaction* or side-effect* or sideeffect* or event* or outcome* or incident*)).tw,kw,kf.	862785
		102	((adverse* or inappropriat* or unnecessar* or undesirabl* or un-desirabl* or unintend* or unintend* or unintent * or un-intent* or unwanted or un-wanted or injurious* or serious*) adj5 (alarm* or anxiet* or anxious* or distress* or emotion* or feeling* or psycholog* or uncertain* or uncertain*)).tw,kw,kf.	13242
		103	exp Neoplasm Metastasis/ and (avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*).ti.	3575
		104	(benefit* or beneficial*).ti,kw,kf.	96339
		105	or/77-104 [BENEFITS/HARMS]	3152378
		106	76 and 105 [nRCTs, OBSERVATIONAL STUDIES, 2014-PRESENT - BENEFITS AND HARMS]	5416
		107	remove duplicates from 106	5404
Ovid Embase <1974 to 2023 September 11>	Sept. 11, 2023 **Results:** 5342	1	exp breast cancer/	569430
		2	((breast* or mamma or mammar*) adj3 (cancer* or carcinoid* or carcinoma* or carcinogen* or adenocarcinoma* or adeno-carcinoma* or malignan* or neoplasia* or neoplasm* or sarcoma* or tumour* or tumor*)).ti,kw,kf.	410111
		3	intraductal carcinoma*.ti,kw,kf.	678
		4	(ductal carcinoma in situ or DCIS).ti,kw,kf.	6290
		5	or/1-4 [BREAST CANCER]	644806
		6	exp breast cancer/di, pc [diagnosis, prevention]	71475
		7	mass screening/ or cancer screening/	157001
		8	screen*.ti,kw,kf.	343605

		9	early cancer diagnosis/	13653
		10	((early or earlier or earliest) adj3 (detect* or diagnos* or identif* or recogni*)).ti,kw,kf.	60364
		11	exp mammography/	67718
		12	(mammograph* or mammogram*).ti,kw,kf.	25217
		13	breast magnetic resonance imaging/	704
		14	(fMRI or fMRIs or MRI or MRIs or NMRI or NMRIs or MR imaging or NMR imaging or magnetic resonance imag* or magnetic resonance tomograph* or MR tomograph*).ti,kw,kf.	363656
		15	(chemical shift imaging or proton spin tomograph* or zeugmatograph*).ti,kw,kf.	690
		16	(ultrasound* or ultrason* or echograph* or echotomograph* or echo-tomograph* or sonograph*).ti,kw,kf.	332932
		17	(echomammogra* or echo-mammogra*).ti,kw,kf.	8
		18	three-dimensional imaging/	117910
		19	((3D or "3-D") adj3 imag*).ti,kw,kf.	8082
		20	(("3" or three) adj dimension* adj3 imag*).ti,kw,kf.	6967
		21	tomosynthes*.ti,kw,kf.	2376
		22	or/6-21 [SCREENING]	1333341
		23	5 and 22 [BREAST CANCER SCREENING]	118838
		24	male/ not female/	3286854
		25	23 not 24 [MALE-ONLY REMOVED]	117134
		26	exp adolescent/ not exp adult/	673829
		27	exp child/ not exp adult/	2234396
		28	or/26-27	2503724
		29	25 not 28 [CHILD-ONLY REMOVED]	116696
		30	(exp animal/ or exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp vertebrate/) not (exp human/ or exp human experimentation/ or exp human experiment/)	7259581
		31	29 not 30 [ANIMAL-ONLY REMOVED]	114205
		32	editorial.pt. or (letter.pt. not randomized controlled trial/)	2061135
		33	conference abstract.pt.	4877774
		34	31 not (32 or 33) [OPINION PIECES, CONFERENCE ABSTRACTS REMOVED]	97539
		35	(case report/ or exp case study/) not randomized controlled trial/	2979143

		36	(case adj (series or study or studies or report or reports)).ti.	515645
		37	34 not (35 or 36) [CASE STUDIES/SERIES REMOVED]	88026
		38	limit 37 to yr="2014-current" [DATE LIMITS APPLICABLE TO OBSERVATIONAL STUDY SEARCH]	38463
		39	controlled clinical trial/	470925
		40	controlled clinical trial (topic)/	13349
		41	(control* adj2 trial).ti,kw,kf.	154850
		42	(nonrandom* or non-random* or quasi-random* or quasi-experiment*).ti,kw,kf.	10518
		43	(nRCT or non-RCT).ti,kw,kf.	13
		44	(control* adj3 ("before and after" or "before after")).ti,kw,kf.	414
		45	time series analysis/	37952
		46	time series.ti,kw,kf.	13968
		47	pretest posttest control group design/	664
		48	(pre- adj5 post-).ti,kw,kf.	10856
		49	((pretest adj5 posttest) or (pre-test adj5 post-test)).ti,kw,kf.	340
		50	controlled study/	9853540
		51	(control* adj2 study).ti,kw,kf.	91626
		52	control group/	110638
		53	(control* adj2 group?).ti,kw,kf.	4289
		54	trial.ti.	400873
		55	or/39-54	1E+07
		56	38 and 55 [nRCTs]	16029
		57	cohort analysis/	1044722
		58	cohort?.ti,kw,kf.	259788
		59	retrospective study/	1484641
		60	longitudinal study/	196998
		61	prospective study/	877418
		62	(longitudinal or prospective or retrospective).ti,kw,kf.	539104
		63	follow up/	2067555
		64	((followup or follow-up) adj (study or studies)).ti,kw,kf.	31327
		65	observational study/	335563

		66	(observation$2 adj (study or studies)).ti,kw,kf.	54094
		67	population research/	135115
		68	((population or population-based) adj (study or studies or analys#s)).ti,kw,kf.	8768
		69	((multidimensional or multi-dimensional) adj (study or studies)).ti,kw,kf.	65
		70	exp comparative study/	1676614
		71	((comparative or comparison) adj (study or studies)).ti,kw,kf.	88994
		72	exp case control study/	225238
		73	((case-control* or case-based or case-comparison or case-compeer or case-referrent or case-referent) adj3 (study or studies)).ti,kw,kf.	57928
		74	major clinical study/	4991488
		75	multicenter study/	371692
		76	((multicenter or multi-center or multicentre or multi-centre) adj (study or studies)).ti,kw,kf.	34050
		77	or/57-76	9020019
		78	38 and 77 [OBSERVATIONAL STUDIES]	23097
		79	56 or 78 [nRCTs, OBSERVATIONAL STUDIES, 2014-PRESENT]	26586
		80	mass screening/ae [adverse drug reaction]	164
		81	exp mammography/ae [adverse drug reaction]	228
		82	exp diagnostic error/	126408
		83	mortality/	898047
		84	cancer mortality/	107182
		85	exp radiation induced neoplasm/	2769
		86	((avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*) adj5 (death* or fatal* or morbidit* or mortalit*)).ti,kw,kf.	26017
		87	((avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*) adj5 (advanced stage? or (advanc* adj3 cancer?) or biopsy or biopsies or chemotherap* or chemo-therap* or disfigur* or exacerbat* or incidental finding? or progress* stage? or progression* or late? stage? or stage? III or stage? 3 or stage? IV or stage? 4)).ti,kw,kf.	12331
		88	((avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*) adj5 (adverse* or harm* or impair* or injur* or invasiv* or side-effect* or sideeffect* or undesirabl* or un-desirabl*)).ti,kw,kf.	44328
		89	((avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*) adj5 (alarm* or anxiet* or anxious* or distress* or emotion* or feeling* or psycholog* or uncertain* or un-certain*)).ti,kw,kf.	9909

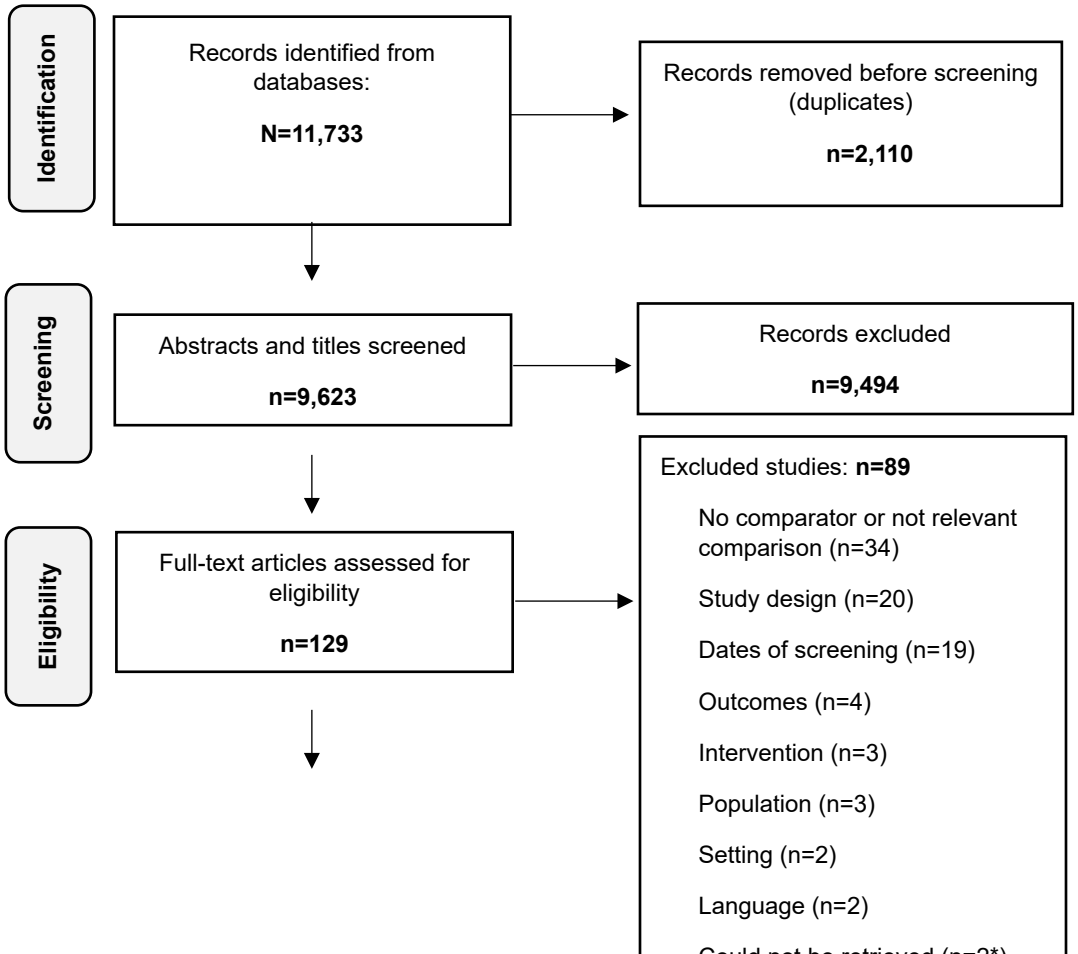
		90	(misdiagnos* or mis-diagnos* or misdetect* or mis-detect* or misidentif* or mis-identif*).ti,kw,kf.	10142
		91	(miss$3 adj3 (detect* or diagnos* or identif*)).ti,kw,kf.	2249
		92	((undetected or un-detected or ("not" adj3 detect*) or undiagnos* or un-diagnos* or ("not" adj3 diagnos*) or unidentif* or un-identif* or ("not" adj3 identif*)) adj3 (cancer* or carcinoid* or carcinoma* or carcinogein* or adenocarcinoma* or adeno-carcinoma* or lump or lumps or malignan* or neoplasia* or neoplasm* or sarcoma* or tumour* or tumor*)).ti,kw,kf.	608
		93	(overdiagnos* or over diagnos*).ti,kw,kf.	2277
		94	(false adj (negative* or positive*)).ti,kw,kf.	11263
		95	((error* or false$2 or wrong$3) adj3 (alarm* or detect* or diagnos*)).ti,kw,kf.	6462
		96	exp medical overuse/	8001
		97	overtreat*.ti,kw,kf.	1425
		98	((medical or health service? or procedur* or therap* or treatment*) adj3 (overuse? or overusing or overutilis* or overutiliz*)).ti,kw,kf.	418
		99	((inappropriate* or unnecessar*) adj3 (followup or follow-up or health care or healthcare or procedur* or therap* or treatment*)).ti,kw,kf.	1420
		100	(inappropriate* or unnecessar* or safe or adverse or adversely or undesirabl* or un-desirabl* or unintend* or un-intend* or unintent* or un-intent* or unsafe* or un-safe* or unwanted or un-wanted or harm* or injurious* or risk or risks or side-effect* or sideeffect* or reaction* or complication*).ti,kw,kf.	1824660
		101	((adverse* or undesirabl* or un-desirabl* or unintend* or un-initend* or unintent* or un-intent* or unwanted or un-wanted or harm* or toxic or injurious* or serious* or fatal) adj5 (affect or affected or affecting or affects or consequence* or effect* or react or reacts or reacted or reacting or reaction* or side-effect* or sideeffect* or event* or outcome* or incident*)).ti,kw,kf.	137246
		102	((adverse* or inappropriat* or unnecessar* or undesirabl* or un-desirabl* or unintend* or unintend* or unintent* or un-intent* or unwanted or un-wanted or injurious* or serious*) adj5 (alarm* or anxiet* or anxious* or distress* or emotion* or feeling* or psycholog* or uncertain* or uncertain*)).ti,kw,kf.	1362
		103	exp metastasis/ and (avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*).ti.	12827
		104	(benefit* or beneficial*).ti,kw,kf.	128770
		105	or/80-104 [BENEFITS/HARMS]	3038175

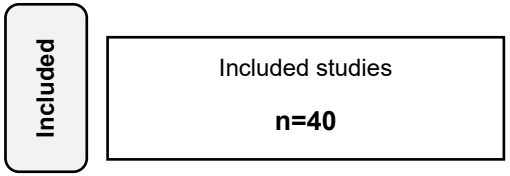
		106 79 and 105 [nRCTs, OBSERVATIONAL STUDIES, 2014-PRESENT - BENEFITS AND HARMS] 5601 107 remove duplicates from 106 5563 108 limit 107 to embase 5342
EBM Reviews - Cochrane Central Register of Controlled Trials <September 11, 2023>	**Results**: 987	1 exp Breast Neoplasms/ (17822) 2 ((breast* or mamma or mammar*) adj3 (cancer* or carcinoid* or carcinoma* or carcinogen* or adenocarcinoma* or adeno-carcinoma* or malignan* or neoplasia* or neoplasm* or sarcoma* or tumour* or tumor*)).ti,ab,kw. (42966) 3 exp Carcinoma, Intraductal, Noninfiltrating/ (268) 4 intraductal carcinoma*.ti,ab,kw. (383) 5 (ductal carcinoma in situ or DCIS).ti,ab,kw. (799) 6 or/1-5 [BREAST CANCER] (44365) 7 exp Breast Neoplasms/di, pc (23) 8 exp Mass Screening/ (5322) 9 screen*.ti,ab,kw. (92978) 10 "Early Detection of Cancer"/ (2019) 11 ((early or earlier or earliest) adj3 (detect* or diagnos* or identif* or recogni*)).ti,ab,kw. (10711) 12 exp Breast Neoplasms/dg (12) 13 exp Mammography/ (1207) 14 (mammograph* or mammogram*).ti,ab,kw. (2716) 15 exp Magnetic Resonance Imaging/ (10900) 16 (fMRI or fMRIs or MRI or MRIs or NMRI or NMRIs or MR imaging or NMR imaging or magnetic resonance imag* or magnetic resonance tomograph* or MR tomograph*).ti,ab,kw. (41032) 17 (chemical shift imaging or proton spin tomograph* or zeugmatograph*).ti,ab,kw. (31) 18 (ultrasound* or ultrason* or echograph* or echotomograph* or echo-tomograph* or sonograph*).ti,ab,kw. (55369) 19 (echomammogra* or echo-mammogra*).ti,ab,kw. (61) 20 Imaging, Three-Dimensional/ (1361) 21 ((3D or "3-D") adj3 imag*).ti,ab,kw. (912) 22 (("3" or three) adj dimension* adj3 imag*).ti,ab,kw. (999) 23 tomosynthes*.ti,ab,kw. (98) 24 or/7-23 (193579) 25 6 and 24 (6537)

		26 exp Infant/ not (exp Adult/ and exp Infant/) (31793) 27 exp Child/ not (exp Adult/ and exp Child/) (56162) 28 Adolescent/ not (exp Adult/ and Adolescent/) (27766) 29 or/26-28 (81116) 30 25 not 29 (6530) 31 conference proceeding.pt. (224121) 32 30 not 31 (5299) 33 limit 32 to yr="2014-current" (2822) 34 exp Mass Screening/ae (0) 35 exp Mass Screening/mo (0) 36 "Early Detection of Cancer"/ae (0) 37 "Early Detection of Cancer"/mo (0) 38 exp Mammography/ae (0) 39 exp Mammography/mo (0) 40 exp Diagnostic Errors/ (3432) 41 exp Neoplasms, Radiation-Induced/ (99) 42 Mortality/ (4569) 43 ((avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*) adj5 (death* or fatal* or morbidit* or mortalit*)).ti,ab,kw. (31982) 44 ((avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*) adj5 (advanced stage? or (advanc* adj3 cancer?) or biopsy or biopsies or chemotherap* or chemo-therap* or disfigur* or exacerbat* or incidental finding? or progress* stage? or progression* or late? stage? or stage? III or stage? 3 or stage? IV or stage? 4)).ti,ab,kw. (18433) 45 ((avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*) adj5 (adverse* or harm* or impair* or injur* or invasiv* or side-effect* or sideeffect* or undesirabl* or un-desirabl*)).ti,ab,kw. (38937) 46 ((avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*) adj5 (alarm* or anxiet* or anxious* or distress* or emotion* or feeling* or psycholog* or uncertain* or un-certain*)).ti,ab,kw. (24948) 47 (misdiagnos* or mis-diagnos* or misdetect* or mis-detect* or misidentif* or mis-identif*).ti,ab,kw. (595) 48 (miss$3 adj3 (detect* or diagnos* or identif*)).ti,ab,kw. (511) 49 ((undetected or un-detected or ("not" adj3 detect*) or undiagnos* or un-diagnos* or ("not" adj3 diagnos*) or unidentif* or un-identif* or ("not" adj3 identif*)) adj3 (cancer* or carcinoid* or carcinoma* or carcinogen* or adenocarcinoma* or adeno-carcinoma* or lump or lumps or malignan* or neoplasia* or neoplasm* or sarcoma* or tumour* or tumor*)).ti,ab,kw. (287) 50 (overdiagnos* or over diagnos*).ti,ab,kw. (484) 51 (false adj (negative* or positive*)).ti,ab,kw. (3294)

		52 ((error* or false$2 or wrong$3) adj3 (alarm* or detect* or diagnos*)).ti,ab,kw. (1443) 53 exp Medical Overuse/ (638) 54 overtreat*.tw,kw,kf. (535) 55 ((medical or health service? or procedur* or therap* or treatment*) adj3 (overuse? or overusing or overutilis* or overutiliz*)).ti,ab,kw. (124) 56 ((inappropriate* or unnecessar*) adj3 (followup or follow-up or health care or healthcare or procedur* or therap* or treatment*)).ti,ab,kw. (970) 57 (inappropriate* or unnecessar* or safe or adverse or adversely or undesirabl* or un-desirabl* or unintend* or un-intend* or unintent* or un-intent* or unsafe* or un-safe* or unwanted or un-wanted or harm* or injurious* or risk or risks or side-effect* or sideeffect* or reaction* or complication*).ti. (76297) 58 ((adverse* or undesirabl* or un-desirabl* or unintend* or un-intend* or unintent* or un-intent* or unwanted or un-wanted or harm* or toxic or injurious* or serious* or fatal) adj5 (affect or affected or affecting or affects or consequence* or effect* or react or reacts or reacted or reacting or reaction* or side-effect* or sideeffect* or event* or outcome* or incident*)).ti,ab,kw. (235248) 59 ((adverse* or inappropriat* or unnecessar* or undesirabl* or un-desirabl* or unintend* or un-intend* or unintent* or un-intent* or unwanted or un-wanted or injurious* or serious*) adj5 (alarm* or anxiet* or anxious* or distress* or emotion* or feeling* or psycholog* or uncertain* or un-certain*)).ti,ab,kw. (2506) 60 exp Neoplasm Metastasis/ and (avoid* or declin* or decreas* or lessen* or lower* or prevent* or reduc*).ti. (191) 61 (benefit* or beneficial*).ti,kw,kf. (18046) 62 or/34-61 (399359) 63 33 and 62 (987)

Supplementary File 2: PRISMA Diagram





* One study was delivered late and was not included in the analysis.

Supplementary File 3: Data Tables

Table S-1. Study characteristics of included non-randomised comparative studies

Author, year	Study design	Setting	Study years Longest FU (years)	Study population	Age (years)	Total participants	Screened definition	Non-screened definition	Screening modality	Screening interval (years)
Cohort studies - general screening population										
Choi et al. 2021 [1]	Prospective Long case accrual	Korea National screening database	1 Jan 2002 to 31 Dec 2015 FU: median 8.7	Women without BC	40-79	13,326,868	Screened at initial invitation or attended another round of screening during study period (includes women who were initially unscreened)	Not screened during study period (includes women who were unscreened initially but underwent screening later)	Film or digital 2D	2
Czwikla et al. 2018 [2]	Retrospective Short case accrual	Germany Insurance claim database	2007 to 31 Dec 2015 FU: mean 3.9	Women with health insurance	50-68	1,247,919	Screening mammogram	Did not undergo screening mammogram	Digital 2D	2
Dunn et al. 2021 [3]	Retrospective Short case accrual	Australia Electoral roll	1 Jan 2000 to 31 Dec 2015 FU: 16	Women on electoral roll	50-65 (age at study entry)	262,350	Screening mammogram during study period	No screening mammogram during study period	NR	2
Garcia-Albeniz et al. 2020 [4]	Retrospective Long case accrual	USA Medicare beneficiaries	1999 to 2008 FU: 8	Women without BC	70-84	264,274	Screening mammogram	No further screening after baseline mammogram	NR	1

Author, year	Study design	Setting	Study years Longest FU (years)	Study population	Age (years)	Total participants	Screened definition	Non-screened definition	Screening modality	Screening interval (years)
Lund et al. 2018 [5]	Retrospective Long case accrual	Norway Random sample of national population-based cohort study participants	1 Jan 2005 to 31 Dec 2013 FU: NR	Women from a Norwegian national population-based cohort study	49-79	124,978	Ever screened	Never screened	Digital 2D	2
Morrell et al. 2017 [6]	Retrospective Long case accrual	New Zealand Screening, cancer, and death registries	1999 to 2011 FU: NR	Women who were ever screened or diagnosed with BC	45-69	NR	Ever screened	Never screened	Film or digital 2D	2
Richman et al. 2023 [7]	Retrospective Short case accrual	USA National Medicare registry	2002-2017 FU: median 13.7	Women without BC	≥70 years	54,635	Screening mammogram within 3 years of previous mammogram	Did not undergo screening mammogram within 3 years of previous mammogram	NR	2
Cohort studies - women with BC										
Barco et al. 2015 [8]	Prospective Long case accrual	Spain Two hospitals	1 Jan 1997 to 31 Jan 2014 FU: 10	Women with BC	50-69	1,821	Breast cancer screening program	Patients referred from regular public healthcare system	Digital in round 6 (otherwise NR)	2
Bayard et al. 2021 [9]	Retrospective Long case accrual	USA Academic cancer programs in two cities	1 Jan 1998 to 31 Dec 2018 FU: median 4.6	Women with BC	≤40 (12%) to >50	756	Scheduled screening mammogram	Clinically detected BC among non-screened participants	NR	NR
Braun et al. 2021 [10]	Retrospective Short case accrual	Germany One of two BC centres in one city	2006 to 2015 FU: NR	Women with newly detected invasive BC	50-69	735	Screen-detected BC (excluding interval BC)	Clinically detected BC among non-screened participants	NR	2
Choi et al. 2018 [11]	Retrospective Long case accrual	Korea National cancer and screening registries	1 Jan 2002 to 31 Dec 2011 FU: NR	Women with BC (DCIS or invasive)	≥41	7,164 (matched); 15,406 (unmatched)	Ever screened	Never screened	NR	2

Author, year	Study design	Setting	Study years Longest FU (years)	Study population	Age (years)	Total participants	Screened definition	Non-screened definition	Screening modality	Screening interval (years)
de Munck et al. 2020 [12]	Retrospective Long case accrual	Netherlands National cancer and screening registries	1 Jan 2004 and 31 Dec 2015 FU: NR	Women with BC (DCIS or invasive)	49-74	88,285	Positive screening mammogram	Diagnosed at screening interval >24 months or had never attended screening	Film or digital 2D	2
Duffy et al. 2021 [13]	Retrospective Long case accrual	Sweden Screening registry (9 counties)	1992 to 2016 FU: 25	Women with BC	40-73 at diagnosis (no upper age limit for mortality)	549,091	Participated in both of last two scheduled screening mammograms	Did not participate in either of two previous screenings	NR	1.5 (age 40-54 years) 2 (age 55-69 years)
Elder et al. 2018 [14]	Retrospective Long case accrual	Australia One hospital	2007 to 2013 FU: NR	Women with BC	50-69	791	Active screeners at diagnosis (includes screen-detected and interval cancers)	Not recently screened (includes never screened and women who last attended screening ≥27 months before diagnosis)	2D (modality NR)	2
Garcia Fernandez et al. 2014 [15]	Prospective Long case accrual	Spain Two hospitals	1 May 2002 to 30 Jul 2012 FU: 10	Women with BC	50-69	904	Recruited from Breast Cancer Early Diagnosis Programme	Recruited from regular public healthcare system	NR	2
Ilenko et al. 2017 [16]	Retrospective Long case accrual	France One hospital	2005 to 2015 FU: 5	Women with BC	≥75	393	Positive screening mammogram	Clinically detected BC	NR	NR
Ip et al. 2020 [17]	Retrospective Short case accrual	New Zealand Regional BC registry	1 Jun 2000 to 23 Nov 2017 FU: median 5.2	Women with BC (DCIS or invasive)	≥70	2,128	Positive screening mammogram	Clinically detected BC	NR	NR
Kobayashi et al. 2017 [18]	Retrospective Long case accrual	Japan One hospital	2003 to 2014 FU: median 5.1	Women with BC	39-70 (note: notation for age ranges not clear)	1,132	Positive screening mammogram	Clinically detected BC	NR	NR
Lim et al. 2022 [19]	Retrospective Long case accrual	Singapore Seven public hospitals	2010 to 2018 FU: ≤10	Women with BC (DCIS or invasive)	≥50	3,739	Last screening mammogram ≤2 years before diagnosis	Did not attend screening or last screen >2 years before diagnosis	NR	2

Author, year	Study design	Setting	Study years Longest FU (years)	Study population	Age (years)	Total participants	Screened definition	Non-screened definition	Screening modality	Screening interval (years)
Luu et al. 2022 [20]	Retrospective Short case accrual	Korea National database	1 Jan 2008 to 31 Dec 2019 FU: median 10.5	Women with BC (DCIS or invasive)	40-79	24,387	Screened	Never screened	NR	Varied from <1 to >3 across participants
Niraula et al. 2020 [21]	Retrospective Long case accrual	Canada Regional cancer and screening registries; national statistics	Jan 2004 to Jun 2010 FU: median 7	Women with invasive BC	50-64	1,687	Positive screening mammography	Did not participate in screening program	NR	2
Oberaigner et al. 2017 [22]	Retrospective Long case accrual	Austria Screening and regional cancer registries	1 Jan 2009 to 31 Dec 2013 FU: NR	Women with BC (mostly invasive)	40-69	1,609	Exposed to screening mammography	Not exposed to screening mammography	NR	1 (age 40-59 years) 2 (age 60-69 years)
Plecha et al. 2014 [23]	Retrospective Long case accrual	USA One breast centre	1 Jan 2008 to 31 Dec 2011 FU: NR	Women with BC	40-49	230	Positive screening mammogram or symptomatic cancer <15 months after negative screening mammogram	Clinically detected BC and no screening mammogram within the last 16 months	Film or digital 2D	NR
Roder et al. 2017 [24]	Retrospective Long case accrual	Australia Regional cancer registry (subset of patients treated at 4 major public hospitals)	1997-2010 FU: 10	Women with invasive BC	50-69	2,039	Participation in screening program	Did not participate in screening program	NR	NR
Seneviratne et al. 2015 [25]	Retrospective Long case accrual	New Zealand Regional cancer registry	1 Jan 1999 and 31 Dec 2013 FU: mean 5.5	Women with BC	45-69	1,846	Positive screening mammogram (89.7%) or opportunistic screening (10.3%)	NR	NR	2
Tomsic et al. 2022 [26]	Retrospective Short case accrual	Slovenia	2008 to 1 July 2021 FU: NR	Women with BC	≥50 years	11,425	At least one mammogram before diagnosis (within or	Did not attend screening after an invitation or	NR	2

Author, year	Study design	Setting	Study years Longest FU (years)	Study population	Age (years)	Total participants	Screened definition	Non-screened definition	Screening modality	Screening interval (years)
		National cancer registry					outside the screening program)	were never invited to screening		
Tvedskov et al. 2016 [27]	Retrospective Long case accrual	Denmark National cancer registry	2008-2010 FU: NR	Women with BC	50-70	955	Registered in screening program database	Not registered in screening program database	NR	2
Ujhelyi et al. 2016 [28]	Retrospective Short case accrual	Hungary Single institution	1 Jan 2002 to 31 Dec 2009 FU: median 6.7	Women with BC	45-65	595	Positive screening mammogram	Self-examination or clinically detected BC	Digital 2D	2
Varga et al. 2023 [29]	Retrospective Short case accrual	Hungary Single institution	2002 to 31 May 2023 FU: mean 12.6	Women with BC	45-65	309	Positive screening mammogram	Self-examination or clinically detected BC	Digital 2D	2
Woods et al. 2016 [30]	Retrospective Short case accrual	Australia/UK Regional cancer registries	Australia: Nov 2003 (median month of diagnosis) to 31 Dec 2008 UK: Aug 2003 (median month of diagnosis) to 31 Dec 2008 FU: 5	Women with primary invasive BC	50-65	12,024 (Australia: 6,396; UK: 5,628)	Positive screening mammogram	Never attended screening	NR	NR
Wozniacki et al. 2017 [31]	Retrospective Long case accrual	Poland Single institution	1 Jan 2007 to 31 Dec 2010 FU: NR	Women with BC (DCIS or invasive)	50-69	643	Participated in screening program	Did not participate in screening program	NR	NR
Case control studies										
Bastos et al. 2017 [32]	Short case accrual	Portugal Regional cancer registry	2000 to 1 Aug 2015 FU: 15	Women who received at least one invitation to screening	50-69	681	Screened after the index invitation or participated in screening round preceding index invitation	Did not attend screening in four years prior to BC diagnosis	NR	NR

Author, year	Study design	Setting	Study years Longest FU (years)	Study population	Age (years)	Total participants	Screened definition	Non-screened definition	Screening modality	Screening interval (years)
Heinavaara et al. 2016 [33]	Long case accrual	Finland National cancer registry	1992-2011 FU: 19.9	Women who received at least one invitation to screening	50-84	20,885	Participated in screening	Did not participate in screening	NR	2
Population-based studies – women with BC										
de Glas et al. 2014 [34]	Long case accrual	Netherlands National cancer registry	1995 to 2011 FU: mean 3,394,055 person years	Women with BC	G1: 70-75 G2: 76-80	38,442	Participated in screening	Did not participate in screening	NR	NR
Hubner et al. 2020 [35]	Long case accrual	Germany National cancer registry	1995-2015 FU: 11	Women with BC	≥30 years	NR	Screening period: 2006-2015	Pre-screening period: 1995-2005	NR	NR
Jacklyn et al. 2017 [36]	Long case accrual	Australia Regional cancer registry	1972-2012 FU: NR	Women with BC	≥20	126,709	Screening period: 1996-2005	Pre-screening period: 1972-1983	Film and digital 2D	2
Jorgensen et al. 2017 [37]	Long case accrual	Denmark National cancer register	1980-2010 FU: >10	Women with invasive BC	35-84	149,833	Screening period: 1991-2010 or 1994-2010 (depending on region)	Pre-screening period: 1980-1990 or 1980-1993 (depending on region)	NR	2
Moller et al. 2019 [38]	Long case accrual	Norway National cancer registry	1987 to Dec 2010 FU: 11.2	Women with invasive BC	30-90	4,903	Screening period: Between 1995 and 2004 up to 2010 (depending on region)	Pre-screening period: 1987 to between 1995 and 2004 (depending on region)	NR	2
Taylor et al. 2019 [39]	Short case accrual	New Zealand National cancer registry	1980-2013 FU: 8	Women with BC	45-69	12,364	Screening period: 1999-2013	Pre-screening period: 1980-1998	NR	2
Wilkinson et al. 2023 [40]	Short case accrual	Canada National cancer registry	2002-2007 FU: 10	Women with BC	40-59	71,990	Regions with screening programs	Regions that did not have screening programs	NR	2

2D: two-dimensional; BC: breast cancer; DCIS: ductal carcinoma in situ; FU: follow up; NR: not reported

Table S-2. Health outcomes reported by included non-randomised comparative studies

	General screening population			Women with breast cancer		
Outcome	**Cohort studies (no. of studies)**	**Case-control studies (no. of studies)**	**Population-based studies (no. of studies)**	**Cohort studies (no. of studies)**	**Case-control studies (no. of studies)**	**Population-based studies (no. of studies)**
Rate of breast cancer specific mortality	LC (3) SC (2)	0	0	LC (10) SC (5)	LC (1) SC (1)	LC (2) SC (2)
Rate of all-cause mortality	SC (2)	0	0	LC (4) SC (4)	0	0
Rate of radiotherapy	LC (1)	0	0	LC (7) SC (3)	0	0
Rate of chemotherapy	LC (1)	0	0	LC (8) SC (3)	0	0
Rate of breast surgery	LC (1)	0	0	LC (9) SC (3)	0	0
Surgical management of axilla	0	0	0	LC (13)	0	0
Breast cancer stage at diagnosis	SC (1) LC (2)	0	0	LC (13) SC (5)	0	LC (4)

Rate of interval cancer	0	0	0	LC (7) SC (2)	0	0
Health-related quality of life	0	0	0	SC (1)	0	0

LC: long case accrual; SC: short case accrual

Table S-3: Effects of screening on breast cancer specific mortality in a general screening population (cohort studies)

Age, years	No. of studies in analysis	Total sample	Screening interval, years	Effect measure (95% CI)[a]
Short case accrual				
50-65	1 [3]	262,350	2	**RR: 0.73 (0.65, 0.81)** **Absolute effect: 2 fewer per 1,000 (2 fewer to 1 fewer)**
70-74	1 [7]	54,635	2	HR: 0.86 (CI 0.44, 1.68) [b]
75-84	1 [7]	54,635	2	HR: 0.87 (CI 0.55, 1.37) [b]
≥85	1 [7]	54,635	2	HR: 1.34 (CI 0.40, 4.49) [b]
Long case accrual				
All ages	2 [1, 6]	114,785,315	2	**RR: 0.40 (0.33 to 0.47)** **Absolute effect: 0 fewer per 1,000** (0 fewer to 0 fewer)
70-74	1 [4]	264,274	1	**HR: 0.78 (0.63, 0.95)** [b]
≥75	1 [4]	264,274	1	HR: 1.00 (0.83, 1.19) [b]

CI: confidence interval; HR: hazard ratio; NR: not reported; RR: risk ratio

[a] Statistically significant results are bolded

[b] Absolute effect could not be calculated because event rates per group were not reported

Table S-4: Effects of screening on breast cancer specific mortality in a population with breast cancer (population-based studies)

Age, years	No. of studies in analysis	Total sample size of study	Screening interval, years	Effect measure (95% CI)[a]
Short case accrual				
50-64	1 [39]	12,364	2	Cumulated incidence per 100,000 women **Rate change: -17.1% (p=0.005)**
65-69				Cumulated incidence per 100,000 women Rate change: -18.9% (p=0.23)
40-44	1 [40]	71,990	2	Incidence-based mortality per 100,000 women Rate ratio: 0.95 (0.85, 1.07)
45-49	2 [39, 40]	12,364 [39]	2	Cumulated incidence per 100,000 women Rate change per 100,000 women: 0% (p=0.99)
		71,990 [40]		Incidence-based mortality per 100,000 women **Rate ratio: 0.89 (0.81, 0.98)**
40-49	1 [40]	71,990	2	Incidence-based mortality rate ratio **0.92 (0.85, 0.99)**
Long case accrual				
All ages	1 [35]	NR	NR	Age-standardised incidence per 100,000 women Screened: 23.3 Non-screened: 26.3
50-69	2 [35, 38]	NR [35]	2 (1) NR (1)	Age-standardised incidence per 100,000 women Screened: 47.1 Non-screened: 60.9
		4,903 [38]		Incidence per 100,000 PY **Adjusted mortality rate ratio: 0.80 (0.73, 0.88)**
≥70	1 [35]	NR	NR	Age-standardised incidence per 100,000 women Screened: 135.3 Non-screened: 137.1
≥75	1 [38]	4,903	2	Incidence per 100,000 PY **Adjusted mortality rate ratio: 0.78 (0.71, 0.84)**

CI: confidence interval; NR: not reported; PY: patient years

[a] Statistically significant results are bolded

Table S-5: Effects of screening on all-cause mortality in a general screening population (cohort studies; short case accrual)

Age, years	No. of studies in analysis	Total sample size	Screening interval, years	Risk ratio (95% CI)[a]	Absolute effect per 1,000 women (95% CI)[a]
All ages	2 [2, 7]	1,302,554	2	**0.57 (0.35, 0.92)** (I^2=99.9%)	**20 fewer (30 fewer to 4 fewer)**
50-68	1 [2]	1,247,919	2	**0.44 (0.43, 0.45)**	**19 fewer (19 fewer to 18 fewer)**
70-74	1 [7]	19,925	2	**0.68 (0.65, 0.71)**	**179 fewer (196 fewer to 162 fewer)**
≥75	1 [7]	34,710	2	**0.81 (0.80, 0.82)**	**160 fewer (168 fewer to 152 fewer)**
≥85	1 [7]	5,390	2	**0.95 (0.93, 0.96)**	**48 fewer (67 fewer to 38 fewer)**

CI: confidence interval; NR: not reported

[a] Statistically significant results are bolded

Table S-6: Effects of screening on radiotherapy treatment in a population with breast cancer (cohort studies)

Age, years	No. of studies in analysis	Total sample size	Screening interval, years (no. of studies)	Risk ratio (95% CI)[a]	Absolute effect per 1,000 women (95% CI)[a]
Short case accrual					
All ages	3 [10, 28, 29]	1,639	2	1.00 (0.93, 1.08) (I^2=61.0%)	0 fewer (59 fewer to 68 more)
45-65 Adjuvant therapy	2 [28, 29]	904	2	0.98 (0.90, 1.07) (I^2=51.9%)	18 fewer (90 fewer to 63 more)
50-69	1 [10]	735	2	1.04 (0.97, 1.13)	31 more (23 fewer to 101 more)
Long case accrual					
All ages	6 [9, 14, 15, 19, 23, 24]	7,708	2 (3), NR (3)	1.04 (0.97, 1.11) (I^2=68.0%)	24 more (18 fewer to 66 more)
50-69 Adjuvant therapy	3 [9, 14, 15]	2,126	2 (2), NR (1)	1.08 (0.99 to 1.18) (I^2=59.6%)	55 more (7 fewer to 124 more)
50-69	3 [14, 15, 24]	3,469	2 (2), NR (1)	**1.08 (1.01, 1.16)** (I^2=65.9%)	**58 more (7 more to 117 more)**
40-49	1 [23]	230	NR	0.95 (0.78 to 1.17)	33 fewer (144 fewer to 111 more)

CI: confidence interval; NR: not reported [a] Statistically significant results are bolded

Table S-7: Effects of screening on chemotherapy treatment in a population with breast cancer (cohort studies)

Age, years	No. of studies in analysis	Total sample size	Screening interval, years (no. of studies)	Risk ratio (95% CI)[a]	Absolute effect per 1,000 women (95% CI)[a]
Short case accrual					
All ages	3 [10, 28, 29]	1,639	2	**0.82 (0.67, 0.99)** (I^2=72.5%)	**100 fewer (182 fewer to 6 fewer)**
45-65 Adjuvant therapy	2 [28, 29]	904	2	0.83 (0.59, 1.18) (I^2=85.1%)	97 fewer (234 fewer to 103 more)
50-69	1 [10]	735	2	**0.80 (0.68 to 0.93)**	**106 fewer (169 fewer to 37 fewer)**
Long case accrual					
All ages	7 [9, 14, 15, 18, 19, 23, 24]	9,500	2 (3), NR (4)	**0.69 (0.60, 0.79)** (I^2=86.9%)	**174 fewer (225 fewer to 118 fewer)**
All ages Adjuvant therapy	3 [9, 14, 15]	2,126	2 (2), NR (1)	0.76 (0.47, 1.23) (I^2=96.97%)	146 fewer (323 fewer to 140 more)
50-69	3 [14, 15, 24]	3,469	2 (2), NR (1)	**0.61 (0.56, 0.66)** (I^2=6.2%)	**216 fewer (243 fewer to 188 fewer)**
50-69 Neoadjuvant therapy	1 [9]	660	NR	1.01 (0.88, 1.14)	6 more (from 70 fewer to 82 more)
40-49	1 [23]	230	NR	**0.67 (0.52, 0.85)**	**216 fewer (314 fewer to 98 fewer)**

CI: confidence interval; NR: not reported

[a] Statistically significant results are bolded

Table S-8: Effects of screening on breast surgery treatment in a population with breast cancer (cohort studies)

Age, years Surgery type	No. of studies in analysis	Total sample size	Screening interval, years (no. of studies)	Risk ratio (95% CI)[a]	Absolute effect per 1,000 women (95% CI)[a]
Short case accrual					
All ages All breast surgery	3 [10, 28, 29]	1,639	2	1.02 (0.98, 1.05) (I^2=60.6%)	17 more (17 fewer to 42 more)
50-69 All breast surgery	1 [10]	735	2	1.07 (0.96, 1.18)	46 more (26 fewer to 118 more)
All ages Breast conserving surgery	3 [10, 28, 29]	1,639	2	1.05 (0.98, 1.12) (I^2=0.0%)	34 more (14 fewer to 82 more)
Long case accrual					
All ages All breast surgery	7 [b 14-16, 18, 19, 23, 24]	8,363	2 (3), NR (4)	1.01 (1.00, 1.03) (I^2=93.3%)	9 more (0 fewer to 28 more)
50-69 All breast surgery	3 [b 14, 15, 24]	4,250	2 (2), NR (1)	1.02 (0.99, 1.06) (I^2=93.5%)	18 more (9 fewer to 53 more)
All ages Breast conserving surgery	6 [8, 14-16, 18, 24]	5,722	2 (3), NR (3)	1.19 (0.93, 1.52) (I^2=99.1%)	111 more (41 fewer to 304 more)
≥75 Breast conserving surgery	1 [16]	340	NR	**0.48 (0.30, 0.77)**	**266 fewer (359 fewer to 118 fewer)**
All ages Mastectomy	6 [8, 14-16, 18, 23]	4,106	2 (3), NR (3)	0.68 (0.33, 1.38) (I^2=97.7%)	127 fewer (266 fewer to 151 more)
40-49 Mastectomy	1 [23]	230	NR	**0.63 (0.45, 0.87)**	**178 fewer (265 fewer to 63 fewer)**
≥75 Mastectomy	1 [16]	340	NR	**4.07 (3.02, 5.49)**	**542 more (357 more to 793 more)**

CI: confidence interval; NR: not reported

[a] Statistically significant results are bolded; [b] One eligible study [8] not included due to a lack of variability between the comparison groups

Table S-9: Effects of screening on surgical management of axilla in a population with breast cancer (cohort studies, long case accrual)

Age, years Surgery type	No. of studies in analysis	Total sample size	Screening interval, years (no. of studies)	Risk ratio (95% CI)[a]	Absolute effect per 1,000 women (95% CI)[a]
All ages Sentinel lymph node biopsy	3 [14, 15, 18]	2,598	2 (2), NR (1)	**1.44 (1.35, 1.54)** (I^2=0.0%)	**231 more (184 more to 284 more)**
All ages Surgery on axilla	3 [14, 15, 18]	2,598	2 (2), NR (1)	1.15 (1.00, 1.31) (I^2=95.6%)	125 more (0 fewer to 259 more)
50-69 years Surgery on axilla	2 [14, 15]	1,466	2	1.24 (0.88 to 1.75) (I^2=96.9%)	151 more (76 fewer to 473 more)

CI: confidence interval; NR: not reported

[a] Statistically significant results are bolded

Table S-10: Effects of screening on stage of cancer at diagnosis in a population with breast cancer (cohort studies)

Age, years Cancer stage	No. of studies in analysis	Total sample size	Screening interval, years (no. of studies)	Risk ratio (95% CI)[a]	Absolute effect per 1,000 women (95% CI)[a]
Short case accrual					
All ages Stage II and higher	4 [20, 26, 28, 30]	46,306	2 (2), NR (1), ≤1, 2, or ≥3 (1)	**0.68 (0.58, 0.79)** (I^2=96.4%)	**138 fewer (181 fewer to 91 fewer)**
All ages Stage III and higher	4 [20, 26, 28, 30]	46,306	2 (2), NR (1), ≤1, 2, or ≥3 (1)	**0.65 (0.55, 0.78)** (I^2=96.5%)	**149 fewer (191 fewer to 93 fewer)**
All ages Stage IV	4 [20, 26, 28, 30]	46,306	2 (2), NR (1), ≤1, 2, or ≥3 (1)	**0.32 (0.20, 0.52)** (I^2=90.1%)	**44 fewer (51 fewer to 31 fewer)**
Long case accrual					
All ages Stage II and higher	11 [8, 11, 12, 16, 18, 19, 21, 23, 24, 27, 31]	107,126	2 (6), NR (5)	**0.61 (0.52, 0.72)** (I^2=97.3%)	**126 fewer (155 fewer to 56 fewer)**
40-49 Stage II and higher	1 [23]	177	NR	**0.66 (0.52, 0.83)**	**259 fewer (365 fewer to 129 fewer)**
≥75 Stage II and higher	1 [16]	340	NR	**0.35 (0.23, 0.55)**	**482 fewer (571 fewer to 334 fewer)**
All ages Stage III and higher	11 [8, 11, 12, 16, 18, 19, 21, 23, 24, 27, 31]	107,126	2 (6), NR (5)	**0.43 (0.32, 0.56)** (I^2=97.4%)	**140 fewer (168 fewer to 108 fewer)**
40-49 Stage III and higher	1 [23]	177	NR	**0.45 (0.26, 0.78)**	**186 fewer (250 fewer to 74 fewer)**
≥75 Stage III and higher	1 [16]	340	NR	**0.23 (0.09, 0.59)**	**239 fewer (283 fewer to 127 fewer)**
All ages Stage IV	8 [11, 16, 19, 21-24, 31]	17,425	2 (3), NR (4), 1 or 2 (1)	**0.28 (0.24, 0.34)** (I^2=5.11%)	**55 fewer (58 fewer to 51 fewer)**
40-49 Stage IV	2 [22, 23]	1,839	NR (1), 1 or 2 (1)	**0.26 (0.16, 0.41)** (I^2=0.0%)	**73 fewer (83 fewer to 58 fewer)[b]**
≥75 Stage IV	1 [16]	340	NR	**0.050 (0.003, 0.810)**	**161 fewer (169 fewer to 32 fewer)**

CI: confidence interval; NR: not reported

[a] Statistically significant results are bolded

[b] Used baseline risk from Plecha et al. 2014 [23] to calculate absolute risk because only a relative risk was reported by Oberaigner et al. 2017 [22]

Table S-11: Effects of screening on stage of cancer at diagnosis in a population with breast cancer (population-based studies, long case accrual)

Age, years Cancer stage	No. of studies in analysis	Total sample size of study	Screening interval, years	Effect measure (95% CI)[a]
50-69 Stage II and higher	1 [37]	149,833	2	Incidence rate ratio (before and after) Screened: 0.96 (0.90, 1.02) **Non-screened: 1.46 (1.41, 1.52)**
≥70 Stage II and higher	2 [34, 37]	149,833 [37]	2 (1), NR (1)	Incidence rate ratio (before and after) **Screened: 1.25 (1.16, 1.34)** **Non-screened: 1.81 (1.72, 1.90)**
		38,442 [34]		**RR: 0.62 (0.60, 0.63**) **Absolute effect: 253 fewer per 1,000 women (267 fewer to 247 fewer)**
All ages Stage III and higher	1 [35]	NR	NR	Incidence per 100,000 women Screened: 22.3 Non-screened: 29.1
50-69 Stage III and higher	1 [35]	NR	NR	Incidence per 100,000 women Screened: 45.7 Non-screened: 66.2
≥70 Stage III and higher	2 [34, 35]	NR [35]	NR	Incidence per 100,000 women (Hubner) Screened: 94.1 Non-screened: 116.1
		38,442 [34]		**RR: 0.66 (0.60, 0.71)** **Absolute effect: 65 fewer per 1,000 women (76 fewer to 55 fewer)**
All ages Stage IV	1 [36]	126,709	2	Age-standardised incidence per 100,000 women Screened: 7.2 (6.9, 7.5) Non-screened: 4.1 (3.9, 4.4)
50-69 Stage IV	1 [36]	126,709	2	Age-standardised incidence per 100,000 women Screened: 16.9 (15.8, 18.0) Non-screened: 9.4 (8.6, 10.2)
40-49 Stage IV	1 [36]	126,709	2	Age-standardised incidence per 100,000 women Screened: 9.3 (8.3, 10.3) Non-screened: 5.8 (5.0, 6.6)
≥70 Stage IV	2 [34, 36]	126,709 [36]	2 (1), NR (1)	Age-standardised incidence per 100,000 women[36] Screened: 22.9 (21.1, 24.7) Non-screened: 12.5 (11.1, 14.0)

		38,442 [34]		**RR: 0.48 (0.41, 0.55)** **Absolute effect: 43 fewer per 1,000 women (49 fewer to 37 fewer)**

CI: confidence interval; NR: not reported; RR: risk ratio

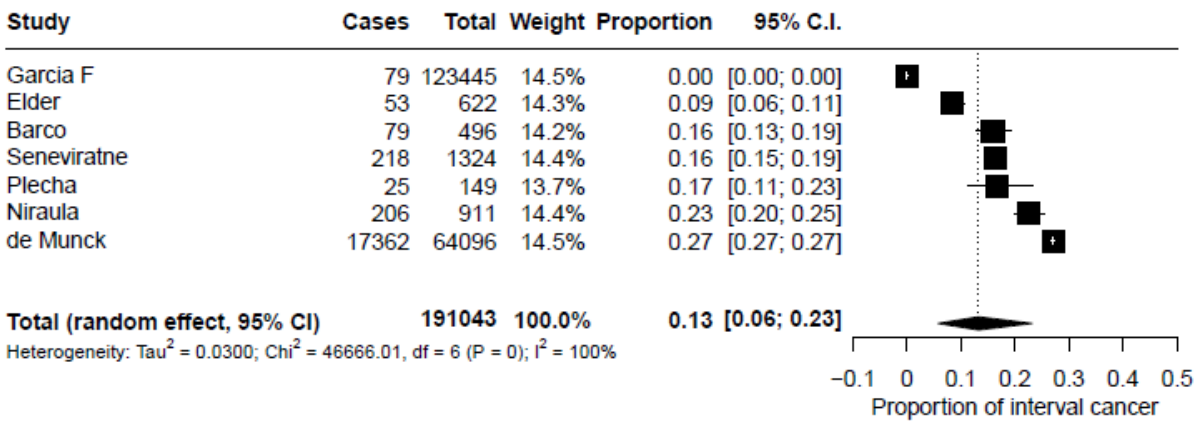
[a] Statistically significant results are bolded

Table S-12: Interval cancer among screening participants in a <u>population with breast cancer</u> (cohort studies)

Age, years	No. of studies in analysis	Total sample size	Screening interval, years (no. of studies)	Proportion (95% CI)[a]
Short case accrual				
50-69	2 [10, 30]	8,159	2 (1) NR (1)	0.22 (0.05 to 0.48)
Long case accrual				
All ages	7 [8, 12, 14, 15, 21, 23, 25]	191,043	2 (6) NR (1)	0.13 (0.06 to 0.23)
50-69	4 [8, 14, 15, 21]	125,474	2 (3) NR (1)	0.003 (0.003 to 0.004)
40-49	1 [23]	149	NR	0.17 (0.11 to 0.23)

CI: confidence interval; NR: not reported

Figure S-1: Interval cancer among screening participants in a <u>population with breast cancer</u> (cohort studies, long case accrual)



References

1. Choi E, Jun JK, Suh M, Jung KW, Park B, Lee K, et al. Effectiveness of the Korean National Cancer Screening Program in reducing breast cancer mortality. *NPJ Breast Cancer* 2021;7(1):83.
2. Czwikla J, Giersiepen K, Langner I, Enders D, Heinze F, Rothgang H, et al. A cohort study of mammography screening finds that comorbidity measures are insufficient for controlling selection bias. *J Clin Epidemiol* 2018;104:1-7.
3. Dunn N, Youl P, Moore J, Harden H, Walpole E, Evans E, et al. Breast-cancer mortality in screened versus unscreened women: Long-term results from a population-based study in Queensland, Australia. *J Med Screen* 2021;28(2):193-199.
4. Garcia-Albeniz X, Hernan MA, Logan RW, Price M, Armstrong K, Hsu J. Continuation of annual screening mammography and breast cancer mortality in women older than 70 years. *Ann Intern Med* 2020;172(6):381-389.
5. Lund E, Nakamura A, Thalabard JC. No overdiagnosis in the Norwegian Breast Cancer Screening Program estimated by combining record linkage and questionnaire information in the Norwegian Women and Cancer study. *Eur J Cancer* 2018;89:102-112.
6. Morrell S, Taylor R, Roder D, Robson B, Gregory M, Craig K. Mammography service screening and breast cancer mortality in New Zealand: A National Cohort Study 1999-2011. *Br J Cancer* 2017;116(6):828-839.
7. Richman IB, Long JB, Soulos PR, Wang SY, Gross CP. Estimating breast cancer overdiagnosis after screening mammography among older women in the United States. *Ann Intern Med* 2023;176(9):1172-1180.

8. Barco I, Chabrera C, Garcia Font M, Gimenez N, Fraile M, Lain JM, et al. Comparison of screened and nonscreened breast cancer patients in relation to age: A 2-institution study. *Clin Breast Cancer* 2015;15(6):482-489.

9. Bayard S, Fasano G, Chen Y, Davis M, Drotman M, Bensenhaver J, et al. Screening mammography mitigates breast cancer disparities through early detection of triple negative breast cancer. *Clin Imaging* 2021;80:430-437.

10. Braun B, Kurosinski MA, Khil L, Tio J, Krause-Bergmann B, Hense HW. The mode of detection is not associated with quality of life in women with breast cancer. *Breast care (Basel)* 2020;15(5):498-505.

11. Choi KS, Yoon M, Song SH, Suh M, Park B, Jung KW, et al. Effect of mammography screening on stage at breast cancer diagnosis: Results from the Korea National Cancer Screening Program. *Sci Rep* 2018;8(1):8882.

12. de Munck L, Siesling S, Fracheboud J, den Heeten GJ, Broeders MJM, de Bock GH. Impact of mammographic screening and advanced cancer definition on the percentage of advanced-stage cancers in a steady-state breast screening programme in the Netherlands. *Br J Cancer* 2020;123(7):1191-1197.

13. Duffy SW, Tabar L, Yen AMF, Dean PB, Smith RA, Jonsson H, et al. Beneficial effect of consecutive screening mammography examinations on mortality from breast cancer: A prospective study. *Radiology* 2021;299(3):541-547.

14. Elder K, Nickson C, Pattanasri M, Cooke S, Machalek D, Rose A, et al. Treatment intensity differences after early-stage breast cancer (ESBC) diagnosis depending on participation in a screening program. *Ann Surg Oncol* 2018;25(9):2563-2572.

15. Garcia-Fernandez A, Chabrera C, Garcia Font M, Fraile M, Lain JM, Gonzalez S, et al. Mortality and recurrence patterns of breast cancer patients diagnosed under a screening programme versus comparable non-screened breast cancer patients from the same population: Analytical survey from 2002 to 2012. *Tumour Biol* 2014;35(3):1945-1953.

16. Ilenko A, Sergent F, Mercuzot A, Zitoun M, Chauffert B, Foulon A, et al. Could patients older than 75 years benefit from a systematic breast cancer screening program? *Anticancer Res* 2017;37(2):903-907.

17. Ip EC, Cohen-Hallaleh RB, Ng AK. Extending screening in "elderly" patients: Should we consider a selective approach? *Clin Breast Cancer* 2020;20(5):377-381.

18. Kobayashi N, Hikichi M, Ushimado K, Sugioka A, Kiriyama Y, Kuroda M, et al. Differences in subtype distribution between screen-detected and symptomatic invasive breast cancer and their impact on survival. *Clin Transl Oncol* 2017;19(10):1232-1240.

19. Lim ZL, Ho PJ, Khng AJ, Yeoh YS, Ong ATW, Tan BKT, et al. Mammography screening is associated with more favourable breast cancer tumour characteristics and better overall survival: Case-only analysis of 3739 Asian breast cancer patients. *BMC Med* 2022;20(1):239.

20. Luu XQ, Lee K, Jun JK, Suh M, Jung KW, Choi KS. Effect of mammography screening on the long-term survival of breast cancer patients: Results from the National Cancer Screening Program in Korea. *Epidemiol Health* 2022;44:e2022094.

21. Niraula S, Biswanger N, Hu P, Lambert P, Decker K. Incidence, characteristics, and outcomes of interval breast cancers compared with screening-detected breast cancers. *JAMA Netw Open* 2020;3(9):e2018179.

22. Oberaigner W, Geiger-Gritsch S, Edlinger M, Daniaux M, Knapp R, Hubalek M, et al. Reduction in advanced breast cancer after introduction of a mammography screening program in Tyrol/Austria. *Breast* 2017;33:178-182.

23. Plecha D, Salem N, Kremer M, Pham R, Downs-Holmes C, Sattar A, et al. Neglecting to screen women between 40 and 49 years old with mammography: What is the impact on treatment morbidity and potential risk reduction? *AJR Am J Roentgenol* 2014;202(2):282-288.

24. Roder D, Farshid G, Gill G, Kollias J, Koczwara B, Karapetis C, et al. Breast cancer screening-opportunistic use of registry and linked screening data for local evaluation. *J Eval Clin Pract* 2017;23(3):508-516.

25. Seneviratne S, Campbell I, Scott N, Shirley R, Lawrenson R. Impact of mammographic screening on ethnic and socioeconomic inequities in breast cancer stage at diagnosis and survival in New Zealand: A cohort study. *BMC Public Health* 2015;15:46.

26. Tomsic S, Zagar T, Mihor A, Mlakar M, Lokar K, Jarm K, et al. Prognostic factors and outcomes in women with breast cancer in Slovenia in relation to step-wise implementation of organized screening. *PLoS One* 2022;17(11):e0278384.

27. Tvedskov TF, Jensen MB, Balslev E, Garne JP, Vejborg I, Christiansen P, et al. Risk of non-sentinel node metastases in patients with symptomatic cancers compared to screen-detected breast cancers. *Acta Oncol* 2016;55(4):455-459.

28. Ujhelyi M, Pukancsik D, Kelemen P, Kovacs E, Kenessey I, Udvarhelyi N, et al. Does breast screening offer a survival benefit? A retrospective comparative study of oncological outcomes of screen-detected and symptomatic early stage breast cancer cases. *Eur J Surg Oncol* 2016;42(12):1814-1820.

29. Varga Z, Balog K, Sebo E, Arkosy P, Toth D. Beyond a decade: A comparative study of 15-year survival rates in screen-detected vs. symptomatic breast cancer patients in Hungary. *Ir J Med Sci* 2024;193(1):57-63.

30. Woods LM, Rachet B, O'Connell DL, Lawrence G, Coleman MP. Are international differences in breast cancer survival between Australia and the UK present amongst both screen-detected women and non-screen-detected women? Survival estimates for women diagnosed in West Midlands and New South Wales 1997-2006. *Int J Cancer* 2016;138(10):2404-2414.

31. Wozniacki P, Skokowski J, Bartoszek K, Kosowska A, Kalinowski L, Jaskiewicz J. The impact of the Polish mass breast cancer screening program on prognosis in the Pomeranian province. *Arch Med Sci* 2017;13(2):441-447.

32. Bastos J, Rodrigues V, Paap E, Broeders M, Pina M, Cruz D, et al. Breast cancer screening effectiveness in Portugal central region. *Eur J Cancer Prev* 2017;26 Joining forces for better cancer registration in Europe: S204-S207.

33. Heinavaara S, Sarkeala T, Anttila A. Impact of organised mammography screening on breast cancer mortality in a case-control and cohort study. *Br J Cancer* 2016;114(9):1038-1044.

34. de Glas NA, de Craen AJM, Bastiaannet E, Op 't Land EG, Kiderlen M, van de Water W, et al. Effect of implementation of the mass breast cancer screening programme in older women in the Netherlands: Population based study. *BMJ* 2014;349:g5410.

35. Hubner J, Katalinic A, Waldmann A, Kraywinkel K. Long-term incidence and mortality trends for breast cancer in Germany. *Geburtshilfe Frauenheilkd* 2020;80(6):611-618.

36. Jacklyn G, McGeechan K, Irwig L, Houssami N, Morrell S, Bell K, et al. Trends in stage-specific breast cancer incidence in New South Wales, Australia: Insights into the effects of 25 years of screening mammography. *Breast Cancer Res Treat* 2017;166(3):843-854.

37. Jorgensen KJ, Gotzsche PC, Kalager M, Zahl PH. Breast cancer screening in Denmark: A cohort study of tumor size and overdiagnosis. *Ann Intern Med* 2017;166(5):313-323.

38. Moller MH, Lousdal ML, Kristiansen IS, Stovring H. Effect of organized mammography screening on breast cancer mortality: A population-based cohort study in Norway. *Int J Cancer* 2019;144(4):697-706.

39. Taylor R, Gregory M, Sexton K, Wharton J, Sharma N, Amoyal G, et al. Breast cancer mortality and screening mammography in New Zealand: Incidence-based and aggregate analyses. *J Med Screen* 2019;26(1):35-43.

40. Wilkinson AN, Ellison LF, Billette J-M, Seely JM. Impact of breast cancer screening on 10-year net survival in Canadian women age 40-49 years. *J Clin Oncol* 2023;41(29):4669-4677.

Supplementary File 4: Summary GRADE Tables

Note: Tables are presented separately by outcome, study design, and accrual period. Within each set of tables, data are presented by age (in the following order: all ages, age intervals specified in the protocol [40-44, 45-49, 50-59, 60-69, 70-74, ≥70], other age groups) and screening interval subgroups.

Table of Contents

Table 1.1. Breast cancer specific mortality (cohort studies, short case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer specific mortality (all ages) **(follow-up: median 4.2 years up to 16 years) (assessed with: n/N (4 studies included in analysis; no raw data provided in 1 study[2]))**												
5[1,2,3,4,5]	non-randomised studies	very serious[a]	very serious[b]	very serious[c]	serious[d]	none	2286/208397 (1.1%)	2961/92492 (3.2%)	**RR 0.44** (0.28 to 0.69)	**18 fewer per 1,000** (from 23 fewer to 10 fewer)	⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age 40-49 years) **(follow-up: median 10.5 years) (assessed with: n/N)**												
1[1]	non-randomised study	serious[e]	not serious	very serious[f]	serious[d]	none	406/6211 (6.5%)	504/4176 (12.1%) Coldman 2014[1] (age 40-49 years): 1.8/1,000 (0.18%)	**RR 0.54** (0.48 to 0.61)	**56 fewer per 1,000** (from 63 fewer to 47 fewer) **1 fewer per 1,000** (from 1 fewer to 1 fewer)	⊕◯◯◯ Very low	CRITICAL

[1] Coldman A, Phillips N, Wilson C, Decker K, Chiarelli AM, Brisson J, et al. Pan-Canadian study of mammography screening and mortality from breast cancer. *J Natl Cancer Inst* 2014;106(11):dju261.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer specific mortality (age 50-59 years) (follow-up: median 10.5 years) (assessed with: n/N)												
1[1]	non-randomised study	serious[e]	not serious	very serious[f]	not serious	none	454/5670 (8.0%)	442/2739 (16.1%) Coldman 2014[1] (age 50-59 years): 3.3/1,000 (0.33%)	**RR 0.50** (0.44 to 0.56)	**81 fewer per 1,000** (from 90 fewer to 71 fewer) **2 fewer per 1,000** (from 2 fewer to 1 fewer)	⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age 60-69 years) (follow-up: median 10.5 years) (assessed with: n/N)												
1[1]	non-randomised study	serious[e]	not serious	very serious[f]	not serious	none	252/2738 (9.2%)	212/1171 (18.1%) Coldman 2014[1] (age 60-69 years): 4.3/1,000 (0.43%)	**RR 0.51** (0.43 to 0.60)	**89 fewer per 1,000** (from 103 fewer to 72 fewer) **2 fewer per 1,000** (from 2 fewer to 2 fewer)	⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age 70-74 years) (follow-up: median 13.7 years) (assessed with: adjusted cumulative incidence per 100 women)												
1[2]	non-randomised study	very serious[g]	not serious	very serious[h]	serious[d]	none	• Screened: 0.35 (95% CI 0.26, 0.48) • Non-screened: 0.41 (95% CI 0.22, 0.76) • HR: 0.86 (95% CI 0.44, 1.68)				⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer specific mortality (age 75-84 years) (follow-up: median 10 years) (assessed with: adjusted cumulative incidence per 100 women)												
1[2]	non-randomised study	very serious[g]	not serious	very serious[h]	serious[d]	none	• Screened: 0.36 (0.29, 0.46) • Non-screened: 0.42 (0.28, 0.64) • HR: 0.87 (95% CI 0.55, 1.37)				⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age 50-65 years) (follow-up: 5 to 16 years) (assessed with: n/N)												
2[3,4]	non-randomised studies	serious[i]	very serious[j]	very serious[k]	very serious[l]	none	1017/192417 (0.5%)	1310/81957 (1.6%)	**RR 0.43** (0.16 to 1.20)	**9 fewer per 1,000** (from 13 fewer to 3 more)	⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age ≥70 years) (follow-up: median 4.2 years to 13.7 years) (assessed with: n/N or HR (no raw data provided in 1 study[2]))												
2[2,5]	non-randomised studies	very serious[m]	not serious	very serious[n]	serious[o]	none	lp: • Screened: 26/416 (6.3%) • Non-screened: 280/1,712 (16.4%) • RR: 0.38 (95% CI 0.26, 0.56) • **Absolute effect (95% CI): 101 fewer per 1,000** (from 121 fewer to 72 fewer) Richman: • Age 70-74 years: HR 0.86 (95% CI 0.44, 1.68) • Age 75-84 years: HR 0.87 (95% CI 0.55, 1.37) • Age ≥85 years: HR 1.34 (95% CI 0.4, 4.49) • No discernible difference for all three age groups.				⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age ≥85 years) (follow-up: median 5.7 years) (assessed with: adjusted cumulative incidence per 100 women)												
1[2]	non-randomised study	very serious[g]	not serious	very serious[h]	serious[d]	none	• Screened: 0.21 (0.09, 0.51) • Non-screened: 0.16 (0.05, 0.50) • HR: 1.34 (95% CI 0.40, 4.49)				⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Retrospective study (n=5); population is a select group of participants (n=1; sample of Medicare beneficiaries in the USA; unclear whether sample is random); study did not correct for major confounding factors (n=1).

b. Point estimates vary widely; insufficient overlap between 95% CIs; magnitude of statistical heterogeneity is high.

c. All participants had breast cancer (n=3); risk level not reported (n=5); mammography type (n=5), screening interval (n=2), and number of screening rounds (n=3) not reported.

d. Wide CI.

e. Retrospective study.

f. All participants had breast cancer; risk level not reported; mammography type not reported; screening interval and number of screening rounds not reported for all participants.

g. Retrospective study; study population is a select group of participants (sample of Medicare beneficiaries in the USA; unclear whether sample is random).

h. Risk level not reported; mammography type not reported.

i. Retrospective study (n=2).

j. Point estimates vary widely; no overlap of 95% CIs; magnitude of statistical heterogeneity is high.

k. All participants had breast cancer (n=1); risk level not reported (n=2); mammography type (n=2), screening interval (n=1), and number of screening rounds (n=2) not reported.

l. Wide CI; 95% CI overlaps no effect (RR=1.0) and CI fails to exclude important benefit or important harm; outcome is a rare event.

m. Retrospective study (n=2); did not correct for major confounding factors (n=1).

n. All participants had breast cancer (n=2); study population is a select group of participants (sample of Medicare beneficiaries in the USA; unclear whether sample is random); risk level of participants not reported (n=2); mammography type (n=2), screening interval (n=1), and number of screening rounds (n=1) not reported.

o. Wide CIs (n=2); 95% CI overlaps no effect (RR=1.0) and CI fails to exclude important benefit or important harm (n=1).

CI: confidence interval; **HR:** hazard ratio; **RR:** risk ratio

References

1. Luu XQ, Lee K, Jun JK, Suh M, Jung KW, Choi KS. Effect of mammography screening on the long-term survival of breast cancer patients: results from the National Cancer Screening Program in Korea. *Epidemiol Health* 2022;44:e2022094.

2. Richman IB, Long JB, Soulos PR, Wang SY, Gross CP. Estimating breast cancer overdiagnosis after screening mammography among older women in the United States. *Ann Intern Med* 2023;176(9):1172-80.

3. Woods LM, Rachet B, O'Connell DL, Lawrence G, Coleman MP. Are international differences in breast cancer survival between Australia and the UK present amongst both screen-detected women and non-screen-detected women? survival estimates for women diagnosed in West Midlands and New South Wales 1997-2006. *Int J Cancer* 2016;138(10):2404-14.

4. Dunn N, Youl P, Moore J, Harden H, Walpole E, Evans E et al. Breast-cancer mortality in screened versus unscreened women: Long-term results from a population-based study in Queensland, Australia. *J Med Screen* 2021;28(2):193-9.

5. Ip EC, Cohen-Hallaleh RB, Ng AK. Extending screening in "elderly" patients: should we consider a selective approach? *Clin Breast Cancer* 2020;20(5):377-81.

Table 1.2. Breast cancer specific mortality (population-based studies, short case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer specific mortality (age 40-44 years) (follow-up: 10 years) (assessed with: incidence-based mortality per 100,000 women)												
1[1]	non-randomised study	very serious[b]	not serious	very serious[c]	serious[a]	none	• Screened: 18.5 • Non-screened: 19.4 • Rate ratio (95% CI): 0.95 (0.85, 1.07); No discernible difference between groups.				⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age 45-49 years) (follow-up: 3 to 10 years) (assessed with: incidence per 100,000 women or incidence-based mortality per 100,000 women)												
2[1,2]	non-randomised studies	very serious[d]	not serious	very serious[e]	serious[a]	none	Taylor: Cumulated incidence per 100,000 women (95% CI) • Screened: 15.4 (11.9, 18.9) • Non-screened: 15.4 (11.6, 19.2) • Rate change per 100,000 women: 0% (p=0.99) Wilkinson: Incidence-based mortality per 100,000 women • Screened: 24.1 • Non-screened: 27.1 • Rate ratio (95% CI): 0.89 (0.81, 0.98) (favours screening)				⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age 40-49 years) (follow-up: 10 years) (assessed with: incidence-based mortality rate ratio)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
1[1]	non-randomised study	very serious[b]	not serious	very serious[c]	serious[a]	none	0.92 (95% CI 0.85, 0.99) (favours screening)				⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer specific mortality (age 50-64 years) (follow-up: 8 years) (assessed with: cumulated incidence per 100,000 women)												
1[2]	non-randomised study	very serious[f]	not serious	very serious[g]	serious[a]	none	• Screened: 48.8 (95% CI 44.4, 53.3) • Non-screened: 58.9 (95% CI 53.5, 64.4) • Rate change per 100,000 women: -17.1% (p=0.005)				⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age 65-69 years) (follow-up: 3 years) (assessed with: cumulated incidence per 100,000 women)												
1[2]	non-randomised study	very serious[f]	not serious	very serious[g]	serious[a]	none	• Screened: 25.7 (95% CI 19.4, 32.0) • Non-screened: 31.7 (95% CI 24.0, 39.4) • Rate change per 100,000 women: -18.9% (p=0.23)				⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Outcome is a rare event.

b. Retrospective study; significant opportunistic screening activity in the comparator group, with rates in some comparator jurisdictions being higher than in the screener provinces; did not correct for major confounding factors.

c. All participants had breast cancer; risk level not reported; type of mammography and number of screening rounds not reported.

d. Retrospective study (n=2); inadequate follow-up length for outcome to occur (n=1); risk of confounding from significant opportunistic screening activity (n=1); did not correct for major confounding factors (n=2).

e. All participants had breast cancer (n=2); risk level not reported (n=2); type of mammography (n=2) and number of screening rounds (n=1) not reported.

f. Retrospective study; inadequate follow-up length for outcome to occur; risk of confounding from significant opportunistic screening activity; did not correct for major confounding factors.

g. All participants had breast cancer; risk level not reported; mammography type not reported.

CI: confidence interval; **RR:** risk ratio

References

1. Wilkinson AN, Ellison LF, Billette JM, Seely JM. Impact of breast cancer screening on 10-year net survival in Canadian women age 40-49 years. *J Clin Oncol* 2023;41(29):4669-77.

2. Taylor R, Gregory M, Sexton K, Wharton J, Sharma N, Amoyal G, Morrell S. Breast cancer mortality and screening mammography in New Zealand: Incidence-based and aggregate analyses. *J Med Screen* 2019;26(1):35-43.

Table 1.3. Breast cancer specific mortality (cohort studies, long case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer specific mortality (all ages) **(follow-up: 5 to 16 years; NR in 2 studies) (assessed with: various measures (8 studies included in analysis; no raw data provided in 2 studies[2,6]))**												
10[1,2,3,4,5,6,7,8,9,10]	non-randomised studies	very serious[a]	very serious[b]	very serious[c]	serious[d]	none	From 5 studies providing n/N: • Screened: 71/2123 • Non-screened: 228/1701 • RR (95% CI): 0.25 (0.19, 0.33) • **Absolute effect (95% CI): 101 fewer per 1,000** (from 109 to 90 fewer) Choi: • Screened: 2,994/51,547,670 PY • Non-screened: 7,271/54,124,644 PY Duffy: • Screened: 2,393/12,210,001 PY • Non-screened: 1,003/2,623,762 PY Morrell: • Screened: 873/3,707,483 PY • Non-screened: 3,511/5,405,518 PY Garcia-Albeniz: • Screened: Mortality risk: range 2.7-3.8 deaths/1,000 women		⊕◯◯◯ Very low	CRITICAL

							• Non-screened: Mortality risk: 3.7 deaths/1,000 women Seneviratne: • HR (95% CI): 2.81 (1.57, 5.04)			

Cernty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer specific mortality (age 40-49 years) (follow-up: NR) (assessed with: n/N)												
1[1]	non-randomised study	very serious[e]	not serious	very serious[f]	very serious[g]	none	1/149 (0.7%)	4/81 (4.9%) Coldman 2014[2] (age 40-49 years): 1.8/1,000 (0.18%)	**RR 0.14** (0.02 to 1.20)	**42 fewer per 1,000** (from 48 fewer to 10 more) **2 fewer per 1,000** (from 2 fewer to 0 more)	⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age 70-74 years) (follow-up: 8 years; assessed with: RD and HR)												
1[2]	non-randomised study	serious[h]	not serious	very serious[i]	serious[j]	none	• RD: -1.0 (95% CI -2.3, 0.1) deaths/1,000 women • HR: 0.78 (95% CI 0.63, 0.95)				⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age ≥75 years) (follow-up: range 5 to 8 years) (assessed with: various measures)												
2[2,3]	non-randomised studies	very serious[j]	not serious	very serious[k]	serious[l]	none	Garcia-Albeniz: • RD: 0.07 (95% CI -0.93, 1.3) deaths/1,000 women • HR: 1.00 (95% CI 0.83, 1.19) Ilenko:				⊕◯◯◯ Very low	CRITICAL

[2] Coldman A, Phillips N, Wilson C, Decker K, Chiarelli AM, Brisson J, et al. Pan-Canadian study of mammography screening and mortality from breast cancer. *J Natl Cancer Inst* 2014;106(11):dju261.

							• Screened: 1/57 (2%) • Not screened: 51/283 (18%) (p<0.05) • RR: 0.10 (95% CI: 0.01, 0.69) • **Absolute effect (95% CI): 162 fewer per 1,000** (from 178 to 56 fewer) • **Absolute effect (95% CI) using Coldman 2014[2] (age 70-79 years) rate of 6.1/1,000: 5 fewer per 1,000** (from 6 fewer to 2 fewer)		

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute* (95% CI)		
Breast cancer specific mortality (age 40-79 years) (follow-up: mean 7.5 years up to 16 years) (assessed with: n/PY)												
2[4,5]	non-randomised studies	serious[m]	very serious[n]	very serious[o]	serious[d]	none	5387/63757671 (0.0001%)	8274/56748406 (0.0001%)	**RR 0.58** (0.56 to 0.60)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age 45-69 years) (follow-up: mean 5.5 years; NR in 1 study) (assessed with: RR or HR)												
2[6,7]	non-randomised studies	serious[p]	not serious	very serious[q]	very serious[l]	none	Morrell: • Screened: 23.5/100,000 PY • Not screened: 65.0/100,000 PY • Adjusted RR: 0.38 (95%CI 0.30, 0.49); p<0.0001 • **Absolute effect (95% CI): 0 fewer per 1,000** PY (from 0 to 0 fewer) Seneviratne: • HR: 2.81 (1.57, 5.04) (non-screened vs screened); p=0.001				⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age 50-69 years) (follow-up: median 7 years up to 10 years) (assessed with: n/N)												
3[8,9,10]	non-randomised studies	very serious[r]	not serious	very serious[s]	serious[t]	none	69/1917 (3.6%)	173/1337 (12.9%)	**RR 0.26** (0.20 to 0.34)	**96 fewer per 1,000**	⊕◯◯◯ Very low	CRITICAL

										(from 104 fewer to 85 fewer)		

*rounded to nearest whole number

Explanations:

a. Retrospective study (n=7); study population is a select group of participants (n=4; one hospital or institution in France and the USA and two hospitals in Spain); inadequate follow-up length for outcome to occur (n=5); did not correct for major confounding factors (n=1).

b. Point estimates vary widely; insufficient overlap between 95% CIs (not all CIs overlap at least one point estimate); magnitude of statistical heterogeneity is high.

c. All participants had breast cancer (n=7); risk level not reported (n=8); used film and digital mammography (n=4); mammography type (n=6), screening interval (n=2) and number of screening rounds (n=6) not reported.

d. Outcome is a rare event.

e. Retrospective study; study population is a select group of participants (one institution in the USA); no description of ascertainment of screening exposure.

f. All participants had breast cancer; used film and digital mammography; screening interval and number of screening rounds not reported.

g. Wide CI; 95% CI overlaps no effect (OR=1.0) and CI fails to exclude important benefit or important harm.

h. Retrospective study.

i. Risk level not reported; mammography type and number of screening rounds not reported.

j. Retrospective study (n=2); study population is a select group of participants (one hospital in France).

k. All participants had breast cancer; risk level not reported; mammography type (n=2), screening interval (n=1), and number of screening rounds (n=2) not reported.

l. Wide CIs; outcome is a rare event.

m. Retrospective study (n=1); inadequate follow-up length for outcome to occur (n=1).

n. No overlap of 95% CIs; magnitude of statistical heterogeneity is high.

o. All participants had breast cancer (n=2); risk level not reported (n=2); used film and digital mammography (n=1); mammography type (n=1) and number of screening rounds (n=2) not reported.

p. Retrospective study (n=2).

q. All participants had breast cancer (n=3); risk level not reported (n=3); used film and digital mammography (n=1); mammography type (n=2) and number of screening rounds (n=1) not reported.

r. Retrospective study (n=1); study population is a select group of participants (two hospitals in Spain); inadequate follow-up length for outcome to occur (n=2).

s. All participants had breast cancer (n=1); risk level not reported (n=2); used film and digital mammography (n=1); mammography type (n=1) not reported.

t. Wide CI.

CI: confidence interval; **HR:** hazard ratio; **NR:** not reported; **PY:** patient years; **RD:** risk difference; **RR:** risk ratio

References

1. Plecha D, Salem N, Kremer M, Pham R, Downs-Holmes C, Sattar A, Lyons J. Neglecting to screen women between 40 and 49 years old with mammography: what is the impact on treatment morbidity and potential risk reduction? *Am J Roentgenol* 2014;202(2):282-8.

2. García-Albéniz X, Hernán MA, Logan RW, Price M, Armstrong K, Hsu J. Continuation of annual screening mammography and breast cancer mortality in women older than 70 years. *Ann Intern Med* 2020;172(6):381-9.

3. Ilenko A, Sergent F, Mercuzot A, Zitoun M, Chauffert B, Foulon A, et al. Could patients older than 75 years benefit from a systematic breast cancer screening program? *Anticancer Res* 2017;37(2):903-7.

4. Duffy SW, Tabár L, Yen AM, Dean PB, Smith RA, Jonsson H et al. Beneficial effect of consecutive screening mammography examinations on mortality from breast cancer: A prospective study. *Radiology* 2021;299(3):541-7.

5. Choi E, Jun JK, Suh M, Jung KW, Park B, Lee K et al. Effectiveness of the Korean National Cancer Screening Program in reducing breast cancer mortality. *NPJ Breast Cancer* 2021;7(1):83.

6. Seneviratne S, Campbell I, Scott N, Shirley R, Lawrenson R. Impact of mammographic screening on ethnic and socioeconomic inequities in breast cancer stage at diagnosis and survival in New Zealand: a cohort study. *BMC Public Health* 2015;15:46

7. Morrell S, Taylor R, Roder D, Robson B, Gregory M, Craig K. Mammography service screening and breast cancer mortality in New Zealand: a national cohort study 1999-2011. *Br J Cancer* 2017;116(6):828-39.

8. García Fernández A, Chabrera C, García Font M, Fraile M, Lain JM, Gónzalez S et al. Mortality and recurrence patterns of breast cancer patients diagnosed under a screening programme versus comparable non-screened breast cancer patients from the same population: analytical survey from 2002 to 2012. *Tumour Biol* 2014;35(3):1945-53.

9. Barco I, Chabrera C, García Font M, Gimenez N, Fraile M, Lain JM et al. Comparison of screened and nonscreened breast cancer patients in relation to age: A 2-institution study. *Clin Breast Cancer* 2015;15(6):482-9.

10. Niraula S, Biswanger N, Hu P, Lambert P, Decker K. Incidence, characteristics, and outcomes of interval breast cancers compared with screening-detected breast cancers. *JAMA Netw Open* 2020;3(9):e2018179.

Table 1.4. Breast cancer specific mortality (population-based studies, long case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer specific mortality (all ages) (follow-up: 11 years) (assessed with: age-standardised incidence per 100,000 women)												
1[1]	non-randomised study	serious[a]	not serious	very serious[b]	serious[c]	none	• Screened: 23.3 • Non-screened: 26.3				⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age ≥75 years) (follow-up: range 6.8 to 11.2 years) (assessed with: n/100,000 PY)												
1[2]	non-randomised study	serious[a]	not serious	serious[d]	serious[c]	none	• Screened: 57.68 (95% CI 54.25, 61.33) • Non-screened: 71.78 (95% CI 67.82, 75.97) • Adjusted mortality rate ratio (95% CI): 0.78 (0.71, 0.84) (favours screening)				⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age 30-49 years) (follow-up: range 6.8 to 11.2 years) (assessed with: age-standardised incidence per 100,000 women or per 100,000 PY)												
2[1,2]	non-randomised studies	serious[e]	not serious	very serious[f]	serious[c]	none	Hubner: Age-standardised incidence per 100,000 women • Screened: 10.7 • Non-screened: 12.3 Moller: Incidence per 100,000 PY (95% CI) • Screened: 6.70 (6.07, 7.39) • Non-screened: 9.15 (8.38, 9.99) • Adjusted mortality rate ratio (95% CI): 0.72 (0.63, 0.82) (favours screening)				⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer specific mortality (age 50-69 years) (follow-up: range 6.8 to 11.2 years) (assessed with: age-standardised incidence per 100,000 women or per 100,000 PY)												
2[1,2]	non-randomised studies	serious[e]	not serious	very serious[f]	serious[c]	none	Hubner: Age-standardised incidence per 100,000 women • Screened: 47.1 • Non-screened: 60.9 Moller: Incidence per 100,000 PY (95% CI) • Screened: 19.21 (17.96, 20.55) • Non-screened: 25.24 (23.69, 26.89) • Adjusted mortality rate ratio (95% CI): 0.80 (0.73, 0.88) (favours screening)			⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (age ≥70 years) (follow-up: 11 years) (assessed with: age-standardised incidence per 100,000 women)												
1[1]	non-randomised study	serious[a]	not serious	very serious[b]	serious[c]	none	• Screened: 135.3 • Non-screened: 137.1 • No apparent difference between groups.				⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Retrospective study.

b. All participants had breast cancer; risk level not reported; type of mammography, screening interval, and number of screening rounds not reported.

c. Outcome is a rare event.

d. All participants had breast cancer; risk level not reported; type of mammography not reported.

e. Retrospective study (n=2).

f. All participants had breast cancer (n=2); risk level not reported (n=2); type of mammography (n=2), screening interval (n=1), and number of screening rounds (n=1) not reported.

CI: confidence interval; **PY:** patient years; **RR:** risk ratio

References

1. Hübner J, Katalinic A, Waldmann A, Kraywinkel K. Long-term Incidence and mortality trends for breast cancer in Germany. *Geburtshilfe Frauenheilkd* 2020;80(6):611-8.

2. Møller MH, Lousdal ML, Kristiansen IS, Støvring H. Effect of organized mammography screening on breast cancer mortality: A population-based cohort study in Norway. *Int J Cancer* 2019;144(4):697-706.

Table 1.5. Breast cancer specific mortality (case-control studies, short and long case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer specific mortality (short case accrual; age 50-69 years) (duration of exposure: range 11 to 15 years) (assessed with: OR (no raw data provided))												
1[1]	non-randomised study	very serious[a]	not serious	very serious[b]	very serious[c]	none	0.67 (95% CI: 0.45, 1.00) (no discernable difference)				⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (long case accrual; age 50-84 years) (duration of exposure: range 0 to 19.9 years) (assessed with: n/N)												
1[2]	non-randomised study	very serious[d]	not serious	very serious[e]	not serious	none	Case event rate: 1,827/1907 (95.8%) Control event rate: 18,185/18,978 (95.8%)				⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Retrospective study; case definition based on record linkage.

b. Risk level not reported; mammography type, screening interval, and number of screening rounds not reported.

c. Wide CI; 95% CI overlaps no effect (OR=1.0) and CI fails to exclude important benefit or important harm.

d. Retrospective study; case definition based on record linkage; potential for selection bias because data were restricted to women living in specific municipalities.

e. Risk level not reported; mammography type and number of screening rounds not reported.

CI: confidence interval; **OR:** odds ratio

References

1. Bastos J, Rodrigues V, Paap E, Broeders M, Pina M, Cruz D et al. Breast cancer screening effectiveness in Portugal central region. *Eur J Cancer Prev* 2017;26 Joining forces for better cancer registration in Europe: S204-7.

2. Heinävaara S, Sarkeala T, Anttila A. Impact of organised mammography screening on breast cancer mortality in a case-control and cohort study. *Br J Cancer* 2016;114(9):1038-44.

Table 2.1. All-cause mortality (cohort studies, short case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
All-cause mortality (all ages) **(follow-up: mean 3.9 years up to median 13.7 years) (assessed with: n/N)**												
4[1,2,3,4]	non-randomised studies	very serious[a]	very serious[b]	very serious[c]	serious[d]	none	37194/761581 (4.9%)	28473/567488 (5.0%) Statistics Canada (all ages): 76.2/1,000 (7.6%)	**RR 0.54** (0.42 to 0.68)	**23 fewer per 1,000** (from 29 fewer to 16 fewer) **35 fewer per 1,000** (from 44 fewer to 24 fewer)	⊕◯◯◯ Very low	CRITICAL
All-cause mortality (age 70-74 years) **(follow-up: median 13.7 years) (assessed with: n/N)**												
1[1]	non-randomised study	very serious[e]	not serious	very serious[f]	not serious	none	6645/17488 (38.0%)	1365/2437 (56.0%)	**RR 0.68** (0.65 to 0.71)	**179 fewer per 1,000** (from 196 fewer to 162 fewer)	⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
								Statistics Canada (age 70-79):189.5/1,000 (19.0%)		**60 fewer per 1,000** (from 66 fewer to 55 fewer)		

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
All-cause mortality (age ≥75 years) **(follow-up: median 5.7 to 10 years) (assessed with: n/N)**												
1[1]	non-randomised study	very serious[e]	not serious	very serious[f]	not serious	none	18427/26997 (68.3%)	6492/7713 (84.2%)	**RR 0.81** (0.80 to 0.82)	**160 fewer per 1,000** (from 168 fewer to 152 fewer)	⨁◯◯◯ Very low	CRITICAL
								Statistics Canada (age 70-79):189.5/1,000 (19.0%)		**36 fewer per 1,000** (from 38 fewer to 34 fewer)		
All-cause mortality (age 50-68 years) **(follow-up: mean 3.9 years) (assessed with: n/N)**												

Table 2.1: All-cause mortality (cohort studies, short case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
1[2]	non-randomised study	very serious[g]	not serious	very serious[h]	not serious	none	10311/701116 (1.5%)	18113/546803 (3.3%)	**RR 0.44** (0.43 to 0.45)	**19 fewer per 1,000** (from 19 fewer to 18 fewer)	⊕◯◯◯ Very low	CRITICAL
All-cause mortality (age ≥70 years) **(follow-up: median 5.2 to 13.7 years) (assessed with: n/N)**												
2[1,3]	non-randomised studies	very serious[i]	very serious[b]	very serious[j]	very serious[d]	none	25154/44901 (56.0%)	8618/11862 (72.7%) Statistics Canada (age 70-79):189.5/1,000 (19.0%)	**RR 0.57** (0.35 to 0.93)	**312 fewer per 1,000** (from 472 fewer to 51 fewer) **81 fewer per 1,000** (from 123 fewer to 13 fewer)	⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Retrospective study (n=4); study population is a select group of participants (n=1; sample of Medicare beneficiaries in the USA; unclear whether sample is random); inadequate follow-up length for outcome to occur (n=1); did not correct for major confounding factors (n=1).

b. Point estimates vary widely; insufficient overlap between 95% CIs (not all CIs overlap at least one point estimate); magnitude of statistical heterogeneity is high.

c. All participants had breast cancer (n=2); risk level not reported (n=4); mammography type (n=3), screening interval (n=1), and number of screening rounds not reported (n=2).

d. Pooled estimate has wide CI.

e. Retrospective study; study population is a select group of participants (sample of Medicare beneficiaries in the USA; unclear whether sample is random).

f. Risk level not reported; mammography type not reported.

g. Retrospective study; inadequate follow-up length for outcome to occur.

h. Risk level not reported; number of screening rounds not reported.

i. Retrospective study (n=2); study population is a select group of participants (sample of Medicare beneficiaries in the USA; unclear whether sample is random); did not correct for major confounding factors (n=1).

j. All participants had breast cancer (n=1); risk level not reported; mammography type (n=2), screening interval (n=1), and number of screening rounds (n=1) not reported.

CI: confidence interval; **RR:** risk ratio

References

1. Richman IB, Long JB, Soulos PR, Wang SY, Gross CP. Estimating breast cancer overdiagnosis after screening mammography among older women in the United States. *Ann Intern Med* 2023;176(9):1172-80.

2. Czwikla J, Giersiepen K, Langner I, Enders D, Heinze F, Rothgang H et al. A cohort study of mammography screening finds that comorbidity measures are insufficient for controlling selection bias. *J Clin Epidemiol* 2018;104:1-7.

3. Ip EC, Cohen-Hallaleh RB, Ng AK. Extending screening in "elderly" patients: should we consider a selective approach? *Clin Breast Cancer*. 2020;20(5):377-81.

4. Luu XQ, Lee K, Jun JK, Suh M, Jung KW, Choi KS. Effect of mammography screening on the long-term survival of breast cancer patients: results from the National Cancer Screening Program in Korea. *Epidemiol Health* 2022;44:e2022094.

Table 2.2. All-cause mortality (cohort studies, short case accrual, screening interval)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
All-cause mortality (screening interval <24 months) (age 40-79 years) (follow-up: median 10.5 years) (assessed with: n/N)												
1[1]	non-randomised study	serious[a]	not serious	very serious[b]	not serious	none	1729/15564 (11.1%)	1742/8823 (19.7%)	**RR 0.56** (0.53 to 0.60)	**87 fewer per 1,000** (from 93 fewer to 79 fewer)	⊕◯◯◯ Very low	CRITICAL
All-cause mortality (screening interval ≥24 months) (all ages) (follow-up: mean 3.9 years up to median 13.7 years) (assessed with: n/N)												
2[2,3]	non-randomised studies	very serious[c]	very serious[d]	very serious[e]	very serious[f]	none	35383/745601 (4.7%)	25970/556953 (4.7%)	**RR 0.57** (0.35 to 0.92)	**20 fewer per 1,000** (from 30 fewer to 4 fewer)	⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Retrospective study.

b. All participants had breast cancer; risk level not reported; mammography type not reported; screening interval and number of rounds varied widely across participants.

c. Retrospective study (n=2); study population is a select group of participants (n=1; sample of Medicare beneficiaries in the USA; unclear whether sample is random); inadequate follow-up length for outcome to occur (n=1).

d. Point estimates vary widely; insufficient overlap between 95% CIs (not all CIs overlap at least one point estimate); magnitude of statistical heterogeneity is high.

e. Risk level not reported (n=2); mammography type (n=1) and number of screening rounds (n=1) not reported.

f. Pooled estimate has wide CI.

CI: confidence interval; **RR:** risk ratio

References

1. Luu XQ, Lee K, Jun JK, Suh M, Jung KW, Choi KS. Effect of mammography screening on the long-term survival of breast cancer patients: results from the National Cancer Screening Program in Korea. *Epidemiol Health* 2022;44:e2022094.

2. Czwikla J, Giersiepen K, Langner I, Enders D, Heinze F, Rothgang H et al. A cohort study of mammography screening finds that comorbidity measures are insufficient for controlling selection bias. *J Clin Epidemiol* 2018;104:1-7.

3. Richman IB, Long JB, Soulos PR, Wang SY, Gross CP. Estimating breast cancer overdiagnosis after screening mammography among older women in the United States. *Ann Intern Med* 2023;176(9):1172-80.

Table 2.3. All-cause mortality (cohort studies, long case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
All-cause mortality (all ages) **(follow-up: median 4.7 years up to 10 years) (assessed with: n/N)**												
4[1,2,3,4]	non-randomised studies	very serious[a]	very serious[b]	very serious[c]	very serious[d]	none	63/2369 (2.7%)	264/3954 (6.7%) Statistics Canada (all ages):76.2/1,000 (7.62%)	**RR 0.33** (0.21 to 0.51)	**45 fewer per 1,000** (from 53 fewer to 33 fewer) **51 fewer per 1,000** (from 60 fewer to 37 fewer)	⊕◯◯◯ Very low	CRITICAL
All-cause mortality (age ≤39-70 years) **(follow-up: median 4.7 to 5.2 years) (assessed with: n/N)**												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
1[1]	non-randomised study	very serious[e]	not serious	very serious[f]	serious[g]	none	5/274 (1.8%)	62/858 (7.2%)	**RR 0.25** (0.10 to 0.62)	**54 fewer per 1,000** (from 65 fewer to 27 fewer)	⊕◯◯◯ Very low	CRITICAL
All-cause mortality (age 50-69 years) **(follow-up: 10 years) (assessed with: n/N)**												
2[2,3]	non-randomised studies	very serious[h]	not serious	very serious[i]	very serious[i]	none	25/1006 (2.5%)	62/836 (7.4%)	**RR 0.26** (0.18 to 0.39)	**55 fewer per 1,000** (from 61 fewer to 45 fewer)	⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
All-cause mortality (age ≥50 years) **(follow-up: 10 years) (assessed with: n/N)**												
1[4]	non-randomised study	very serious[k]	not serious	very serious[l]	serious[l]	none	25/1089 (2.3%)	96/2260 (4.2%)	**RR 0.54** (0.35 to 0.83)	**20 fewer per 1,000** (from 28 fewer to 7 fewer)	⊕◯◯◯ Very low	CRITICAL

Explanations:

a. Retrospective study (n=2); study population is a select group of participants (n=4; one hospital in Japan, two hospitals in Spain, and seven public hospitals in Singapore); inadequate follow-up length for outcome to occur (n=2); ascertainment of exposure via self-report (interview or questionnaire) (n=2).

b. Point estimates vary widely; insufficient overlap between 95% CIs (not all CIs overlap at least one point estimate).

c. All participants had breast cancer (n=4); risk level not reported (n=2), no criteria provided for unscreened group (n=1), or participants included women of all risk levels (including high risk) (n=1); used film and digital mammography (n=1) or mammography type not reported (n=3); screening interval (n=1) and number of screening rounds (n=2) not reported.

d. Pooled estimate has wide CI.

e. Retrospective study; study population is a select group of participants (one hospital in Japan); ascertainment of exposure by self-report (interview).

f. All participants had breast cancer; risk level not reported; mammography type, screening interval, and number of screening rounds not reported.

g. Single study with small sample size.

h. Study population is a select group of participants (n=2; two hospitals in Spain in each study); inadequate follow-up length for outcome to occur (n=1).

i. All participants had breast cancer; risk level not reported (n=1) or no criteria provided for unscreened group (n=1); used film and digital mammography (n=1) or mammography type not reported (n=1).

j. Outcome is a rare event.

k. Retrospective study; study population is a select group of participants (seven public hospitals in Singapore); ascertainment of exposure by self-report (questionnaire).

l. All participants had breast cancer patients; participants included women of all risk levels (including high risk); mammography type and number of screening rounds not reported.

CI: confidence interval; **RR:** risk ratio

References

1. Kobayashi N, Hikichi M, Ushimado K, Sugioka A, Kiriyama Y, Kuroda M, Utsumi T. Differences in subtype distribution between screen-detected and symptomatic invasive breast cancer and their impact on survival. *Clin Transl Oncol* 2017;19(10):1232-40.

2. García Fernández A, Chabrera C, García Font M, Fraile M, Lain JM, Gónzalez S et al. Mortality and recurrence patterns of breast cancer patients diagnosed under a screening programme versus comparable non-screened breast cancer patients from the same population: analytical survey from 2002 to 2012. *Tumour Biol* 2014;35(3):1945-53.

3. Barco I, Chabrera C, García Font M, Gimenez N, Fraile M, Lain JM et al. Comparison of screened and nonscreened breast cancer patients in relation to age: a 2-institution study. *Clin Breast Cancer* 2015;15(6):482-9.

4. Lim ZL, Ho PJ, Khng AJ, Yeoh YS, Ong ATW, Tan BKT et al. Mammography screening is associated with more favourable breast cancer tumour characteristics and better overall survival: case-only analysis of 3739 Asian breast cancer patients. *BMC Med* 2022;20(1):239.

Table 3.1. Radiotherapy (cohort studies, short case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Radiotherapy (all ages) **(follow-up: median 5.4 years up to mean 12.6 years; NR in 1 study) (assessed with: n/N)**												
3[1,2,3]	non-randomised studies	very serious[a]	serious[b]	very serious[c]	serious[d]	none	771/921 (83.7%)	609/718 (84.8%)	**RR 1.00** (0.93 to 1.08)	**0 fewer per 1,000** (from 59 fewer to 68 more)	⊕◯◯◯ Very low	CRITICAL
Adjuvant radiotherapy only (age 45-65 years) **(follow-up: median 5.4 years up to mean 12.6 years) (assessed with: n/N)**												
2[1,2]	non-randomised studies	serious[e]	serious[f]	very serious[g]	very serious[h]	none	417/487 (85.6%)	374/417 (89.7%)	**RR 0.98** (0.90 to 1.07)	**18 fewer per 1,000** (from 90 fewer to 63 more)	⊕◯◯◯ Very low	CRITICAL
Radiotherapy (age 50-69 years) **(follow-up: NR) (assessed with: n/N)**												
1[3]	non-randomised study	very serious[i]	not serious	very serious[i,k]	very serious[h]	none	354/434 (81.6%)	235/301 (78.1%)	**RR 1.04** (0.97 to 1.13)	**31 more per 1,000** (from 23 fewer to 101 more)	⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Retrospective study (n=3); ascertainment of exposure by self-report (questionnaire) (n=1).

b. Some overlap of 95% CIs; magnitude of statistical heterogeneity is high.

c. All participants had breast cancer (n=3); study population is a select group of participants (n=3; one breast care centre in Munster, Germany and one institution each in Hungary); HDI <0.9 (Hungary) (n=2); risk level not reported (n=3); type of mammography (n=1) and number of screening rounds (n=3) not reported.

d. 95% CI overlaps no effect and CI fails to exclude important benefit or important harm.

e. Retrospective study (n=2).

f. Direction of effect is not consistent; magnitude of statistical heterogeneity is moderate.

g. All participants had breast cancer (n=2); study population is a select group of participants (n=2; one institution each); HDI <0.9 (n=2); risk level not reported (n=2); number of screening rounds (n=2) not reported.

h. Small sample size; 95% CI overlaps no effect and CI fails to exclude important benefit or important harm.

i. Retrospective study; ascertainment of exposure by self-report (questionnaire).

j. All participants had breast cancer; study population is a select group of participants (one breast care centre in Munster, Germany); risk level not reported; mammography type and number of screening rounds not reported.

CI: confidence interval; **HDI**: Human Development Index; **NR**: not reported; **RR:** risk ratio

References

1. Újhelyi M, Pukancsik D, Kelemen P, Kovács E, Kenessey I, Udvarhelyi N, Bak M, Kovács T, Mátrai Z. Does breast screening offer a survival benefit? A retrospective comparative study of oncological outcomes of screen-detected and symptomatic early stage breast cancer cases. *Eur J Surg Oncol* 2016;42(12):1814-20.

2. Varga Z, Balog K, Sebő É, Árkosy P, Tóth D. Beyond a decade: a comparative study of 15-year survival rates in screen-detected vs. symptomatic breast cancer patients in Hungary. *Ir J Med Sci* 2023;193(1):57-63.

3. Braun B, Kurosinski MA, Khil L, Tio J, Krause-Bergmann B, Hense HW. The mode of detection is not associated with quality of life in women with breast cancer. *Breast Care (Basel)* 2020;15(5):498-505.

Table 3.2. Radiotherapy (cohort studies, long case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Radiotherapy (all ages) **(follow-up: median 4.2 years up to 10 years; NR in 2 studies) (assessed with: n/N (6 studies included in analysis; no raw data provided in 1 study[3]))**												
7[1,2,3,4,5,6,7]	non-randomised studies	very serious[a]	very serious[b]	very serious[c]	not serious[d]	none	2609/3825 (68.2%)	2319/3883 (59.7%)	**RR 1.04** (0.97 to 1.11)	**24 more per 1,000** (from 18 fewer to 66 more)	⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Radiotherapy (all ages (including ≤40 years)) (follow-up: median 4.2 to 4.6 years) (assessed with: n/N)												
1[1]	non-randomised study	very serious[e]	not serious	very serious[f]	very serious[g]	none	181/301 (60.1%)	209/359 (58.2%)	**RR 1.03** (0.91 to 1.17)	**17 more per 1,000** (from 52 fewer to 99 more)	⊕◯◯◯ Very low	CRITICAL
Radiotherapy (age 40-49 years) (follow-up: NR) (assessed with: n/N)												
1[2]	non-randomised study	very serious[h]	not serious	very serious[i]	very serious[g]	none	93/149 (62.4%)	53/81 (65.4%)	**RR 0.95** (0.78 to 1.17)	**33 fewer per 1,000** (from 144 fewer to 111 more)	⊕◯◯◯ Very low	CRITICAL
Radiotherapy (age 70-74 years) (follow-up: 8 years) (assessed with: standardised percentage)												
1[3]	non-randomised study	serious[j]	not serious	very serious[k]	not serious	none	• Screened: 51.0% (95%CI: 50.3-51.8) • Not screened: 39.9% (95% CI: 38.6, 41.3)				⊕◯◯◯ Very low	CRITICAL

Table 6.1: Surgical management of axilla (cohort studies, short case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Radiotherapy (age 75-84 years) (follow-up: 8 years) (assessed with: standardised percentage)												
1[3]	non-randomised study	serious[i]	not serious	very serious[k]	not serious	none	• Screened: 41.2% (95% CI: 40.4-41.9) • Not screened: 31.9% (95% CI: 30.7-33.1)				⊕◯◯◯ Very low	CRITICAL
Radiotherapy (age 50-69 years) (follow-up: mean 4.3 years up to 10 years; NR in 1 study) (assessed with: n/N)												
3[4,5,6]	non-randomised studies	serious[l]	serious[m]	very serious[n]	not serious	none	1787/2286 (78.2%)	865/1183 (73.1%)	**RR 1.08** (1.01 to 1.16)	**58 more per 1,000** (from 7 more to 117 more)	⊕◯◯◯ Very low	CRITICAL
Radiotherapy (age ≥50 years) (follow-up: mean 10 years) (assessed with: n/N)												
1[7]	non-randomised study	very serious[o]	not serious	very serious[p]	serious[q]	none	548/1089 (50.3%)	1192/2260 (52.7%)	**RR 0.95** (0.89 to 1.02)	**26 fewer per 1,000** (from 58 fewer to 11 more)	⊕◯◯◯ Very low	CRITICAL
Adjuvant radiotherapy only (age 50-69 years in 2 studies; all ages in 1 study) (follow-up: mean 4.3 years up to median 4.6 years; NR in 1 study) (assessed with: n/N)												
3[1,4,5]	non-randomised studies	serious[l]	serious[r]	very serious[s]	serious[q]	none	939/1206 (77.9%)	634/920 (68.9%)	**RR 1.08** (0.99 to 1.18)	**55 more per 1,000** (from 7 fewer to 124 more)	⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Retrospective study (n=6); ascertainment of exposure by self-report (questionnaire) (n=1).

b. Some variability in point estimates; magnitude of statistical heterogeneity is high.

c. All participants had breast cancer (n=6); study population was a select group of participants (n=6; one hospital in Australia, one institution in the USA; two hospitals in Spain; seven public hospitals in Singapore; one academic cancer program in two cities in the USA; and four major public hospitals in Australia); risk

level not reported (n=5) or participants included women of all risk levels (including high risk) (n=1); used film and digital mammography (n=1); mammography type (n=5), screening interval (n=3), and number of screening rounds (n=6) not reported.

d. 95% CI overlaps no effect (RR=1.0) (n=5) and CI fails to exclude important benefit or important harm.

e. Retrospective study; unclear whether participants with recurrent cancer were excluded.

f. All participants had breast cancer; study population is a select group of participants (academic cancer programs in two cities in the USA); risk level not reported; type of mammography, screening interval, and number of screening rounds not reported.

g. Small sample size; 95% CI overlaps no effect and CI fails to exclude important benefit or important harm.

h. Retrospective study; no description of ascertainment of exposure.

i. All participants had breast cancer; study population was a select group of participants (one institution in the USA); risk level not reported; used film (14% of women) and digital mammography; screening interval and number of screening rounds not reported.

j. Retrospective study.

k. Risk level not reported; mammography type and number of screening rounds not reported.

l. Retrospective study (n=2).

m. Magnitude of statistical heterogeneity is high.

n. All participants had breast cancer (n=3); study population is a select group of participants (n=3; one hospital in Australia, two hospitals in Spain, and four major public hospitals in Australia); and one study population was somewhat representative (subset of patients treated at four major public hospitals); risk level not reported (n=2) or no criteria provided for risk in unscreened group (n=1); mammography type (n=3), screening interval (n=1), and number of screening rounds (n=2) not reported.

o. Retrospective study; ascertainment of exposure by self-report (questionnaire).

p. All participants had breast cancer; study population is a select group of participants (seven public hospitals in Singapore); participants included women of all risk levels (including high risk); mammography type and number of screening rounds not reported.

q. 95% CI overlaps no effect and CI fails to exclude important benefit or important harm.

r. Some overlap of 95% CIs; magnitude of statistical heterogeneity is high.

s. All participants had breast cancer (n=3); study population is a select group of participants (n=3; one hospital in Australia, two hospitals in Spain, and an academic cancer program in the USA); risk level not reported (n=2) or no criteria provided for risk level in the unscreened group (n=1); mammography type (n=3), screening interval (n=2), and number of screening rounds (n=2) not reported.

CI: confidence interval; **NR**: not reported; **RR:** risk ratio

References

1. Bayard S, Fasano G, Chen Y, Davis M, Drotman M, Bensenhaver J et al. Screening mammography mitigates breast cancer disparities through early detection of triple negative breast cancer. *Clin Imaging* 2021;80:430-7.

2. Plecha D, Salem N, Kremer M, Pham R, Downs-Holmes C, Sattar A, Lyons J. Neglecting to screen women between 40 and 49 years old with mammography: what is the impact on treatment morbidity and potential risk reduction? *Am J Roentgenol* 2014;202(2):282-8.

3. García-Albéniz X, Hernán MA, Hsu J. Continuation of annual screening mammography and breast cancer mortality in women older than 70 years. *Ann Intern Med* 2020;173(3):247.

4. García Fernández A, Chabrera C, García Font M, Fraile M, Lain JM, Gónzalez S et al. Mortality and recurrence patterns of breast cancer patients diagnosed under a screening programme versus comparable non-screened breast cancer patients from the same population: analytical survey from 2002 to 2012. *Tumour Biol* 2014;35(3):1945-53.

5. Elder K, Nickson C, Pattanasri M, Cooke S, Machalek D, Rose A et al. Treatment intensity differences after early-stage breast cancer (ESBC) diagnosis depending on participation in a screening program. *Ann Surg Oncol* 2018;25(9):2563-72.

6. Roder D, Farshid G, Gill G, Kollias J, Koczwara B, Karapetis C, Adams J, Joshi R, Keefe D, Powell K, Fusco K, Eckert M, Buckley E, Beckmann K. Breast cancer screening-opportunistic use of registry and linked screening data for local evaluation. *J Eval Clin Pract* 2017;23(3):508-16.

7. Lim ZL, Ho PJ, Khng AJ, Yeoh YS, Ong ATW, Tan BKT et al. Mammography screening is associated with more favourable breast cancer tumour characteristics and better overall survival: case-only analysis of 3739 Asian breast cancer patients. *BMC Med* 2022;20(1):239.

Table 4.1. Chemotherapy (cohort studies, short case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Chemotherapy (all ages) **(follow-up: median 5.4 years up to mean 12.6 years; NR in 1 study) (assessed with: n/N)**												
3[1,2,3]	non-randomised studies	very serious[a]	serious[b]	very serious[c]	serious[d]	none	413/921 (44.8%)	397/718 (55.3%)	**RR 0.82** (0.67 to 0.99)	**100 fewer per 1,000** (from 182 fewer to 6 fewer)	⊕◯◯◯ Very low	CRITICAL
Adjuvant chemotherapy only (age 45-65 years) **(follow-up: median 5.4 years up to mean 12.6 years) (assessed with: n/N)**												
2[1,2]	non-randomised studies	very serious[e]	very serious[f]	very serious[g]	very serious[h]	none	230/487 (47.2%)	238/417 (57.1%)	**RR 0.83** (0.59 to 1.18)	**97 fewer per 1,000** (from 234 fewer to 103 more)	⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Chemotherapy (age 50-69 years) (follow-up: NR) (assessed with: n/N)												
1[3]	non-randomised study	very serious[i]	not serious	very serious[j]	serious[k]	none	183/434 (42.2%)	159/301 (52.8%)	**RR 0.80** (0.68 to 0.93)	**106 fewer per 1,000** (from 169 fewer to 37 fewer)	⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Retrospective study (n=3); study population is a select group of participants (n=3; one breast care centre in Munster, Germany and two institution in Hungary); ascertainment of exposure by self-report (questionnaire with 64% participation rate) (n=1).

b. Magnitude of statistical heterogeneity is high.

c. All participants had breast cancer (n=3); HDI <0.9 (Hungary) (n=2); risk level not reported (n=3); mammography type (n=1) and number of screening rounds (n=3) not reported.

d. Small sample size.

e. Retrospective study (n=2); study population is a select group of participants (n=2; single institutions in Hungary).

f. Direction of the effect is not consistent; magnitude of statistical heterogeneity is high.

g. All participants had breast cancer (n=2); HDI <0.9 (Hungary) (n=2); risk level not reported (n=2); number of screening rounds not reported (n=2).

h. Small sample size; 95% CI overlaps no effect (RR=1.0) and CI fails to exclude important benefit or important harm.

i. Retrospective study; study population is a select group of participants (one breast care centre in Munster, Germany); ascertainment of exposure by self-report (questionnaire with 64% participation rate).

j. All participants had breast cancer; risk level not reported; mammography type and number of screening rounds not reported.

k. Single study with small sample size.

CI: confidence interval; **HDI:** Human Development Index; **NR**: not reported; **RR:** risk ratio

References

1. Újhelyi M, Pukancsik D, Kelemen P, Kovács E, Kenessey I, Udvarhelyi N et al. Does breast screening offer a survival benefit? A retrospective comparative study of oncological outcomes of screen-detected and symptomatic early stage breast cancer cases. *Eur J Surg Oncol* 2016;42(12):1814-20.

2. Varga Z, Balog K, Sebő É, Árkosy P, Tóth D. Beyond a decade: a comparative study of 15-year survival rates in screen-detected vs. symptomatic breast cancer patients in Hungary. *Ir J Med Sci* 2023;193(1):57-63.

3. Braun B, Kurosinski MA, Khil L, Tio J, Krause-Bergmann B, Hense HW. The mode of detection is not associated with quality of life in women with breast cancer. *Breast Care (Basel)* 2020;15(5):498-505.

Table 4.2. Chemotherapy (cohort studies, long case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Chemotherapy (all ages) **(follow-up: median 4.2 up to 10 years; NR in 2 studies) (assessed with: n/N (7 studies included in analysis; (no raw data provided in 1 study[2]))**												
8[1,2,3,4,5,6,7,8]	non-randomised studies	very serious[a]	very serious[b]	very serious[c]	not serious	none	1725/4400 (39.2%)	2863/5100 (56.1%)	**RR 0.69** (0.60 to 0.79)	**174 fewer per 1,000** (from 225 fewer to 118 fewer)	⊕◯◯◯ Very low	CRITICAL
Chemotherapy (age 40-49 years) **(follow-up: NR) (assessed with: n/N)**												
1[1]	non-randomised study	very serious[d]	not serious	very serious[e]	very serious[f]	none	65/149 (43.6%)	53/81 (65.4%)	**RR 0.67** (0.52 to 0.85)	**216 fewer per 1,000** (from 314 fewer to 98 fewer)	⊕◯◯◯ Very low	CRITICAL
Chemotherapy (age 70-74 years) **(follow-up: 8 years) (assessed with: standardised percentage (no raw data provided))**												
1[2]	non-randomised study	serious[g]	not serious	very serious[h]	not serious	none	Percentage (95% CI): • Screened: 15.2% (14.7%, 15.8%) • Non-screened: 21.1% (20.0%, 22.1%)				⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Chemotherapy (age 75-84 years) (follow-up: 8 years) (assessed with: standardised percentage (no raw data provided))												
1[2]	non-randomised study	serious[g]	not serious	very serious[h]	not serious	none	Percentage (95% CI): • Screened: 8.6% (8.3%, 9.1%) • Non-screened: 11.5% (10.6%, 12.3%)				⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Chemotherapy (age ≤39-70 years) (follow-up: median 4.7 to 5.2 years) (assessed with: n/N)												
1[3]	non-randomised study	very serious[i]	not serious	very serious[j]	serious[k]	none	87/274 (31.8%)	437/858 (50.9%)	**RR 0.62** (0.52 to 0.75)	**194 fewer per 1,000** (from 244 fewer to 127 fewer)	⊕◯◯◯ Very low	CRITICAL
Chemotherapy (age 50-69 years) (follow-up: mean 4.3 up to 10 years; NR in 1 study) (assessed with: n/N)												
3[4,5,6]	non-randomised studies	very serious[l]	not serious	very serious[m]	not serious	none	741/2286 (32.4%)	654/1183 (55.3%)	**RR 0.61** (0.56 to 0.66)	**216 fewer per 1,000** (from 243 fewer to 188 fewer)	⊕◯◯◯ Very low	CRITICAL
Chemotherapy (age ≥50 years) (follow-up: up to 10 years) (assessed with: n/N)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
1[7]	non-randomised study	very serious[n]	not serious	very serious[o]	not serious	none	548/1089 (50.3%)	1192/2260 (52.7%)	**RR 0.92** (0.86 to 0.97)	**42 fewer per 1,000** (from 74 fewer to 16 fewer)	⊕◯◯◯ Very low	CRITICAL
Neoadjuvant chemotherapy only (age 50-69) **(follow-up: median 4.2 to 4.6 years) (assessed with: n/N)**												
1[8]	non-randomised study	very serious[p]	not serious	very serious[q]	very serious[k]	none	181/301 (60.1%)	209/359 (58.2%)	**RR 1.01** (0.88 to 1.14)	**6 more per 1,000** (from 70 fewer to 82 more)	⊕◯◯◯ Very low	CRITICAL
Adjuvant chemotherapy only (all ages) **(follow-up: mean 4.3 years; NR in 1 study) (assessed with: n/N)**												
3[4,5,8]	non-randomised studies	very serious[r]	very serious[s]	very serious[t]	very serious[u]	none	540/1206 (44.8%)	560/920 (60.9%)	**RR 0.76** (0.47 to 1.23)	**146 fewer per 1,000** (from 323 fewer to 140 more)	⊕◯◯◯ Very low	CRITICAL

Explanations:

a. Retrospective study (n=7); study population is a select group of participants (n=7; one institution in the USA; cancer program in two cities in the USA; one hospital each in Australia and Japan; two hospitals in Spain; seven public hospitals in Singapore; four major public hospitals in Australia); ascertainment of exposure by self-report (interview or questionnaire) (n=2); no description of ascertainment of screening exposure (n=1); length of follow-up in the non-screened group was unclear (n=1).

b. Point estimates vary widely; insufficient overlap between CIs (not all CIs overlap with at least one point estimate); magnitude of statistical heterogeneity is high.

c. All participants had breast cancer (n=7); risk level not reported (n=6); used film (14% of women) and digital mammography (n=1); mammography type (n=7) not reported; screening interval (n=4) and number of screening rounds (n=7) not reported.

d. Retrospective study; study population is a select group of participants (one institution in the USA); no description of ascertainment of screening exposure; length of follow-up in the non-screened group was unclear.

e. All participants had breast cancer; risk level not reported; used film (14% of women) and digital mammography; screening interval and number of screening rounds not reported.

f. Single study with small sample size; wide CI.

g. Retrospective study.

h. Risk level not reported; mammography type and number of screening rounds not reported.

i. Retrospective study, study population is a select group of participants (one hospital in Japan); ascertainment of exposure by self-report (interview).

j. All participants had breast cancer; risk level not reported; mammography type, screening interval, and number of screening rounds not reported.

k. Single study with small sample size; wide CI; 95% CI overlaps no effect (RR=1.0) and CI fails to exclude important benefit or important harm.

l. Retrospective study (n=2); study population is a select group of participants (n=3; one hospital in Australia, two hospitals in Spain, and four major public hospitals in Australia).

m. All participants had breast cancer; risk level not reported (n=2); mammography type (n=3), screening interval (n=1), and number of screening rounds (n=2) not reported.

n. Retrospective study; all participants had breast cancer; study population is a select group of participants (seven hospitals in Singapore); ascertainment of exposure by self-report (questionnaire).

o. All participants had breast cancer; participants included women of all risk levels (including high risk); mammography type and number of screening rounds not reported.

p. Retrospective study; study population is a select group of participants (academic cancer programs in two cities in the USA); no demonstration that the outcome was not present at the start of the study.

q. All participants had breast cancer; risk level not reported; type of mammography, screening interval, and number of screening rounds not reported.

r. Retrospective study (n=2); study population is a select group of participants (n=3; cancer program in two cities in the USA, one hospital in Australia, and two hospitals in Spain).

s. Point estimates vary widely; insufficient overlap between 95% CIs (not all CIs overlap at least one point estimate); magnitude of statistical heterogeneity is high.

t. All participants had breast cancer (n=3); risk level not reported (n=2); mammography type (n=3), screening interval (n=1), and number of screening rounds (n=2) not reported.

u. Wide confidence interval around effect estimate; 95% CI overlaps no effect (RR=1.0) and CI fails to exclude important benefit or important harm.

CI: confidence interval; **NR**: not reported; **RR:** risk ratio

References

1. Plecha D, Salem N, Kremer M, Pham R, Downs-Holmes C, Sattar A, Lyons J. Neglecting to screen women between 40 and 49 years old with mammography: what is the impact on treatment morbidity and potential risk reduction? *Am J Roentgenol* 2014;202(2):282-8.

2. García-Albéniz X, Hernán MA, Hsu J. Continuation of annual screening mammography and breast cancer mortality in women older than 70 years. *Ann Intern Med* 2020;173(3):247.

3. Kobayashi N, Hikichi M, Ushimado K, Sugioka A, Kiriyama Y, Kuroda M, Utsumi T. Differences in subtype distribution between screen-detected and symptomatic invasive breast cancer and their impact on survival. *Clin Transl Oncol* 2017;19(10):1232-40.

4. García Fernández A, Chabrera C, García Font M, Fraile M, Lain JM, Gónzalez S et al. Mortality and recurrence patterns of breast cancer patients diagnosed under a screening programme versus comparable non-screened breast cancer patients from the same population: analytical survey from 2002 to 2012. *Tumour Biol* 2014;35(3):1945-53.

5. Elder K, Nickson C, Pattanasri M, Cooke S, Machalek D, Rose A et al. Treatment intensity differences after early-stage breast cancer (ESBC) diagnosis depending on participation in a screening program. *Ann Surg Oncol* 2018;25(9):2563-72.

6. Roder D, Farshid G, Gill G, Kollias J, Koczwara B, Karapetis C et al. Breast cancer screening-opportunistic use of registry and linked screening data for local evaluation. *J Eval Clin Pract* 2017;23(3):508-16.

7. Lim ZL, Ho PJ, Khng AJ, Yeoh YS, Ong ATW, Tan BKT et al. Mammography screening is associated with more favourable breast cancer tumour characteristics and better overall survival: case-only analysis of 3739 Asian breast cancer patients. *BMC Med* 2022;20(1):239.

8. Bayard S, Fasano G, Chen Y, Davis M, Drotman M, Bensenhaver J et al. Screening mammography mitigates breast cancer disparities through early detection of triple negative breast cancer. *Clin Imaging* 2021;80:430-7.

Table 5.1: Breast surgery (cohort studies, short case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
All types of breast surgery (all ages) **(follow-up: median 5.4 years up to mean 12.6 years; NR in 1 study) (assessed with: n/N)**												
3[1,2,3]	non-randomised studies	very serious[a]	not serious	very serious[b]	serious[c]	none	788/921 (85.6%)	610/718 (85.0%)	**RR 1.02** (0.98 to 1.05)	**17 more per 1,000** (from 17 fewer to 42 more)	⊕◯◯◯ Very low	CRITICAL
All types of breast surgery (age 50-69 years) **(follow-up: NR) (assessed with: n/N)**												
1[1]	non-randomised study	very serious[d]	not serious	very serious[e]	serious[f]	none	303/434 (69.8%)	197/301 (65.4%)	**RR 1.07** (0.96 to 1.18)	**46 more per 1,000** (from 26 fewer to 118 more)	⊕◯◯◯ Very low	CRITICAL
Breast conserving surgery (all ages) **(follow-up: median 5.4 years up to mean 12.6 years; NR in 1 study) (assessed with: n/N)**												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
3[1,2,3]	non-randomised studies	very serious[a]	not serious	very serious[b]	serious[c]	none	657/921 (71.3%)	493/718 (68.7%)	**RR 1.05** (0.98 to 1.12)	**34 more per 1,000** (from 14 fewer to 82 more)	⊕◯◯◯ Very low	CRITICAL
Mastectomy (age 45-65 years) **(follow-up: median 5.4 years up to mean 12.6 years) (assessed with: n/N)**												
2[2,3]	non-randomised studies	very serious[g]	not serious	very serious[h]	serious[i]	none	131/487 (26.9%)	117/417 (28.1%)	**RR 0.90** (0.73 to 1.12)	**28 fewer per 1,000** (from 76 fewer to 34 more)	⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Retrospective study (n=3); study populations is a select group of participants (n=3; one breast care centre in Munster, Germany and one institution each in Hungary; ascertainment of exposure by self-report (participation rate 64%) (n=1).

b. All participants had breast cancer (n=3); HDI <0.9 (Hungary) (n=2); risk level of participants not reported (n=3); mammography type not reported (n=1) and number of screening rounds (n=3) not reported.

c. 95% CI overlaps no effect (RR=1.0) and CI fails to exclude important benefit or important harm.

d. Retrospective study; study population is a select group of participants (one breast care centre in Munster, Germany); ascertainment of exposure by questionnaire (participation rate 64%).

e. All participants had breast cancer; risk level not reported; mammography type and number of screening rounds not reported.

f. Single study with small sample size; wide CI.

g. Retrospective study (n=2); study population is a select group of participants (n=2; one institution each in Hungary).

h. All participants had breast cancer (n=2); HDI <0.9 (Hungary) (n=2); risk level (n=2) and number of screening rounds (n=2) not reported.

i. 95% CI overlaps no effect (RR=1.0) and CI fails to exclude important benefit or important harm; small sample size and wide CI.

CI: confidence interval; **HDI**: Human Development Index; **NR**: not reported; **RR:** risk ratio

References

1. Braun B, Kurosinski MA, Khil L, Tio J, Krause-Bergmann B, Hense HW. The mode of detection is not associated with quality of life in women with breast cancer. *Breast Care (Basel)* 2020;15(5):498-505.

2. Újhelyi M, Pukancsik D, Kelemen P, Kovács E, Kenessey I, Udvarhelyi N, Bak M, Kovács T, Mátrai Z. Does breast screening offer a survival benefit? A retrospective comparative study of oncological outcomes of screen-detected and symptomatic early stage breast cancer cases. *Eur J Surg Oncol* 2016;42(12):1814-20.

3. Varga Z, Balog K, Sebő É, Árkosy P, Tóth D. Beyond a decade: a comparative study of 15-year survival rates in screen-detected vs. symptomatic breast cancer patients in Hungary. *Ir J Med Sci* 2023;193(1):57-63.

Table 5.2: Breast surgery (cohort studies, long case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
All types of breast surgery (all ages) (follow-up: mean 2.9 years up to 10 years; NR in 2 studies) (assessed with: n/N; 7 studies included in analysis (no raw data in 1 study[7]; no variability between groups in 1 study)) [1]												
9[1,2,3,4,5,6,7,8,9]	non-randomised studies	very serious[a]	very serious[b]	very serious[c]	serious[d]	none	3329/3747 (88.8%)	4257/4616 (92.2%)	**RR 1.01** (1.00 to 1.03)	**9 more per 1,000** (from 0 fewer to 28 more)	⊕◯◯◯ Very low	CRITICAL
All types of breast surgery (age 50-69 years) (follow-up: mean 2.9 years up to 10 years; NR in 1 study) (assessed with: n/N; (3 studies included in analysis (no variability between groups in 1 study)) [1]												
4[1,2,3,4]	non-randomised studies	very serious[e]	very serious[f]	very serious[g]	serious[d]	none	2378/2674 (88.9%)	1386/1576 (87.9%)	**RR 1.02** (0.99 to 1.06)	**18 more per 1,000** (from 9 fewer to 53 more)	⊕◯◯◯ Very low	CRITICAL
All types of breast surgery (age ≥50 years) (follow-up: ≤10 years) (assessed with: n/N)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
1[5]	non-randomised study	very serious[h]	not serious	very serious[i]	not serious	none	1084/1089 (99.5%)	2239/2260 (99.1%)	**RR 1.00** (1.00 to 1.01)	**0 fewer per 1,000** (from 0 fewer to 10 more)	⊕◯◯◯ Very low	CRITICAL
Breast conserving surgery (all ages) **(follow-up: mean 1.3 years up to 10 years; NR in 1 study) (assessed with: n/N; 6 studies included in analysis (no raw data in 1 study[7]))**												
7[1,2,3,4,7,8,9]	non-randomised studies	very serious[j]	very serious[b]	very serious[k]	very serious[d]	none	2374/3005 (79.0%)	1591/2717 (58.6%)	**RR 1.19** (0.93 to 1.52)	**111 more per 1,000** (from 41 fewer to 304 more)	⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast conserving surgery (age 70-74 years) **(follow-up: 8 years) (assessed with: percentage)**												
1[7]	non-randomised study	serious[l]	not serious	very serious[m]	not serious	none	Standardised percentage (95% CI): • Screened: 52.6% (51.8%, 53.4%) • Non-screened: 36.5% (35.2, 38.0%)				⊕◯◯◯ Very low	CRITICAL
Breast conserving surgery (age ≥75 years) **(follow-up: median 1.3 years up to 8 years) (assessed with: percentage or n/N)**												

Table 6.1: Surgical management of axilla (cohort studies, short case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
2[7,9]	non-randomised studies	very serious[n]	not serious	very serious[o]	not serious	none	Garcia-Albeniz: Standardised percentage (95% CI) (lumpectomy) • Screened: 48.8% (47.9%, 49.5%) • Non-screened: 32.6% (31.5%, 33.8%) Ilenko (lumpectomy plus sentinel lymphadenectomy): • Screened: 14/57 (24.6%) • Non-screened: 145/283 (51.2%) • RR (95% CI): 0.48 (0.30, 0.77) • **Absolute effect (95% CI): 266 fewer per 1,000** (from 359 fewer to 118 fewer)				⊕◯◯◯ Very low	CRITICAL
Breast conserving surgery (age ≤39-70 years) **(follow-up: median 5.1 years) (assessed with: n/N)**												
1[8]	non-randomised study	very serious[p]	not serious	very serious[q]	serious[r]	none	209/274 (76.3%)	463/858 (54.0%)	**RR 1.41** (1.29 to 1.55)	**221 more per 1,000** (from 156 more to 297 more)	⊕◯◯◯ Very low	CRITICAL
Mastectomy (all ages) **(follow-up: mean 2.9 years to 5.8 years; NR in 2 studies) (assessed with: n/N)**												
6[1,2,3,6,8,9]	non-randomised studies	very serious[s]	very serious[b]	very serious[t]	very serious[u]	none	378/1881 (20.1%)	885/2225 (39.8%)	**RR 0.68** (0.33 to 1.38)	**127 fewer per 1,000** (from 266 fewer to 151 more)	⊕◯◯◯ Very low	CRITICAL

Table 6.1: Surgical management of axilla (cohort studies, short case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Mastectomy (age 40-49 years) (follow-up: NR) (assessed with: n/N)												
1[6]	non-randomised study	very serious[v]	not serious	very serious[w]	serious[r]	none	45/149 (30.2%)	39/81 (48.1%)	**RR 0.63** (0.45 to 0.87)	**178 fewer per 1,000** (from 265 fewer to 63 fewer)	⊕◯◯◯ Very low	CRITICAL
Mastectomy (age 70-74 years) (follow-up: 8 years) (assessed with: percentage)												
1[7]	non-randomised study	serious[l]	not serious	very serious[m]	not serious	none	Standardised percentage (95% CI): Simple mastectomy: • Screened: 11.3% (10.8,% 11.8%) • Non-screened: 10.4% (9.5%, 11.3%) Radical mastectomy: • Screened: 13.9% (13.4%, 14.5%) • Non-screened: 18.2% (17.0%, 19.4%)				⊕◯◯◯ Very low	CRITICAL
Mastectomy (age ≥75 years) (follow-up: median 1.3 years up to 8 years) (assessed with: percentage or n/N)												
2[7,9]	non-randomised studies	very serious[n]	not serious	very serious[o]	not serious	none	Garcia-Albeniz: Standardised percentage (95% CI) Simple mastectomy: • Screened: 10.8% (10.3,% 11.2%) • Non-screened: 10.1% (9.4%, 10.9%) Radical mastectomy: • Screened: 14.2% (13.7%, 14.6%) • Non-screened: 17.0% (16.0%, 17.9%) Ilenko: • Screened: 41/57 (71.9%) • Non-screened: 50/283 (17.7%) • RR (95% CI): 4.07 (3.02, 5.49) • **Absolute effect (95% CI): 542 more per 1,000** (from 357 more to 793 more)				⊕◯◯◯ Very low	CRITICAL

Table 6.1: Surgical management of axilla (cohort studies, short case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Mastectomy (age ≤39-70 years) (follow-up: median 5.1 years) (assessed with: n/N)												
1[8]	non-randomised study	very serious[p]	not serious	very serious[q]	serious[r]	none	65/274 (23.7%)	393/858 (45.8%)	**RR 0.52** (0.41 to 0.65)	**220 fewer per 1,000** (from 270 fewer to 160 fewer)	⊕◯◯◯ Very low	CRITICAL

Explanations:

a. Retrospective study (n=7); study population is a select group of participants (n=8; one hospital each in Australia, France, and Japan; one institution in the USA; two hospitals in Spain; seven public hospitals in Singapore; and four major public hospitals in Australia); ascertainment of exposure by self -report (interview or questionnaire) (n=2) or not reported (n=1); study did not correct for major confounding factors (n-1).

b. Point estimates vary widely; insufficient overlap between 95% CIs (not all CIs overlap at least one point estimate); direction of the effect is not consistent; magnitude of statistical heterogeneity is high.

c. All participants had breast cancer (n=8); all participants ≥75 years of age (n=1); participants included women of all risk levels (including high risk) (n=1) or risk level not reported (n=8); used film and digital mammography (n=2); mammography type (n=7), screening interval (n=4), and number of screening rounds (n=7) not reported.

d. 95% CI overlaps no effect (RR=1.0) and CI fails to exclude important benefit or important harm.

e. Retrospective study (n=2); study population is a select group of participants (n=4; one hospital in Australia, two hospitals each in Spain, and four major public hospitals in Australia).

f. Insufficient overlap between 95% CIs (not all CIs overlap at least one point estimate); magnitude of statistical heterogeneity is high.

g. All participants had breast cancer; used film and digital mammography (n=1); risk level not reported (n=3); mammography type (n=3), screening interval (n=1), and number of screening rounds (n=2) not reported.

h. Retrospective study; study population is a select group of participants (seven public hospitals in Singapore); ascertainment of exposure by self-report (questionnaire).

i. All participants had breast cancer; participants included women of all risk levels (including high risk); mammography type and number of screening rounds not reported.

j. Retrospective study (n=5); study population is a select group of participants (n=6; one hospital each in Australia, France, and Japan, two hospitals each in Spain, and four major public hospitals in Australia); ascertainment of exposure by self-report (interview) (n=1); study did not correct for major confounding factors (n=1).

k. All participants had breast cancer (n=6); all participants ≥75 years (n=1); risk level not reported (n=6); used film (14% of women) and digital mammography (n=1); mammography type (n=6), screening interval (n=3), and number of screening rounds (n=5) not reported.

l. Retrospective study.

m. Risk level not reported; mammography type and number of screening rounds not reported.

n. Retrospective study (n=2); study population is a select group of participants (n=1; one hospital in France); study did not correct for major confounding factors (n=1).

o. All participants had breast cancer (n=1); risk level not reported (n=2); mammography type (n=2), screening interval (n=1), and number of screening rounds (n=2) not reported.

p. Retrospective study; study population is a select group of participants (one hospital in Japan); ascertainment of exposure by self-report (interview).

q. All participants had breast cancer; risk level not reported; mammography type, screening interval, and number of screening rounds not reported.

r. Single study with small sample size; wide CI.

s. Retrospective study (n=4); study population is a select group of participants (n=6; one hospital each in Australia, France, and Japan, two hospitals in Spain, and one institution in the USA); ascertainment of exposure by self-report (interview or questionnaire) (n=2); study did not correct for major confounding factors (n=1).

t. All participants had breast cancer; included participants ≥75 years (n=1); risk level not reported (n=5); used film and digital mammography (n=2); mammography type (n=4), screening interval (n=3), and number of screening rounds (n=4) not reported.

u. 95% CI overlaps no effect (RR=1.0) and CI fails to exclude important benefit or important harm; one extreme outlier (Ilenko).

v. Retrospective study; study population is a select group of participants (one institution in USA); no description of ascertainment of exposure.

w. All participants had breast cancer; risk level not reported; used film mammography (14% of women) and digital mammography; screening interval and number of screening rounds not reported.

CI: confidence interval; **NR**: not reported; **RR:** risk ratio

References

1. Barco I, Chabrera C, García Font M, Gimenez N, Fraile M, Lain JM, Piqueras M, Vidal MC, Torras M, González S, Pessarrodona A, Barco J, Cassadó J, García Fernández A. Comparison of screened and nonscreened breast cancer patients in relation to age: A 2-institution study. *Clin Breast Cancer* 2015;15(6):482-9.

2. García Fernández A, Chabrera C, García Font M, Fraile M, Lain JM, Gónzalez S, Corral C, Torras M, Torres J, Teixido M, Barco I, López R, Gónzalez C, Pessarrodona A, Giménez N. Mortality and recurrence patterns of breast cancer patients diagnosed under a screening programme versus comparable non-screened breast cancer patients from the same population: analytical survey from 2002 to 2012. *Tumour Biol* 2014;35(3):1945-53.

3. Elder K, Nickson C, Pattanasri M, Cooke S, Machalek D, Rose A, Mou A, Collins JP, Park A, De Boer R, Phillips C, Pridmore V, Farrugia H, Bruce Mann G. Treatment intensity differences after early-stage breast cancer (ESBC) diagnosis depending on participation in a screening program. *Ann Surg Oncol* 2018;25(9):2563-72.

4. Roder D, Farshid G, Gill G, Kollias J, Koczwara B, Karapetis C, Adams J, Joshi R, Keefe D, Powell K, Fusco K, Eckert M, Buckley E, Beckmann K. Breast cancer screening-opportunistic use of registry and linked screening data for local evaluation. *J Eval Clin Pract* 2017;23(3):508-16.

5. Lim ZL, Ho PJ, Khng AJ, Yeoh YS, Ong ATW, Tan BKT, Tan EY, Tan SM, Lim GH, Lee JA, Tan VK, Hu J, Li J, Hartman M. Mammography screening is associated with more favourable breast cancer tumour characteristics and better overall survival: case-only analysis of 3739 Asian breast cancer patients. *BMC Med* 2022;20(1):239.

6. Plecha D, Salem N, Kremer M, Pham R, Downs-Holmes C, Sattar A, Lyons J. Neglecting to screen women between 40 and 49 years old with mammography: what is the impact on treatment morbidity and potential risk reduction? *Am J Roentgenol* 2014;202(2):282-8.

7. García-Albéniz X, Hernán MA, Hsu J. Continuation of annual screening mammography and breast cancer mortality in women older than 70 years. *Ann Intern Med* 2020;173(3):247.

8. Kobayashi N, Hikichi M, Ushimado K, Sugioka A, Kiriyama Y, Kuroda M, Utsumi T. Differences in subtype distribution between screen-detected and symptomatic invasive breast cancer and their impact on survival. *Clin Transl Oncol* 2017;19(10):1232-40.

9. Ilenko A, Sergent F, Mercuzot A, Zitoun M, Chauffert B, Foulon A, Gondry J, Chevreau J. Could patients older than 75 years benefit from a systematic breast cancer screening program? *Anticancer Res* 2017;37(2):903-7.

Table 6.1: Surgical management of axilla (cohort studies, short case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Sentinel lymph node biopsy (age 45-65 years) **(follow-up: mean 12.6 years) (assessed with: n/N)**												
1[1]	non-randomised study	very serious[a]	not serious	very serious[b]	very serious[c]	none	18/208 (8.7%)	6/101 (5.9%)	**RR 1.46** (0.60 to 3.56)	**27 more per 1,000** (from 24 fewer to 152 more)	⊕◯◯◯ Very low	CRITICAL
Surgery on axilla (age 45-65 years) **(follow-up: mean 12.6 years) (assessed with: n/N)**												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
1[1]	non-randomised study	very serious[a]	not serious	very serious[b]	serious[d]	none	190/208 (91.3%)	95/101 (94.1%)	**RR 0.97** (0.91 to 1.04)	**28 fewer per 1,000** (from 85 fewer to 38 more)	⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Retrospective study; study population is select group of participants (one institution in Hungary).

b. All participants had breast cancer; HDI index <0.9 (Hungary); risk level and number of screening rounds not reported.

c. Single study with small sample size; wide CI; 95% CI overlaps no effect (RR=1.0) and CI fails to exclude important benefit or important harm.

d. Single study with small sample size; 95% CI overlaps no effect (RR=1.0) and CI fails to exclude important benefit or important harm.

CI: confidence interval; **HDI**: Human Development Index; **RR:** risk ratio

References

1. Varga Z, Balog K, Sebő É, Árkosy P, Tóth D. Beyond a decade: a comparative study of 15-year survival rates in screen-detected vs. symptomatic breast cancer patients in Hungary. *Ir J Med Sci* 2023;193(1):57-63.

Table 6.2: Surgical management of axilla (cohort studies, long case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Sentinel lymph node biopsy (age ≤39 to 70 years) (follow-up: mean 4.3 years up to median 5.1 years; NR in 1 study) (assessed with: n/N)												
3[1,2,3]	non-randomised studies	very serious[a]	not serious	very serious[b]	not serious	none	897/1179 (76.1%)	746/1419 (52.6%)	**RR 1.44** (1.35 to 1.54)	**231 more per 1,000** (from 184 more to 284 more)	⊕◯◯◯ Very low	CRITICAL
Sentinel lymph node biopsy and/or axillary lymph node dissection (age ≤39 to 70 years) (follow-up: median 5.1 years) (assessed with: n/N)												
1[1]	non-randomised study	very serious[c]	not serious	very serious[c]	serious[e]	none	270/274 (98.5%)	833/858 (97.1%)	**RR 1.01** (1.00 to 1.03)	**10 more per 1,000** (from 0 fewer to 29 more)	⊕◯◯◯ Very low	CRITICAL
Surgery on axilla (all ages) (follow-up: mean 2.9 years up to median 5.2 years; NR in 1 study) (assessed with: n/N (3 studies included in analysis; no raw data provided in 1 study[4]))												
4[1,2,3,4]	non-randomised studies	very serious[f]	very serious[g]	very serious[h]	serious[i]	none	1036/1179 (87.9%)	1187/1419 (83.7%)	**RR 1.15** (1.00 to 1.31)	**125 more per 1,000** (from 0 fewer to 259 more)	⊕◯◯◯ Very low	CRITICAL
Surgery on axilla and/or mastectomy (age ≥75 years) (follow-up: mean 3.1 years) (assessed with: no raw data provided)												
1[4]	non-randomised study	very serious[j]	not serious	very serious[d]	not serious	none	• Included in Invasive surgery (mastectomy and/or axillary dissection) outcome. • Study noted that the outcome favoured screening (p<0.05).				⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Surgery on axilla (age ≤39 to 70 years) (follow-up: median 5.1 years; NR in 1 study) (assessed with: n/N)												
2[1,3]	non-randomised studies	very serious[k]	not serious	very serious[l]	serious[m]	none	139/669 (20.8%)	441/1025 (43.0%)	**RR 0.52** (0.44 to 0.62)	**207 fewer per 1,000** (from 241 fewer to 163 fewer)	⊕◯◯◯ Very low	CRITICAL
Surgery on axilla (age 50-69 years) (follow-up: mean 4.3 years; NR in 1 study) (assessed with: n/N)												
2[2,3]	non-randomised studies	very serious[n]	very serious[g]	very serious[o]	very serious[p]	none	766/905 (84.6%)	354/561 (63.1%)	**RR 1.24** (0.88 to 1.75)	**151 more per 1,000** (from 76 fewer to 473 more)	⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Retrospective study (n=2); study population is a select group of participants (n=3; one hospital each in Australia and Japan and two hospitals in Spain); ascertainment of exposure by self-report (interview) (n=1).

b. All participants had breast cancer (n=3); risk level not reported (n=3); mammography type (n=3), screening interval (n=1), and number of screening rounds (n=2) not reported.

c. Retrospective study; study population is a select group of participants (one hospital in Japan); ascertainment of exposure by self-report (interview).

d. All participants had breast cancer; risk level not reported; mammography type, screening interval, and number of screening rounds not reported.

e. 95% CI overlaps no effect (RR=1.0) and CI fails to exclude important benefit or important harm.

f. Retrospective study (n=3); study population is a select group of participants (n=4; one hospital in Australia, France, and Japan and two hospitals in Spain); ascertainment of exposure by self-report (interview) (n=1); study did not correct for major confounding factors (n=1).

g. Point estimates vary widely; insufficient overlap between CIs (not all CIs overlap at least one point estimate); magnitude of statistical heterogeneity is high.

h. All participants had breast cancer (n=3); risk level not reported (n=3); mammography type (n=4), screening interval (n=2), and number of screening rounds (n=3) not reported.

i. Wide CI; 95% CI overlaps no effect (RR=1.0) and CI fails to exclude important benefit or important harm.

j. Retrospective study; all participants had breast cancer; study population is a select group of participants (one hospital in France); study did not correct for major confounding factors.

k. Retrospective study (n=2); study population is a select group of participants (n=2; one hospital each in Australia and Japan); ascertainment of exposure by self-report (interview) (n=1).

l. All participants had breast cancer (n=2); risk level not reported (n=2); mammography type (n=2), screening interval (n=1), and number of screening rounds (n=2) not reported.

m. Small sample size and wide CI.

n. Retrospective study (n=1); study population is a select group of participants (n=2; one hospital in Australia and two hospitals in Spain).

o. All participants had breast cancer (n=2); risk level not reported (n=2); mammography type (n=2) and number of screening rounds (n=1) not reported.

p. Small sample size and wide CI; 95% CI overlaps no effect (RR=1.0) and CI fails to exclude important benefit or important harm.

CI: confidence interval; **NR:** not reported; **RR:** risk ratio

References

1. Kobayashi N, Hikichi M, Ushimado K, Sugioka A, Kiriyama Y, Kuroda M, Utsumi T. Differences in subtype distribution between screen-detected and symptomatic invasive breast cancer and their impact on survival. *Clin Transl Oncol* 2017;19(10):1232-40.

2. García Fernández A, Chabrera C, García Font M, Fraile M, Lain JM, Gónzalez S, et al. Mortality and recurrence patterns of breast cancer patients diagnosed under a screening programme versus comparable non-screened breast cancer patients from the same population: analytical survey from 2002 to 2012. *Tumour Biol* 2014;35(3):1945-53.

3. Elder K, Nickson C, Pattanasri M, Cooke S, Machalek D, Rose A et al. Treatment intensity differences after early-stage breast cancer (ESBC) diagnosis depending on participation in a screening program. *Ann Surg Oncol* 2018;25(9):2563-72.

4. Ilenko A, Sergent F, Mercuzot A, Zitoun M, Chauffert B, Foulon A, et al. Could patients older than 75 years benefit from a systematic breast cancer screening program? *Anticancer Res* 2017;37(2):903-7.

Table 7.1: Stage of cancer (cohort studies, short case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer staging, stage II (age 70-74 years) (follow-up: median 13.7 years) (assessed with: cumulative incidence rate per 100 women)												
1[1]	non-randomised study	very serious[a]	not serious	very serious[b]	serious[c]	none	Localised invasive, adjusted cumulative incidence per 100 women (95% CI): • Screened: 3.84 (3.58, 4.11) • Non-screened: 2.56 (2.05, 3.20)				⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage II (age 75-84 years) (follow-up: median 10 years) (assessed with: cumulative incidence rate per 100 women)												
1[1]	non-randomised study	very serious[a]	not serious	very serious[b]	serious[c]	none	Localised invasive, adjusted cumulative incidence per 100 women (95% CI): • Screened: 3.15 (2.95, 3.38) • Non-screened: 1.50 (1.21, 1.86)				⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage II and higher (all ages) (follow-up: median 5.4 to 13.7 years; NR in 2 studies) (assessed with: n/N (4 studies included in analysis; no raw data provided in 1 study[1])												
5[1,2,3,4,5]	non-randomised studies	very serious[d]	very serious[e]	very serious[f]	serious[g]	none	7076/23522 (30.1%)	9821/22784 (43.1%)	**RR 0.68** (0.58 to 0.79)	**138 fewer per 1,000** (from 181 fewer to 91 fewer)	⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage III and higher (all ages) (follow-up: median 5.4 to 13.7 years; NR in 2 studies) (assessed with: n/N (4 studies included in analysis; no raw data provided in 1 study[1]))												
5[1,2,3,4,5]	non-randomised studies	very serious[d]	very serious[e]	very serious[f]	serious[c]	none	6974/23522 (29.6%)	9672/22784 (42.5%)	**RR 0.65** (0.55 to 0.78)	**149 fewer per 1,000** (from 191 fewer to 93 fewer)	⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Certainty assessment							**№ of patients**		**Effect**		**Certainty**	**Importance**
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**mammography**	**no screening**	**Relative (95% CI)**	**Absolute (95% CI)**		
Breast cancer staging, stage III and IV (age 70-74 years) (follow-up: median 13.7 years) (assessed with: cumulative incidence rate per 100 women)												
1[1]	non-randomised study	very serious[a]	not serious	very serious[b]	serious[c]	none	Regional/distant, adjusted cumulative incidence per 100 women (95% CI): • Screened: 1.00 (0.85, 1.17) • Non-screened: 0.90 (0.61, 1.34)				⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage III and IV (age 75-84 years) (follow-up: median 10 years) (assessed with: cumulative incidence per 100 women)												
1[1]	non-randomised study	very serious[a]	not serious	very serious[b]	serious[c]	none	Regional/distant, adjusted cumulative incidence per 100 women (95% CI): • 0.78 (0.66, 0.92) • 0.74 (0.55, 1.00)				⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage IV (all ages) (follow-up: median 5.4 to 10.5 years; NR in 2 studies) (assessed with: n/N)												
4[2,3,4,5]	non-randomised studies	very serious[h]	very serious[i]	very serious[j]	serious[c]	none	532/23522 (2.3%)	1461/22784 (6.4%)	**RR 0.32** (0.20 to 0.52)	**44 fewer per 1,000** (from 51 fewer to 31 fewer)	⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Retrospective study; study population is a select group of participants (sample of Medicare beneficiaries in the USA; unclear whether the sample is random).

b. Risk level not reported; type of mammography not reported.

c. Wide CI.

d. Retrospective study (n=5); study population was a select group of participants (n=2; one institution in Hungary and sample of Medicare beneficiaries in the USA (unclear whether the sample is random)); inadequate follow-up length for outcome to occur (n=1); did not correct for major confounding factors (n=1).

e. Point estimates vary widely; insufficient overlap between 95% CIs (not all CIs overlap at least one point estimate); magnitude of statistical heterogeneity is high.

f. All participants had breast cancer (n=4); HDI <0.9 (Hungary) (n=1); risk level not reported (n=5); mammography type (n=4), screening interval (n=1), and number of screening rounds (n=3) not reported.

g. Wide CI; outcome is a rare event.

h. Retrospective study (n=4); study population was a select group of participants (n=1; one institution in Hungary); inadequate follow-up length for outcome to occur (n=1); study did not correct for major confounding factors (n=1).

i. Point estimates vary widely; insufficient overlap between 95% CIs (not all CIs overlap at least one point estimate); direction of the effect is not consistent; magnitude of statistical heterogeneity is high.

j. All participants had breast cancer (n=4); HDI <0.9 (Hungary) (n=1); risk level not reported (n=4); mammography type (n=3), screening interval (n=1), and number of screening rounds (n=3) not reported.

CI: confidence interval; **HDI:** Human Development Index; **NR:** not reported; **RR:** risk ratio

References

1. Richman IB, Long JB, Soulos PR, Wang SY, Gross CP. Estimating breast cancer overdiagnosis after screening mammography among older women in the United States. *Ann Intern Med* 2023;176(9):1172-80.

2. Tomšič S, Žagar T, Mihor A, Mlakar M, Lokar K, Jarm K, Zadnik V. Prognostic factors and outcomes in women with breast cancer in Slovenia in relation to step-wise implementation of organized screening. *PLoS One* 2022;17(11):e0278384.

3. Újhelyi M, Pukancsik D, Kelemen P, Kovács E, Kenessey I, Udvarhelyi N et al. Does breast screening offer a survival benefit? A retrospective comparative study of oncological outcomes of screen-detected and symptomatic early stage breast cancer cases. *Eur J Surg Oncol* 2016;42(12):1814-20.

4. Woods LM, Rachet B, O'Connell DL, Lawrence G, Coleman MP. Are international differences in breast cancer survival between Australia and the UK present amongst both screen-detected women and non-screen-detected women? survival estimates for women diagnosed in West Midlands and New South Wales 1997-2006. *Int J Cancer* 2016;138(10):2404-14.

5. Luu XQ, Lee K, Jun JK, Suh M, Jung KW, Choi KS. Effect of mammography screening on the long-term survival of breast cancer patients: results from the National Cancer Screening Program in Korea. *Epidemiol Health* 2022;44:e2022094.

Table 7.2: Stage of cancer (cohort studies, long case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer staging, stage II and higher (all ages) **(follow-up: mean 2.9 years up to 10 years; NR in 6 studies) (assessed with: n/N or RR (13 studies included in analysis; no raw data provided in 1 study, but reported RR included in analysis[4]))**												
13[1,2,3,4,5,6,7,8,9,10,11,12,13]	non-randomised studies	very serious[a]	very serious[b]	very serious[c]	serious[d]	none	23433/120816 (19.4%)	24261/71128 (34.1%)	**RR 0.59** (0.48 to 0.74)	**140 fewer per 1,000** (from 177 fewer to 89 fewer)	⨁◯◯◯ Very low	CRITICAL
Breast cancer staging, stage II and higher (age 40-49 years) **(follow-up: NR) (assessed with: n/N)**												
1[1]	non-randomised studies	very serious[e]	not serious	very serious[f]	serious[g]	none	53/106 (50.0%)	54/71 (76.1%)	**RR 0.66** (0.52 to 0.83)	**259 fewer per 1,000** (from 365 fewer to 129 fewer)	⨁◯◯◯ Very low	CRITICAL
Breast cancer staging, stage II and higher (age ≥75 years) **(follow-up: median 3.1 years) (assessed with: n/N)**												
1[2]	non-randomised studies	very serious[h]	not serious	very serious[i]	serious[g]	none	15/57 (26.3%)	210/283 (74.2%)	**RR 0.35** (0.23 to 0.55)	**482 fewer per 1,000** (from 571 fewer to 334 fewer)	⨁◯◯◯ Very low	CRITICAL
Breast cancer staging, stage III and higher (all ages) **(follow-up: mean 2.9 years up to 10 years; NR in 6 studies) (assessed with: n/N or RR (13 studies included in analysis; no raw data provided in 1 study, but reported RR included in analysis[4]))**												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
13[1,2,3,4,5,6,7,8,9,10,11,12,13]	non-randomised studies	very serious[a]	very serious[b]	very serious[c]	serious[d]	none	21627/120816 (17.9%)	21618/71128 (30.4%)	**RR 0.43** (0.33 to 0.58)	**173 fewer per 1,000** (from 204 fewer to 128 fewer)	⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer staging, stage III and higher (age 40-49 years) (follow-up: NR) (assessed with: n/N)												
1[1]	non-randomised studies	very serious[e]	serious[i]	very serious[f]	serious[g]	none	16/106 (15.1%)	24/71 (33.8%)	**RR 0.45** (0.26 to 0.78)	**186 fewer per 1,000** (from 250 fewer to 74 fewer)	⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage III and higher (age ≥75 years) (follow-up: median 3.1 years) (assessed with: n/N)												
1[2]	non-randomised studies	very serious[h]	not serious	very serious[i]	serious[g]	none	4/57 (7.0%)	88/283 (31.1%)	**RR 0.23** (0.09 to 0.59)	**239 fewer per 1,000** (from 283 fewer to 127 fewer)	⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage IV (all ages) (follow-up: mean 2.9 years up to 10 years; NR in 4 studies) (assessed with: n/N or RR (no raw data provided in 1 study, but reported RR included in analysis[4]))												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
9[1,2,4,5,6,7,9,10,12]	non-randomised studies	very serious[k]	very serious[b]	very serious[l]	serious[d]	none	1502/55476 (2.7%)	2824/45158 (6.3%)	**RR 0.29** (0.22 to 0.39)	**44 fewer per 1,000** (from 49 fewer to 38 fewer)	⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage IV (age 40-49 years) (follow-up: NR) (assessed with: n/N or RR (no raw data not provided in 1 study, but reported RR included in analysis[4]))												
2[1,4]	non-randomised studies	very serious[m]	serious[i]	very serious[n]	serious[d]	none	Total sample size: 1839 • RR: 0.26 (95% CI 0.16, 0.41) • **Absolute effect (95% CI): 73 fewer per 1,000** (from 83 fewer to 58 fewer) (using the baseline risk from Plecha)				⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage IV (age ≥75 years) (follow-up: median 3.1 years) (assessed with: n/N)												
1[2]	non-randomised studies	very serious[h]	not serious	very serious[i]	serious[g]	none	0/57 (0.0%)	48/283 (17.0%)	**RR 0.050** (0.003 to 0.810)	**161 fewer per 1,000** (from 169 fewer to 32 fewer)	⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Retrospective study (n=11); study population was a select group of participants (n=6; one hospital in France and Japan; one institution in Poland and the USA; two hospitals in Spain; and seven public hospitals in Singapore); inadequate follow-up rate (n=1); did not correct for major confounding factors (n=2).

b. Point estimates vary widely; insufficient overlap between 95% CIs (not all CIs overlap at least one point estimate); magnitude of statistical heterogeneity is high.

c. All participants had breast cancer (n=12); HDI <0.9 (Poland) (n=1); participants included women of all risk levels (including high risk) (n=1) or risk level not reported (n=11); used film and digital mammography (n=4); type of mammography (n=9), screening interval (n=5), and number of screening rounds (n=10) not reported.

d. Wide CI.

e. Retrospective study; study population is a select group of participants (one institution in the USA); no description of ascertainment of screening exposure; length of follow-up in the non-screened group was unclear.

f. All participants had breast cancer; risk level not reported; used film (14% of women) and digital mammography; screening interval and number of screening rounds not reported.

g. Single study with small sample size; wide CI.

h. Retrospective study; study population was a select group of participants (one hospital in France); did not correct for major confounding factors.

i. All participants had breast cancer; risk level not reported; mammography type, screening interval, and number of screening rounds not reported.

j. Point estimates vary widely.

k. Retrospective studies (n=8); study population was a select group of participants (n=5; one hospital in France; one institution each in Poland and the USA; seven public hospitals in Singapore; and four major public hospitals in Australia); inadequate rate of follow-up (n=1); did not correct for major confounding factors (n=2).

l. All participants had breast cancer (n=8); study population was a select group of participants (n=5; one hospital in France; one institution in Poland and the USA; seven public hospitals in Singapore; and four major public hospitals in Australia); HDI <0.9 (Poland) (n=1); participants included women of all risk levels (including high risk) (n=1) or risk level not reported (n=7); used film and digital mammography (n=2); mammography type (n=7), screening interval (n=4), and number of screening rounds (n=7) not reported.

m. Retrospective study (n=2); study population was a select group of participants (n=1; one institution in the USA).

n. All participants had breast cancer (n=2); study population was a select group of participants (n=1; one institution in the USA); risk level not reported (n=2); used film and digital mammography (n=2); mammography type (n=2), screening interval (n=1), and number of screening rounds (n=2) not reported.

CI: confidence interval; **HDI:** Human Development Index; **RR:** risk ratio

References

1. Plecha D, Salem N, Kremer M, Pham R, Downs-Holmes C, Sattar A, Lyons J. Neglecting to screen women between 40 and 49 years old with mammography: what is the impact on treatment morbidity and potential risk reduction? *Am J Roentgenol* 2014;202(2):282-8.

2. Ilenko A, Sergent F, Mercuzot A, Zitoun M, Chauffert B, Foulon A et al. Could patients older than 75 years benefit from a systematic breast cancer screening program? *Anticancer Res* 2017;37(2):903-7.

3. Tvedskov TF, Jensen MB, Balslev E, Garne JP, Vejborg I, Christiansen P et al. Risk of non-sentinel node metastases in patients with symptomatic cancers compared to screen-detected breast cancers. *Acta Oncol.*2016;55(4):455-9.

4. Oberaigner W, Geiger-Gritsch S, Edlinger M, Daniaux M, Knapp R, Hubalek M et al. Reduction in advanced breast cancer after introduction of a mammography screening program in Tyrol/Austria. *Breast* 2017;33:178-182.

5. Woźniacki P, Skokowski J, Bartoszek K, Kosowska A, Kalinowski L, Jaśkiewicz J. The impact of the Polish mass breast cancer screening program on prognosis in the Pomeranian Province. *Arch Med Sci* 2017;13(2):441-7.

6. Choi KS, Yoon M, Song SH, Suh M, Park B, Jung KW, Jun JK. Effect of mammography screening on stage at breast cancer diagnosis: results from the Korea National Cancer Screening Program. *Sci Rep* 2018;8(1):8882.

7. Roder D, Farshid G, Gill G, Kollias J, Koczwara B, Karapetis C et al. Breast cancer screening-opportunistic use of registry and linked screening data for local evaluation. *J Eval Clin Pract* 2017;23(3):508-16.

8. de Munck L, Siesling S, Fracheboud J, den Heeten GJ, Broeders MJM, de Bock GH. Impact of mammographic screening and advanced cancer definition on the percentage of advanced-stage cancers in a steady-state breast screening programme in the Netherlands. *Br J Cancer* 2020;123(7):1191-7.

9. Niraula S, Biswanger N, Hu P, Lambert P, Decker K. Incidence, characteristics, and outcomes of interval breast cancers compared with screening-detected breast cancers. *JAMA Netw Open* 2020;3(9):e2018179.

10. Lim ZL, Ho PJ, Khng AJ, Yeoh YS, Ong ATW, Tan BKT et al. Mammography screening is associated with more favourable breast cancer tumour characteristics and better overall survival: case-only analysis of 3739 Asian breast cancer patients. *BMC Med* 2022;20(1):239.

11. Kobayashi N, Hikichi M, Ushimado K, Sugioka A, Kiriyama Y, Kuroda M, Utsumi T. Differences in subtype distribution between screen-detected and symptomatic invasive breast cancer and their impact on survival. *Clin Transl Oncol* 2017;19(10):1232-40.

12. Choi E, Jun JK, Suh M, Jung KW, Park B, Lee K et al. Effectiveness of the Korean National Cancer Screening Program in reducing breast cancer mortality. *NPJ Breast Cancer* 2021;7(1):83.

13. Barco I, Chabrera C, García Font M, Gimenez N, Fraile M, Lain JM et al. Comparison of screened and nonscreened breast cancer patients in relation to age: A 2-institution study. *Clin Breast Cancer* 2015;15(6):482-9.

Table 7.3: Stage of cancer (population-based studies, long case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer staging, stage II (all ages) **(follow-up: NR) (assessed with: incidence per 100,000 women)**												
1[1]	non-randomised study	very serious[a]	not serious	very serious[b]	serious[c]	none	• Screened: 47.2 • Non-screened: 42.2				⨁◯◯◯ Very low	CRITICAL
Breast cancer staging, stage II (50-69 years) **(follow-up: NR) (assessed with: incidence per 100,000 women)**												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
1[1]	non-randomised study	very serious[a]	not serious	very serious[b]	serious[c]	none	Incidence per 100,000 women • Screened: 104.0 • Non-screened: 101.4				⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage II (≥70 years) (follow-up: NR) (assessed with: incidence per 100, 000 women)												
1[1]	non-randomised study	very serious[a]	not serious	very serious[b]	serious[c]	none	• Screened: 144.4 • Non-screened: 126.3				⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage II and higher (50-69 years) (follow-up: >10 years) (assessed with: incidence rate ratio)												
1[2]	non-randomised study	serious[d]	not serious	very serious[e]	serious[c]	none	Before and after incidence rate ratio (95% CI) • Screened: 0.96 (0.90, 1.02) • Non-screened: 1.46 (1.41, 1.52)				⊕◯◯◯ Very low	CRITICAL

Table 7.3: Stage of cancer (population-based studies, long case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer staging, stage II and higher (≥70 years) (follow-up: range 2,386,061 to 3,394,055 PY (1 study); >10 years (1 study)) (assessed with: n/N or incidence rate ratio)												
2[2,3]	non-randomised studies	very serious[f]	not serious	very serious[g]	not serious	none	Jørgensen: Before and after incidence rate ratio (95% CI) • Screened: 1.25 (1.16, 1.34) • Non-screened: 1.81 (1.72, 1.90) de Glas: • Screened: 5774/14075 (41.0%) • Non-screened: 2286/3428 (66.7%) • RR 0.62 (95% CI 0.60, 0.63) • **Absolute effect (95% CI): 253 fewer per 1,000** (from 267 fewer to 247 fewer)			⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage III (all ages) (follow-up: NR) (assessed with: incidence per 100,000 women)												
1[4]	non-randomised study	serious[d]	not serious	very serious[h]	serious[c]	none	Age-standardised incidence per 100,000 women relative to prescreening (95% CI) • Screened: 44.4 (43.6, 45.2) • Non-screened: 22.6 (22.0, 23.2) Incident rate ratio per 100,000 women relative to prescreening (95% CI): 1.96 (1.90, 2.03)			⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage III (age 40-49 years) (follow-up: NR) (assessed with: incidence per 100,000 women)												
1[4]	non-randomised study	serious[d]	not serious	very serious[h]	serious[c]	none	Age-standardised incidence per 100,000 women relative to prescreening (95% CI) • Screened: 62.3 (60.0, 64.5) • Non-screened: 39.8 (37.7, 42.0) Incident rate ratio per 100,000 women relative to prescreening (95% CI): 1.82 (1.70, 1.94)			⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer staging, stage III (age ≥70 years) (follow-up: NR) (assessed with: incidence per 100,000 women)												
1[4]	non-randomised study	very serious[d]	not serious	very serious[h]	serious[c]	none	Age-standardised incidence per 100,000 women relative to prescreening (95% CI) • Screened: 100.9 (97.0, 104.7) • Non-screened: 48.1 (45.3, 51.0) Incident rate ratio per 100,000 women relative to prescreening (95% CI): 2.10 (1.95, 2.23)				⨁◯◯◯ Very low	CRITICAL
Breast cancer staging, stage III (50-69 years) (follow-up: NR) (assessed with: incidence per 100,000 women)												
1[4]	non-randomised study	very serious[d]	not serious	very serious[h]	serious[c]	none	Age-standardised incidence per 100,000 women relative to prescreening (95% CI) • Screened: 106.9 (104.2, 109.7) • Non-screened: 52.5 (50.6, 54.4) Incident rate ratio per 100,000 women relative to prescreening (95% CI): 2.04 (1.95, 2.13)				⨁◯◯◯ Very low	CRITICAL
Breast cancer staging, stage III and higher (all ages) (follow-up: NR) (assessed with: incidence per 100,000 women)												
1[1]	non-randomised study	very serious[a]	not serious	very serious[b]	serious[c]	none	• Screened: 22.3 • Non-screened: 29.1				⨁◯◯◯ Very low	CRITICAL
Breast cancer staging, stage III and higher (50-69 years) (follow-up: NR) (assessed with: incidence per 100,000 women)												
1[1]	non-randomised study	very serious[a]	not serious	very serious[b]	serious[c]	none	• Screened: 45.7 • Non-screened: 66.2				⨁◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer staging, stage III and higher (≥70 years) **(follow-up: range 2,386,061 to 3,394,055 PY (1 study); NR (1 study)) (assessed with: n/N or incidence per 100,000 women)**												
2[1,3]	non-randomised studies	very serious[i]	not serious	very serious[j]	serious[k]	none	de Glas: • Screened: 1759/14075 (12.5%) • Non-screened: 654/3428 (19.1%) • RR 0.66 (95% CI 0.60, 0.71) • **Absolute effect (95% CI): 65 fewer per 1,000** (from 76 fewer to 55 fewer) Hubner: Incidence per 100,000 women • Screened: 94.1 • Non-screened: 116.1				⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage IV (all ages) **(follow-up: NR) (assessed with: incidence per 100,000 women)**												
1[4]	non-randomised study	very serious[d]	not serious	very serious[h]	serious[c]	none	Age-standardised incidence per 100,000 women relative to prescreening (95% CI) • Screened: 7.2 (6.9, 7.5) • Non-screened: 4.1 (3.9, 4.4) Incident rate ratio per 100,000 women relative to prescreening (95% CI): 1.74 (1.61, 1.87)				⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage IV (age 40-49 years) **(follow-up: NR) (assessed with: incidence per 100,000 women)**												
1[4]	non-randomised study	very serious[d]	not serious	very serious[h]	serious[c]	none	Age-standardised incidence per 100,000 women relative to prescreening (95% CI) • Screened: 9.3 (8.3, 10.3) • Non-screened: 5.8 (5.0, 6.6) Incident rate ratio per 100,000 women relative to prescreening (95% CI): 1.60 (1.34, 1.91)				⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer staging, stage IV (50-69 years) (follow-up: NR) (assessed with: incidence per 100,000 women)												
1[4]	non-randomised study	very serious[d]	not serious	very serious[h]	serious[c]	none	Age-standardised incidence per 100,000 women relative to prescreening (95% CI) • Screened: 16.9 (15.8, 18.0) • Non-screened: 9.4 (8.6, 10.2) Incident rate ratio per 100,000 women relative to prescreening (95% CI): 1.80 (1.62, 2.00)				⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage IV (≥70 years) (follow-up: range 2,386,061 to 3,394,055 PY (1 study); NR (1 study)) (assessed with: n/N or incidence per 100,000 women)												
2[3,4]	non-randomised studies	very serious[i]	serious[l]	very serious[m]	serious[k]	none	de Glas: • Screened: 553/14075 (3.9%) • Non-screened: 283/3428 (8.3%) • RR 0.48 (95% CI 0.41, 0.55) • **Absolute effect (95% CI): 43 fewer per 1,000** (from 49 fewer to 37 fewer) Jacklyn: Age-standardised incidence per 100,000 women relative to prescreening (95% CI) • Screened: 22.9 (21.1, 24.7) • Non-screened: 12.5 (11.1, 14.0) Incident rate ratio per 100,000 women relative to prescreening (95% CI): 1.83 (1.59, 2.11)				⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. Retrospective study; potentially confounded by opportunistic screening in the screened group prior to the start of screening and in the non-screened group.

b. All participants had breast cancer; risk level not reported; type of mammography, screening interval, and number of screening rounds not reported.

c. Outcome is a rare event.

d. Retrospective study.

e. All participants had breast cancer; risk level not reported; mammography type and number of screening rounds not reported.

f. Retrospective study (n=2); age ranges of screened and non-screened groups were different (range 70-84 years versus 70-75 years) (n=1).

g. All participants had breast cancer (n=2); risk level not reported (n=2); type of mammography type (n=2), screening interval (n=1), and number of screening rounds (n=2) not reported.

h. All participants had breast cancer; risk level not reported; used film and digital mammography; number of screening rounds not reported.

i. Retrospective study (n=2); age ranges of screened and non-screened groups were different (n=1).

j. All participants had breast cancer (n=2); risk level not reported (n=2); mammography type (n=2), screening interval (n=2), and number of screening rounds (n=2).

k. Outcome is a rare event (n=1).

l. Direction of effect is not consistent.

m. All participants had breast cancer (n=2); risk level not reported (n=2); used film and digital mammography (n=1); mammography type (n=1), screening interval (n=1), and number of screening rounds (n=2) not reported.

CI: confidence interval; **NR:** not reported; **PY:** patient years; **RR:** risk ratio

References

1. Hübner J, Katalinic A, Waldmann A, Kraywinkel K. Long-term incidence and mortality trends for breast cancer in Germany. *Geburtshilfe Frauenheilkd* 2020;80(6):611-8.

2. Jørgensen KJ, Gøtzsche PC, Kalager M, Zahl PH. Breast cancer screening in Denmark: A cohort study of tumor size and overdiagnosis. *Ann Intern Med* 2017;166(5):313-23.

3. de Glas NA, de Craen AJ, Bastiaannet E, Op 't Land EG, Kiderlen M, van de Water W, et al. Effect of implementation of the mass breast cancer screening programme in older women in the Netherlands: population based study *BMJ*. 2014;349:g5410.

4. Jacklyn G, McGeechan K, Irwig L, Houssami N, Morrell S, Bell K, Barratt A. Trends in stage-specific breast cancer incidence in New South Wales, Australia: insights into the effects of 25 years of screening mammography. *Breast Cancer Res Treat* 2017;166(3):843-54.

Table 8. Health-related quality of life (cohort studies, short case accrual)

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Health-related quality of life (age 50-69 years) (follow-up: NR) (assessed with: scale)[a]									
1[1]	non-randomised study	very serious[b]	not serious	very serious[c]	serious[d]	none	• Screened (n=346): mean 68.8 • Non-screened (n=301): mean 69.8 • Study reported no difference between groups (p-value not reported).	⊕◯◯◯ Very low	CRITICAL
Health-related quality of life (age 50-59 years) (follow-up: NR) (assessed with: scale)[a]									
1[1]	non-randomised study	very serious[b]	not serious	very serious[c]	serious[d]	none	• Screened (n=346): mean 66.9 • Non-screened (n=301): mean 70.7 • Study reported no difference between groups (p-value not reported).	⊕◯◯◯ Very low	CRITICAL
Health-related quality of life (age 60-69 years) (follow-up: NR) (assessed with: scale)[a]									
1[1]	non-randomised study	very serious[b]	not serious	very serious[c]	serious[d]	none	• Screened (n=346): mean 69.0 • Non-screened (n=301): mean 69.8 • Study reported no difference between groups (p-value not reported).	⊕◯◯◯ Very low	CRITICAL

***Explanations*:**

a. EORTC QLQ-C30 v. 3 and parts of the QLQ-BR23 were used to assess quality of life, score range 0 to 100 (higher scores correspond to better functioning).

b. Retrospective study; study population was a select group of participants (one breast care centre in Munster, Germany); ascertainment of exposure by self-report (questionnaire with 64% participation rate).

c. All participants had breast cancer; risk level not reported; mammography type and number of screening rounds not reported.

d. Single study with small sample size.

NR: not reported

References

1. Braun B, Kurosinski MA, Khil L, Tio J, Krause-Bergmann B, Hense HW. The mode of detection is not associated with quality of life in women with breast cancer. *Breast Care (Basel)* 2020;15(5):498-505.

Table 9.1. Interval cancer in the screening group (cohort studies, short case accrual)

Certainty assessment							№ of patients	Proportion (95%CI)	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations				
Interval cancer (age 50-69 years) (follow-up: NR) (assessed with: n/N (screening group only))										
2[1,2]	non-randomised studies	very serious[b]	very serious[a]	very serious[c]	very serious[d]	none	2653/8159 (32.5%)	**0.22** (0.05 to 0.48)	⊕◯◯◯ Very low	IMPORTANT

***Explanations*:**

a. Wide range of values reported across the studies.

b. Retrospective study (n=2); study population is a select group of participants (n=1; one breast care centre in Munster, Germany); ascertainment of exposure by self-report (questionnaire with 64% participation rate) (n=1).

c. All participants had breast cancer (n=2); risk level not reported (n=2); mammography type (n=2), screening interval (n=1), and number of screening rounds (n=2) not reported.

d. Wide CIs.

CI: confidence interval; **NA:** not applicable; **NR**: not reported

References

1.Braun B, Kurosinski MA, Khil L, Tio J, Krause-Bergmann B, Hense HW. The mode of detection is not associated with quality of life in women with breast cancer. *Breast Care (Basel)* 2020;15(5):498-505.

2. Woods LM, Rachet B, O'Connell DL, Lawrence G, Coleman MP. Are international differences in breast cancer survival between Australia and the UK present amongst both screen-detected women and non-screen-detected women? survival estimates for women diagnosed in West Midlands and New South Wales 1997-2006. *Int J Cancer* 2016;138(10):2404-14.

Table 9.2. Interval cancer in the screening group (cohort studies, long case accrual)

Certainty assessment							№ of patients	Proportion (95%CI)	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations				
Interval cancer (all ages) (follow-up: mean 4.3 years up to median 7 years; NR in 3 studies) (assessed with: n/N)										
7[1,2,3,4,5,6,7]	non-randomised study	very serious[a]	very serious[b]	very serious[c]	very serious[d]	none	18022/191043 (9.4%)	**0.13** (0.06 to 0.23)	⊕◯◯◯ Very low	IMPORTANT
Interval cancer (age 40-49 years) (follow-up: NR) (assessed with: n/N)										
1[2]	non-randomised study	very serious[e]	not serious	very serious[f]	serious[g]	none	25/149 (16.8%)	**0.17** (0.11 to 0.23)	⊕◯◯◯ Very low	IMPORTANT
Interval cancer (age 45-69 years) (follow-up: mean 5.5 years) (assessed with: n/N)										
1[3]	non-randomised study	serious[h]	not serious	very serious[i]	not serious	none	218/1324 (16.5%)	**0.16** (0.15 to 0.19)	⊕◯◯◯ Very low	IMPORTANT

Certainty assessment							№ of patients	Proportion (95%CI)	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations				
Interval cancer (age 49-74 years) (follow-up: NR) (assessed with: n/N)										
1[4]	non-randomised study	serious[h]	not serious	very serious[i]	not serious	none	17362/64096 (27.1%)	**0.27** (0.27 to 0.27)	⊕◯◯◯ Very low	IMPORTANT
Interval cancer (age 50-69 years) (follow-up: mean 4.3 years up to 7 years; NR in 1 study) (assessed with: n/N)										
4[1,5,6,7]	non-randomised study	very serious[k]	serious[l]	serious[m]	serious[n]	none	417/125474 (0.3%)	**0.003** (0.003 to 0.004)	⊕◯◯◯ Very low	IMPORTANT

***Explanations*:**

a. Retrospective study (n=5); study population is a select group of participants (n=4; one hospital in Australia, one institution in the USA, and two hospitals in Spain).

b. Point estimates vary widely; insufficient overlap between 95% CIs (not all CIs overlap at least one point estimate); magnitude of statistical heterogeneity is high.

c. All participants had breast cancer (n=7); risk level not reported (n=6); used film and digital mammography (n=3); mammography type (n=4), screening interval (n=1), and number of screening rounds (n=5) not reported.

d. Wide CI of pooled point estimate.

e. Retrospective study; study population is select group of participants (one institution in the USA); no description of ascertainment of screening exposure.

f. All participants had breast cancer; risk level not reported; used film mammography (14% of women) and digital mammography; screening interval and number of screening rounds not reported.

g. Single study with small sample size.

h. Retrospective study.

i. All participants had breast cancer; risk level not reported; mammography type and number of screening rounds not reported.

j. All participants had breast cancer; risk level not reported; used film and digital mammography; number of screening rounds not reported.

k. Retrospective study (n=2); study population is a select group of participants (n=3; one hospital in Australia and two hospitals in Spain).

l. Wide range of values reported across the studies.

m. All participants had breast cancer (n=4); risk level not reported (n=3); used film and digital mammography (n=1); mammography type (n=3) and number of screening rounds (n=2) not reported.

n. Outcome is rare event.

CI: confidence interval; **NA:** not applicable; **NR**: not reported

References

1. Niraula S, Biswanger N, Hu P, Lambert P, Decker K. Incidence, characteristics, and outcomes of interval breast cancers compared with screening-detected breast cancers. *JAMA Netw Open* 2020;3(9):e2018179.

2. Plecha D, Salem N, Kremer M, Pham R, Downs-Holmes C, Sattar A, Lyons J. Neglecting to screen women between 40 and 49 years old with mammography: what is the impact on treatment morbidity and potential risk reduction? *Am J Roentgenol* 2014;202(2):282-8.

3. Seneviratne S, Campbell I, Scott N, Shirley R, Lawrenson R. Impact of mammographic screening on ethnic and socioeconomic inequities in breast cancer stage at diagnosis and survival in New Zealand: a cohort study. *BMC Public Health* 2015;15:46.

4. de Munck L, Siesling S, Fracheboud J, den Heeten GJ, Broeders MJM, de Bock GH. Impact of mammographic screening and advanced cancer definition on the percentage of advanced-stage cancers in a steady-state breast screening programme in the Netherlands. *Br J Cancer* 2020;123(7):1191-7.

5. García Fernández A, Chabrera C, García Font M, Fraile M, Lain JM, Gónzalez S et al. Mortality and recurrence patterns of breast cancer patients diagnosed under a screening programme versus comparable non-screened breast cancer patients from the same population: analytical survey from 2002 to 2012. *Tumour Biol* 2014;35(3):1945-53.

6. Elder K, Nickson C, Pattanasri M, Cooke S, Machalek D, Rose A et al. Treatment intensity differences after early-stage breast cancer (ESBC) diagnosis depending on participation in a screening program. *Ann Surg Oncol* 2018;25(9):2563-72.

7. Barco I, Chabrera C, García Font M, Gimenez N, Fraile M, Lain JM et al. Comparison of screened and nonscreened breast cancer patients in relation to age: A 2-institution study. *Clin Breast Cancer* 2015;15(6):482-9.

Table 10. General screening population, all outcomes (cohort studies, short and long case accrual)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute* (95% CI)		
Breast cancer specific mortality (short case accrual; all ages) (follow-up: median 5.7 years up to 16 years) (assessed with: n/N or adjusted cumulative incidence per 100 women (1 study included in analysis; no raw data in 1 study[1]))												
2[1,2]	non-randomised studies	serious[a]	not serious	very serious[b]	serious[c]	none	873/187558 (0.5%)	479/74792 (0.6%)	**HR 0.61** (0.55 to 0.68)	**2 fewer per 1,000** (from 3 fewer to 2 fewer)	⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (short case accrual; age 70-74 years) (follow-up: median 13.7 years) (assessed with: adjusted cumulative incidence per 100 women)												
1[1]	non-randomised study	very serious[d]	not serious	very serious[e]	serious[c]	none	• Screened: 0.35 (95% CI 0.26, 0.48) • Not screened: 0.41 (0.22, 0.76) HR: 0.86 (95% CI 0.44, 1.68)				⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (short case accrual; age 75-84 years) (follow-up: median 10 years) (assessed with: adjusted cumulative incidence per 100 women)												
1[1]	non-randomised studies	very serious[d]	not serious	very serious[e]	serious[c]	none	• Screened: 0.36 (0.29, 0.46) • Not screened: 0.42 (0.28, 0.64) HR: 0.87 (95% CI 0.55, 1.37)				⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (long case accrual; all ages) (follow-up: median 7.5 to 8.4 years; NR in 1 study) (assessed with: n/N)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute* (95% CI)		
2[3,4]	non-randomised studies	very serious[f]	serious[g]	very serious[h]	serious[c]	none	3867/55255153 (0.00007%)	10782/59530162 (0.00018%)	**RR 0.40** (0.33 to 0.47)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer specific mortality (long case accrual; age 70-74 years) **(follow-up: 8 years; assessed with: RD or HR)**												
1[5]	non-randomised study	serious[i]	not serious	very serious[j]	serious[c]	none	RD: -1.0 (95% CI: -2.3, 0.1) deaths/1,000 women HR: 0.78 (95% CI 0.63, 0.95)				⊕◯◯◯ Very low	CRITICAL
Breast cancer specific mortality (long case accrual; age ≥75 years) **(follow-up: 8 years) (assessed with: risk difference or hazard ratio)**												
1[5]	non-randomised study	serious[i]	not serious	very serious[j]	serious[c]	none	RD: 0.07 (95% CI -0.93, 1.3) deaths/1,000 women HR: 1.00 (95% CI 0.83, 1.19)				⊕◯◯◯ Very low	CRITICAL
All-cause mortality (short case accrual; all ages) **(follow-up: mean 3.9 years up to 3.7 years) (assessed with: n/N)**												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
2[1,6]	non-randomised studies	very serious[k]	very serious[l]	very serious[m]	not serious[n]	none	35383/745601 (4.7%)	25970/556953 (4.7%) Statistics Canada (all ages): 76.2/1000 (7.62%)	**RR 0.57** (0.35 to 0.92)	**20 fewer per 1,000** (from 30 fewer to 4 fewer) **33 fewer per 1,000** (from 50 fewer to 6 fewer)	⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
All-cause mortality (short case accrual; age 70-74) (follow-up: median 13.7 years) (assessed with: n/N)												
1[1]	non-randomised study	very serious[d]	not serious	very serious[e]	not serious	none	6645/17488 (38.0%)	1365/2437 (56.0%) Statistics Canada (age 70-79 years): 189.5/1,000 (18.95%)	**RR 0.68** (0.65 to 0.71)	**179 fewer per 1,000** (from 196 fewer to 162 fewer) **61 fewer per 1,000** (from 66 fewer to 55 fewer)	⊕◯◯◯ Very low	CRITICAL
All-cause mortality (short case accrual; age ≥75 years) (follow-up: median 5.7 years to median 10 years) (assessed with: n/N)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
1[1]	non-randomised study	very serious[d]	not serious	very serious[e]	not serious	none	18427/26997 (68.3%)	6492/7713 (84.2%) Statistics Canada (age 70-79 years): 189.5/1,000 (18.95%)	**RR 0.81** (0.80 to 0.82)	**160 fewer per 1,000** (from 168 fewer to 152 fewer) **36 fewer per 1,000** (from 38 fewer to 34 fewer)	⊕◯◯◯ Very low	CRITICAL
Radiotherapy (long case accrual; age 70-74 years) (follow-up: 8 years) (assessed with: standardised percentage)												
1[5]	non-randomised studies	serious[i]	not serious	very serious[j]	not serious	none	Standardised percentage (95% CI) • Screened: 51.0% (95%CI: 50.3-51.8) • Not screened: 39.9% (95% CI: 38.6, 41.3)				⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Radiotherapy (long case accrual; age 75-84 years) (follow-up: 8 years) (assessed with: standardised percentage)												
1[5]	non-randomised study	serious[i]	not serious	very serious[j]	not serious	none	Standardised percentage (95% CI) • Screened: 41.2% (95% CI: 40.4-41.9) • Not screened: 31.9% (95% CI: 30.7-33.1)				⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Chemotherapy (long case accrual; age 70-74 years) (follow-up: 8 years) (assessed with: standardised percentage)												
1[5]	non-randomised study	serious[i]	not serious	very serious[j]	not serious	none	Standardised percentage (95% CI) • Screened: 15.2% (14.7%, 15.8%) • Non-screened: 21.1% (20.0%, 22.1%)				⊕◯◯◯ Very low	CRITICAL
Chemotherapy (long case accrual; age 75-84 years) (follow-up: 8 years) (assessed with: standardised percentage)												
1[5]	non-randomised study	serious[i]	not serious	very serious[j]	not serious	none	Standardised percentage (95% CI) • Screened: 8.6% (8.3%, 9.1%) • Non-screened: 11.5% (10.6%, 12.3%)				⊕◯◯◯ Very low	CRITICAL
Breast conserving surgery (long case accrual; age 70-74 years) (follow-up: 8 years) (assessed with: standardised percentage)												
1[5]	non-randomised study	serious[i]	not serious	very serious[j]	not serious	none	Standardised percentage (95% CI) • Screened: 52.6% (51.8%, 53.4%) • Non-screened: 36.5% (35.2, 38.0%)				⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast conserving surgery (long case accrual; age ≥75 years) (follow-up: 8 years (assessed with: standardised percentage)												
1[5]	non-randomised study	serious[i]	not serious	very serious[j]	not serious	none	Standardised percentage (95% CI) • Screened: 48.8% (47.9%, 49.5%) • Non-screened: 32.6% (31.5%, 33.8%)				⊕◯◯◯ Very low	CRITICAL
Mastectomy (long case accrual; age 70-74 years) (follow-up: 8 years) (assessed with: standardised percentage)												
1[5]	non-randomised study	serious[i]	not serious	very serious[j]	not serious	none	Standardised percentage (95% CI) Simple mastectomy: • Screened: 11.3% (10.8,% 11.8%) • Non-screened: 10.4% (9.5%, 11.3%) Radical mastectomy: • Screened: 13.9% (13.4%, 14.5%) • Non-screened: 18.2% (17.0%, 19.4%)				⊕◯◯◯ Very low	CRITICAL
Mastectomy (long case accrual; age ≥75 years) (follow-up: 8 years) (assessed with: standardised percentage)												
1[5]	non-randomised study	serious[i]	not serious	very serious[j]	not serious	none	Standardised percentage (95% CI) Simple mastectomy: • Screened: 10.8% (10.3,% 11.2%) • Non-screened: 10.1% (9.4%, 10.9%) Radical mastectomy: • Screened: 14.2% (13.7%, 14.6%) • Non-screened: 17.0% (16.0%, 17.9%)				⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage II (short case accrual; age 70-74 years) (follow-up: median 13.7 years) (assessed with: cumulative incidence rate per 100 women)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
1[1]	non-randomised study	very serious[d]	not serious	very serious[j]	not serious	none	Localised invasive (stage II), adjusted cumulative incidence per 100 women (95% CI): • Screened: 3.84 (3.58, 4.11) • Non-screened: 2.56 (2.05, 3.20)				⊕◯◯◯ Very low	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
Breast cancer staging, stage II (short case accrual; age 75-84 years) (follow-up: median 10 years) (assessed with: cumulative incidence rate per 100 women)												
1[1]	non-randomised study	very serious[d]	not serious	very serious[j]	not serious	none	Localised invasive (stage II), adjusted cumulative incidence per 100 women (95% CI): • Screened: 3.15 (2.95, 3.38) • Non-screened: 1.50 (1.21, 1.86)				⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage III and IV (short case accrual; age 70-74 years) (follow-up: median 13.7 years) (assessed with: cumulative incidence rate per 100 women)												
1[1]	non-randomised study	very serious[d]	not serious	very serious[j]	not serious	none	Regional/distant (stage III/IV), adjusted cumulative incidence per 100 women (95% CI): • Screened: 1.00 (0.85, 1.17) • Non-screened: 0.90 (0.61, 1.34)				⊕◯◯◯ Very low	CRITICAL
Breast cancer staging, stage III and IV (short case accrual; age 75-84 years) (follow-up: median 10 years) (assessed with: cumulative incidence per 100 women)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	mammography	no screening	Relative (95% CI)	Absolute (95% CI)		
1[1]	non-randomised study	very serious[d]	not serious	very serious[j]	not serious	none	Regional/distant (stage III/IV), adjusted cumulative incidence per 100 women (95% CI): • Screened: 0.78 (0.66, 0.92) • Non-screened: 0.74 (0.55, 1.00)				⨁◯◯◯ Very low	CRITICAL
Breast cancer staging, stage III and higher (long case accrual; all ages) (follow-up: median 7.5 to 8.4 years) (assessed with: n/N)												
1[4]	non-randomised study	serious[o]	not serious	very serious[p]	not serious	none	14358/6125603 (0.23%)	13208/7201265 (0.18%)	**RR 1.28** (1.25 to 1.31)	**1 more per 1,000** (from 0 fewer to 1 more)	⨁◯◯◯ Very low	CRITICAL
Breast cancer staging, stage IV (long case accrual; all ages) (follow-up 7.5 to 8.4 years) (assessed with: n/N)												
1[4]	non-randomised study	serious[o]	not serious	very serious[p]	not serious	none	1325/6125603 (0.02%)	2213/7201265 (0.03%)	**RR 0.70** (0.66 to 0.75)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	CRITICAL

*rounded to nearest whole number

***Explanations*:**

a. Retrospective study (n=2).

b. Risk level not reported; mammography type (n=2) and number of screening rounds (n=1) not reported.

c. Outcome is a rare event.

d. Retrospective study; study population is a select group of participants (n=1; sample of Medicare beneficiaries in the USA; unclear whether sample is random).

e. Risk level not reported; mammography type not reported.

f. Retrospective study (n=1); inadequate follow-up of participants (n=1).

g. Magnitude of statistical heterogeneity is high.

h. Risk level not reported (n=2); used film and digital mammography (n=2); number of screening rounds not reported (n=1).

i. Retrospective study.

j. Risk level not reported; mammography type and number of screening rounds not reported.

k. Retrospective study (n=2); inadequate follow-up length for outcome to occur (n=1).

l. Point estimates vary widely; insufficient overlap between confidence intervals (not all confidence intervals overlap at least one point estimate); magnitude of statistical heterogeneity is high.

m. Study population is a select group of participants (n=1; sample of Medicare beneficiaries in the USA; unclear whether sample is random); risk level not reported (n=2); mammography type (n=1) and number of screening rounds (n=1) not reported.

n. Pooled estimate has wide confidence interval.

o. Inadequate follow-up of participants.

p. Risk level not reported; used film and digital mammography.

CI: confidence interval; **HR:** hazard ratio; **NR:** not reported**; RD:** risk difference; **RR:** risk ratio

References

1. Richman IB, Long JB, Soulos PR, Wang SY, Gross CP. Estimating breast cancer overdiagnosis after screening mammography among older women in the United States. *Ann Intern Med* 2023;176(9):1172-80.

2. Dunn N, Youl P, Moore J, Harden H, Walpole E, Evans E, Taylor K, Philpot S, Furnival C. Breast-cancer mortality in screened versus unscreened women: Long-term results from a population-based study in Queensland, Australia. *J Med Screen* 2021;28(2):193-9.

3. Morrell S, Taylor R, Roder D, Robson B, Gregory M, Craig K. Mammography service screening and breast cancer mortality in New Zealand: a national cohort study 1999-2011. *Br J Cancer* 2017;116(6):828-39.

4. Choi E, Jun JK, Suh M, Jung KW, Park B, Lee K, Jung SY, Lee ES, Choi KS. Effectiveness of the Korean National Cancer Screening Program in reducing breast cancer mortality. *NPJ Breast Cancer* 2021;7(1):83.

5. García-Albéniz X, Hernán MA, Hsu J. Continuation of annual screening mammography and breast cancer mortality in women older than 70 years. *Ann Intern Med* 2020;173(3):247.

6. Czwikla J, Giersiepen K, Langner I, Enders D, Heinze F, Rothgang H, Haug U, Zeeb H, Hense HW. A cohort study of mammography screening finds that comorbidity measures are insufficient for controlling selection bias. *J Clin Epidemiol* 2018;104:1-7.