

Supplementary Materials to the article
«Cardiovascular outcomes in breast cancer survivors: systematic review and meta-analysis.»

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Appendix. Supplementary search strategy.

PubMed

#1 - (("Cardiovascular Diseases"[Mesh] OR "Coronary Thrombosis"[Mesh] OR "Myocardial Revascularization"[Mesh] OR "Coronary Stenosis"[Mesh] OR "Acute Coronary Syndrome"[Mesh] OR "Coronary Artery Disease"[Mesh] OR "Coronary Disease"[Mesh] OR "Myocardial Infarction"[Mesh] OR "angina, stable"[Mesh] OR "Myocardial Ischemia"[Mesh] OR "Heart Failure"[Mesh] OR "Atrial Fibrillation"[Mesh] OR "Stroke"[Mesh] OR "Stroke, Lacunar"[Mesh] OR "Hemorrhagic Stroke"[Mesh] OR "Embolic Stroke"[Mesh] OR "Thrombotic Stroke"[Mesh] OR "Ischemic Stroke"[Mesh] OR "Death, Sudden, Cardiac"[Mesh] OR "Heart Arrest"[Mesh] OR "acute coronary syndrome"[Title/Abstract] OR "chronic coronary syndrome"[Title/Abstract] OR "coronary artery disease"[Title/Abstract] OR "Myocardial Infarction"[Title/Abstract] OR "ischemic heart disease"[Title/Abstract] OR "ischaemic heart disease"[Title/Abstract] OR "percutaneous coronary intervention"[Title/Abstract] OR "unstable angina"[Title/Abstract] OR "stable angina"[Title/Abstract] OR "Intracranial bleeding"[Title/Abstract] OR "hemorrhagic stroke"[Title/Abstract])

#2 - (("Incidence"[Mesh] OR "Epidemiology"[Mesh] OR "epidemiology"[Subheading] OR "Cohort Studies"[Mesh] OR "Follow-Up Studies"[Mesh] OR "Follow-Up Studies"[Mesh] OR "Kaplan-Meier Estimate"[Mesh] OR "Proportional Hazards Models"[Mesh] OR "Heart Disease Risk Factors"[Mesh] OR "Risk Factors"[Mesh] OR "Cardiometabolic Risk Factors"[Mesh] OR "Prospective Studies"[Mesh] OR "Risk"[Mesh] OR "Survival Analysis"[Mesh] OR "Survival Rate"[Mesh] OR "Longitudinal Studies"[Mesh] OR "Risk Assessment"[Mesh] OR "Cause of Death"[Mesh] OR "Mortality"[Mesh] OR "Causality"[Majr] OR "Registries"[Mesh] OR "National Program of Cancer Registries"[Mesh] OR "Prognosis"[Mesh]) OR (incident[Title/Abstract] OR incidence[Title/Abstract] OR "general population"[Title/Abstract] OR "population based"[Title/Abstract] OR epidemiol*[Title/Abstract] OR registr*[Title/Abstract] OR "primary care"[Title/Abstract] OR "long-term prognos*"[Title/Abstract] OR "long-term outcom*"[Title/Abstract] OR "long-term surviv*"[Title/Abstract] OR "long-term adverse outcom*"[Title/Abstract] OR "long term prognos*"[Title/Abstract] OR "long term outcom*"[Title/Abstract] OR "long term adverse outcom*"[Title/Abstract] OR "long term surviv*"[Title/Abstract] OR "cardiovascular outcom*"[Title/Abstract] OR "cardio-vascular outcom*"[Title/Abstract] OR "cardiac outcom*"[Title/Abstract] OR "cerebral outcom*"[Title/Abstract] OR "cerebrovascular outcom*"[Title/Abstract] OR "thrombotic outcom*"[Title/Abstract] OR "ischemic outcom*"[Title/Abstract] OR "ischaemic outcom*"[Title/Abstract] OR "cardiovascular endpoint*"[Title/Abstract] OR "cardiac endpoint*"[Title/Abstract] OR "cerebrovascular endpoint*"[Title/Abstract] OR "thrombotic endpoint*"[Title/Abstract] OR "ischaemic endpoint*"[Title/Abstract] OR "ischemic endpoint*"[Title/Abstract] OR "cardiovascular end point*"[Title/Abstract] OR "cardiac end point*"[Title/Abstract] OR "cerebrovascular endpoint*"[Title/Abstract] OR "cerebrovascular end point*"[Title/Abstract] OR "ischaemic end point*"[Title/Abstract] OR "ischemic end point*"[Title/Abstract] OR "cardiovascular end- point*"[Title/Abstract] OR "cardiac end-point*"[Title/Abstract] OR "cerebrovascular end- point*"[Title/Abstract] OR "ischaemic end-point*"[Title/Abstract] OR "ischemic end-point*"[Title/Abstract] OR "cardiovascular complication*"[Title/Abstract] OR "cardio-vascular complication*"[Title/Abstract] OR "cardiac complication*"[Title/Abstract] OR "cerebral complication*"[Title/Abstract] OR "cerebrovascular complication*"[Title/Abstract] OR "cerebro-vascular complication*"[Title/Abstract] OR "thrombotic complication*"[Title/Abstract] OR "ischaemic complication*"[Title/Abstract] OR "ischemic complication*"[Title/Abstract] OR "adverse cardiac event*"[Title/Abstract] OR "adverse cardiovascular event*"[Title/Abstract] OR "adverse cardio-vascular event*"[Title/Abstract] OR

"cerebral event"[Title/Abstract] OR "cerebrovascular event"[Title/Abstract] OR "survival analys*"[Title/Abstract] OR "kaplan meir curve*"[Title/Abstract] OR "kaplan meir analys*"[Title/Abstract] OR "kaplan meir surviv*"[Title/Abstract] OR "proportional hazard model*"[Title/Abstract] OR "cardiovascular death"[Title/Abstract] OR "cardio-vascular death"[Title/Abstract] OR "cardiac death"[Title/Abstract] OR "cardiovascular risk"[Title/Abstract] OR "cardio-vascular risk"[Title/Abstract] OR "cerebrovascular risk"[Title/Abstract] OR "cerebro-vascular risk"[Title/Abstract] OR "atherothrombotic risk"[Title/Abstract] OR "thrombotic risk"[Title/Abstract] OR "ischemic risk"[Title/Abstract] OR "ischaemic risk"[Title/Abstract] OR "Mortality"[Title/Abstract]))

#3 - (("Breast Neoplasms"[Mesh] OR "Triple Negative Breast Neoplasms"[Mesh] OR "Inflammatory Breast Neoplasms"[Mesh] OR "Breast Neoplasms, Male"[Mesh] OR "Breast Cancer Lymphedema"[Mesh] OR "Unilateral Breast Neoplasms"[Mesh] OR "Carcinoma, Intraductal, Noninfiltrating"[Mesh] OR "Carcinoma, Ductal, Breast"[Mesh] OR "Carcinoma, Lobular"[Mesh] OR "Paget's Disease, Mammary"[Mesh] OR "Mastectomy, Simple"[Mesh] OR "Mastectomy"[Mesh] OR "Mastectomy, Subcutaneous"[Mesh] OR "Mastectomy, Extended Radical"[Mesh] OR "Mastectomy, Radical"[Mesh] OR "Mastectomy, Modified Radical"[Mesh] OR "Mastectomy, Segmental"[Mesh] OR "ductal carcinoma in situ"[Title/Abstract]) OR ((breast[Title/Abstract] OR breasts[Title/Abstract] OR mamma[Title/Abstract] OR mamma*[Title/Abstract] OR ductal[Title/Abstract] OR lobular[Title/Abstract] OR "Breast"[Mesh] OR "Mammary Glands, Human"[Mesh]) AND (carcino*[Title/Abstract] OR tumor[Title/Abstract] OR tumor*[Title/Abstract] OR tumour[Title/Abstract] OR tumour*[Title/Abstract] OR malignanc*[Title/Abstract] OR neoplasm[Title/Abstract] OR neoplasms[Title/Abstract] OR neoplasms[Mesh Terms] OR oncol*[Title/Abstract])))

#1 AND #2 AND #3

Scopus

#1 - ((TITLE-ABS-KEY ((breast OR breasts OR mamma OR mamma* OR ductal OR lobular) W/3 (carcino* OR tumor OR tumor* OR tumour OR tumour* OR malignanc* OR neoplasm OR oncol*)) OR TITLE-ABS-KEY (carcino* W/1 (intraductal OR ductal OR lobular)) OR TITLE-ABS-KEY ("paget's disease" OR "mastectomy")))

#2 - (TITLE-ABS-KEY ("cardiovascular diseases" OR "Myocardial Revascularization" OR "myocardial infarction" OR "acute coronary syndrome" OR "coronary artery disease" OR "ischemic heart disease" OR "ischaemic heart disease" OR "chronic coronary syndrome" OR "stable angina" OR "unstable angina" OR "Coronary Thrombosis" OR "Coronary Stenosis" OR "hemorrhagic stroke" OR "ischemic stroke" OR "stroke" OR "intracranial bleeding" OR "heart failure" OR "atrial fibrillation" OR "cardiac death" OR "percutaneous coronary intervention" OR arrhythmia))

#3 - ((TITLE-ABS-KEY (incident OR incidence OR "general population" OR "population based" OR epidemiol* OR registr* OR "primary care") OR TITLE-ABS-KEY (long-term PRE/1 (prognosis OR outcome OR survival)) OR TITLE-ABS-KEY ((cardiovascular OR cardio-vascular OR cardiac OR cerebral OR cerebrovascular OR cerebro-vascular OR atherothrombotic OR athero-thrombotic OR atherothromb* OR athero-thromb* OR thrombotic OR thrombo* OR ischemic OR ischaemic OR arrhythm*) PRE/1 (outcome OR endpoint OR complication OR end-point OR "end point" OR event OR occurrence OR onset)) OR TITLE-ABS-KEY ((cardiovascular OR cardio-vascular OR cardiac OR cerebral OR cerebrovascular OR cerebro-vascular OR atherothrombotic OR athero-thrombotic OR

atherothromb* OR athero-thromb* OR thrombotic OR thrombo* OR ischemic OR ischaemic OR arrhythm*) W/2 risk) OR TITLE-ABS-KEY ((cardiovascular OR cardio-vascular OR cardiac OR cerebral OR cerebrovascular OR cerebro-vascular OR atherothrombotic OR athero-thrombotic OR atherothromb* OR athero-thromb* OR thrombotic OR thrombo* OR ischemic OR ischaemic OR arrhythm*) W/2 death) OR TITLE-ABS-KEY (proportional PRE/1 hazard PRE/1 (model OR analysis)) OR TITLE-ABS-KEY ("kaplan-meir" PRE/2 (curve OR analysis)) OR TITLE-ABS-KEY (survival PRE/0 (analysis OR rate))) OR TITLE-ABS-KEY (mortality))

#1 AND #2 AND #3

Web of Science

Query #1

((TS=((breast OR breasts OR mamma OR mamma* OR ductal OR lobular) NEAR/4 (carcino* OR tumor OR tumor* OR tumour OR tumour* OR malignanc* OR neoplasm OR oncol*))) OR TS=(carcino* NEAR/1 (intraductal OR ductal OR lobular))) OR TS=("paget's disease" OR "mastectomy")

Query #2

TS=("cardiovascular diseases" OR "heart diseases" OR "cardiac diseases" OR "Myocardial Revascularization" OR "myocardial infarction" OR "acute coronary syndrome" OR "coronary artery disease" OR "ischemic heart disease" OR "ischaemic heart disease" OR "chronic coronary syndrome" OR "stable angina" OR "unstable angina" OR "Coronary Thrombosis" OR "Coronary Stenosis" OR "hemorrhagic stroke" OR "ischemic stroke" OR "stroke" OR "intracranial bleeding" OR "heart failure" OR "atrial fibrillation" OR "cardiac death" OR "percutaneous coronary intervention" OR arrhythmia)

Query #3

(((((TS=(incident OR incidence OR "general population" OR "population based" OR epidemiol* OR registr* OR "primary care")) OR TS=(long-term NEAR/1 ((prognos* OR outcom* OR surviv*) OR (prognosis OR outcome OR survival)))) OR TS=((cardiovascular OR cardio-vascular OR cardiac OR cerebral OR cerebrovascular OR cerebro-vascular OR atherothromb* OR atherothrombotic OR athero-thromb* OR thromb* OR thrombotic OR isch\$emic OR ischemic OR arrhythm*) NEAR/2 (outcom* OR outcome OR endpoint* OR endpoint OR end-pont* OR end-pont OR complicat* OR complication OR event OR occurrence OR onset))) OR TS=((cardiovascular OR cardio-vascular OR cardiac OR cerebral OR cerebrovascular OR cerebro-vascular OR atherothromb* OR atherothrombotic OR athero-thromb* OR thromb* OR thrombotic OR isch\$emic OR ischemic OR arrhythm*) NEAR/2 risk)) OR TS=((cardiovascular OR cardio-vascular OR cardiac OR cerebral OR cerebrovascular OR cerebro-vascular OR atherothromb* OR atherothrombotic OR athero-thromb* OR thromb* OR thrombotic OR isch\$emic OR ischemic OR arrhythm*) NEAR/2 death)) OR TS=(mortality)) OR TS=((proport* OR proportional) NEAR/1 (hazard* OR hazard) NEAR/1 (model* OR model OR analys\$s OR analysis))) OR TS=(kaplan-meir NEAR/2 (curve* OR analys\$s OR curve OR analysis))

Query #4

#1 AND #2 AND #3

Supplementary Tables.

Table S1. Search strategy in additional sources and its results.

Name	Last search date	Search strategy	Number of results
Registries			
ClinicalTrials.gov, https://clinicaltrials.gov/	13/03/2022	breast cancer AND ("cardiovascular death" OR "myocardial infarction" OR "heart failure" OR "atrial fibrillation" OR "stroke" AND Adult, Older Adult)	107
The Australian New Zealand Clinical Trials Registry, https://www.anzctr.org.au/	13/03/2022	"Breast cancer" AND "cardiovascular disease"	104
The European Union Clinical Trials Register, https://www.clinicaltrialsregister.eu/	13/03/2022	"Breast Cancer" AND "cardiovascular disease"	7
German Clinical Trial Registry, https://www.drks.de/	13/03/2022	"breast cancer" AND "cardiovascular disease"	13
Japan Primary Registries Network, https://rctportal.niph.go.jp/	13/03/2022	"breast cancer AND cardiovascular disease"	1
Clinical Research Information Service, Republic of Korea, https://cris.nih.go.kr/cris/	13/03/2022	"breast cancer"	116
Peruvian Clinical Trial Registry, https://ensayosclnicos-repec.ins.gob.pe/en/	13/03/2022	"breast cancer"	128
Brazilian Registry of Clinical Trials http://www.ensaiosclinicos.gov.br/	13/03/2022	"breast cancer"	97
International Standard Randomised Controlled Trial Number registry,	13/03/2022	"breast cancer" AND "cardiovascular disease"	20

https:// www.isrctn.com/			
Journal websites			
Journal of clinical oncology, https:// ascopubs.org/ journal/jco	14/03/2022	"breast cancer" AND "cardiovascular disease"	456
Cancer, https:// acsjournals.onlineli brary.wiley.com/ journal/10970142	14/03/2022	"breast cancer" AND "cardiovascular disease"	375
Journal of the National Cancer Institute, https:// academic.oup.com/ jnci	14/03/2022	"breast cancer" AND "cardiovascular disease". Article type: Research Article Published: After January 1990	333
Breast cancer research and treatment, https:// www.springer.com/ journal/10549	14/03/2022	"breast cancer" AND "cardiovascular disease". 1990-2022	394
Annals of oncology, https:// www.annalsofoncol ogy.org/	14/03/2022	"breast cancer" AND "cardiovascular disease". Filters: Research article.	102
European Journal of Cancer, https:// www.ejancer.com/	14/03/2022	"breast cancer" AND "cardiovascular disease". Filters: Research article. 1990-2022	202
European Heart Journal, https:// academic.oup.com/ eurheartj	14/03/2022	"breast cancer". Format: Journal Article. Article type: Research Article	193
BMC cancer, https:// bmccancer.biomedc entral.com/	14/03/2022	"breast cancer" AND "cardiovascular disease"	267
The Breast, https:// www.thebreastonlin e.com/	14/03/2022	"breast cancer" AND "cardiovascular disease". Filters: Research article.	88
Lancet Oncology, https:// www.thelancet.com	14/03/2022	"breast cancer" AND "cardiovascular disease". Filters: Research article.	48

/journals/lanonc/home			
Other sources			
Biomed Explorer, https://sites.research.google/biomedexplorer/	14/03/2022	What is the risk of cardiovascular disease in breast cancer patients?	100
Dimensions, https://app.dimensions.ai/	14/03/2022	"breast cancer" AND "cardiovascular disease". Publication type: Article	500
Conferences from the European Society of Cardiology, https://esc365.escardio.org/	14/03/2022	"breast cancer"	349
SnowGlobe website, https://snowglobe.soc.northwestern.edu/	15/03/2022	Citations related to the included publications	320
CoCites tool, https://www.cocites.com/	15/03/2022	Citations related to the included publications	850
Connected Papers, https://www.connectedpapers.com/	15/03/2022	Citations related to the included publications	300

Table S2. Some potentially relevant studies for the meta-analysis and reasons for exclusion.

First author, year	Citation	Reasons for exclusion
Advani PP, 2015	Advani PP, Ballman KV, Dockter TJ, Colon-Otero G, Perez EA. Long-Term Cardiac Safety Analysis of NCCTG N9831 (Alliance) Adjuvant Trastuzumab Trial. J Clin Oncol. 2016 Feb 20;34(6):581-7. doi: 10.1200/JCO.2015.61.8413. Epub 2015 Sep 21.	The study was performed on the same cohort of patients that has already been included in the meta-analysis
Asdahl PH, 2021	Asdahl PH, Sundbøll J, Adelborg K, et al. Cardiovascular events in cancer patients with bone metastases-A Danish population-based cohort study of 23,113	The study population was diagnosed with breast cancer in a period from 1978 to 2013

	patients. Cancer Med. 2021;10(14):4885-4895. doi:10.1002/cam4.4027	
Ben Kridis W, 2020	Ben Kridis W, Sghaier S, Charfeddine S, et al. Prospective Study About Trastuzumab-induced Cardiotoxicity in HER2-positive Breast Cancer. Am J Clin Oncol. 2020 Jul;43(7):510-516. doi: 10.1097/COC.0000000000000699.	Median follow-up was not reported.
Berkman A, 2014	Berkman A, F Cole B, Ades PA, et al. Racial differences in breast cancer, cardiovascular disease, and all-cause mortality among women with ductal carcinoma in situ of the breast. Breast Cancer Res Treat. 2014;148(2):407-413. doi:10.1007/s10549-014-3168-3	Median follow-up was not reported for the cohort of patients enrolled after 1990.
Chang W, 2021	Chang WT, Chen PW, Lin HW, Lin SH, Li YH. Risks of trastuzumab-related cardiotoxicity in breast cancer patients in Taiwan. ESC Heart Fail. 2021;8(6):5149-5158. doi:10.1002/ehf2.13591	The median follow-up was not clearly reported. The study was conducted on the cohort that was already included in the meta-analysis.
Chapman JA, 2016	Chapman JA, Shepherd LE, Ingle JN, et al. Competing risks of death in women treated with adjuvant aromatase inhibitors for early breast cancer on NCIC CTG MA.27. Breast Cancer Res Treat. 2016;156(2):343-349. doi:10.1007/s10549-016-3761-8	Some patients were randomized to treatment with celecoxib which then was discontinued due to cardiac toxicity
Chavez-MacGregor M, 2013	Chavez-MacGregor M, Zhang N, Buchholz TA, et al. Trastuzumab-related cardiotoxicity among older patients with breast cancer. J Clin Oncol. 2013;31(33):4222-4228. doi:10.1200/JCO.2013.48.7884	The median follow-up was not reported

Chen J, et al	Chen J, Long JB, Hurria A, Owusu C, Steingart RM, Gross CP. Incidence of heart failure or cardiomyopathy after adjuvant trastuzumab therapy for breast cancer. J Am Coll Cardiol. 2012 Dec 18;60(24):2504-12. doi: 10.1016/j.jacc.2012.07.068.	The reported data were not adequate for conducting the meta-analysis
de Azambuja E, 2014	de Azambuja E, Procter MJ, van Veldhuisen DJ, et al. Trastuzumab-associated cardiac events at 8 years of median follow-up in the Herceptin Adjuvant trial (BIG 1-01). J Clin Oncol. 2014 Jul 10;32(20):2159-65. doi: 10.1200/JCO.2013.53.9288. Epub 2014 Jun 9.	The study was performed on the same cohort of patients that has already been included in the meta-analysis
Doyle JJ, 2005	Doyle JJ, Neugut AI, Jacobson JS, Grann VR, Hershman DL. Chemotherapy and cardiotoxicity in older breast cancer patients: a population-based study. J Clin Oncol. 2005 Dec 1;23(34):8597-605. doi: 10.1200/JCO.2005.02.5841. PMID: 16314622.	Median follow-up was not reported
Du XL, 2008	Du XL, Fox EE, Lai D. Competing causes of death for women with breast cancer and change over time from 1975 to 2003. Am J Clin Oncol. 2008;31(2):105-116. doi:10.1097/COC.0b013e318142c865	The study population were enrolled in a period from 1975 to 2003
Du XL, 2016	Du XL, Zhang Y, Hardy D. Associations between hematopoietic growth factors and risks of venous thromboembolism, stroke, ischemic heart disease and myelodysplastic syndrome: findings from a large population-based cohort of women with breast cancer. Cancer Causes	The median follow-up was not reported. The incidence rates were provided without confidence intervals.

	Control. 2016 May;27(5):695-707. doi: 10.1007/s10552-016-0742-5. Epub 2016 Apr 8. PMID: 27059219.	
Earl HM, 2016	Earl HM, Vallier AL, Dunn J, et al. Trastuzumab-associated cardiac events in the Persephone trial. Br J Cancer. 2016;115(12):1462-1470. doi:10.1038/bjc.2016.357	The overall median follow-up was not reported
Forbes JF, 2016	Forbes JF, Sestak I, Howell A, et al. Anastrozole versus tamoxifen for the prevention of locoregional and contralateral breast cancer in postmenopausal women with locally excised ductal carcinoma in situ (IBIS-II DCIS): a double-blind, randomised controlled trial. Lancet. 2016;387(10021):866-873. doi:10.1016/S0140-6736(15)01129-0	The study did not provided utilized definitions for reporting of adverse cardiovascular events. If the study follow Common Terminology Criteria for Adverse Events, then asymptomatic and symptomatic events were combined
Gegechkori N, 2019	Gegechkori N, Egorova N, Mhango G, Wisnivesky JP, Lin JJ. Bisphosphonate use and incident cardiovascular events among older breast cancer survivors. Breast. 2019 Oct;47:28-32. doi: 10.1016/j.breast.2019.06.006.	The median follow-up was not reported
Gianni L, 2001	Gianni L, Dombernowsky P, Sledge G, et al. Cardiac function following combination therapy with paclitaxel and doxorubicin: an analysis of 657 women with advanced breast cancer. Ann Oncol. 2001 Aug;12(8):1067-73. doi: 10.1023/a:1011655503511. PMID: 11583187.	The overall median follow-up was not reported
Gong IY, 2016	Gong IY, Verma S, Yan AT, et al. Long-term cardiovascular outcomes and overall survival of early-stage breast cancer patients with early discontinuation of trastuzumab: a	The primary endpoint of the study combined heart failure with all-cause mortality

	population-based study. Breast Cancer Res Treat. 2016 Jun;157(3):535-44. doi: 10.1007/s10549-016-3823-y. Epub 2016 Jun 6. PMID: 27271767.	
Goss PE, 2005	Goss PE, Ingle JN, Martino S. Randomized Trial of Letrozole Following Tamoxifen as Extended Adjuvant Therapy in Receptor-Positive Breast Cancer: Updated Findings from NCIC CTG MA.17. JNCI: Journal of the National Cancer Institute. 2005;97(17):1262–1271' doi:10.1093/jnci/dji250	The grades for cardiovascular adverse events were not provided. The study provided outcomes that combined symptomatic and asymptomatic endpoints
Guo A, 2020	Guo A, Zhang KW, Reynolds K, Foraker RE. Coronary heart disease and mortality following a breast cancer diagnosis. BMC Med Inform Decis Mak. 2020;20(1):88. Published 2020 May 13. doi:10.1186/s12911-020-1127-y	Median follow-up was not reported
Haque R, 2009	Haque R, Yood MU, Geiger AM, et al. Long-term safety of radiotherapy and breast cancer laterality in older survivors. Cancer Epidemiol Biomarkers Prev. 2011;20(10):2120-2126. doi:10.1158/1055-9965.EPI-11-0348	The reported study outcomes combined some endpoints that were not of interest for our meta-analysis.
Harlan, 2009	Harlan LC, Klabunde CN, Ambbs AH, et al. Comorbidities, therapy, and newly diagnosed conditions for women with early stage breast cancer. J Cancer Surviv. 2009;3(2):89-98. doi:10.1007/s11764-009-0084-3	Median follow-up was not reported
Henry ML, 2018	Henry ML, Niu J, Zhang N, Giordano SH, Chavez-MacGregor M. Cardiotoxicity and Cardiac Monitoring Among Chemotherapy-	The study provided outcomes that combined symptomatic and asymptomatic endpoints

	Treated Breast Cancer Patients. JACC Cardiovasc Imaging. 2018 Aug;11(8):1084-1093. doi: 10.1016/j.jcmg.2018.06.005. PMID: 30092967; PMCID: PMC6149535.	
Henson KE, 2016	Henson KE, Reulen RC, Winter DL, et al. Cardiac Mortality Among 200 000 Five-Year Survivors of Cancer Diagnosed at 15 to 39 Years of Age: The Teenage and Young Adult Cancer Survivor Study. Circulation. 2016 Nov 15;134(20):1519-1531. doi: 10.1161/CIRCULATIONAHA.116.022514. Epub 2016 Nov 7.	The study did not provide sufficient data for conducting statistical analyses
Hernandez K, 2008	Rohini K. Hernandez, Henrik Toft Sørensen, Jacob Jacobsen, Lars Pedersen, Timothy L. Lash; Tamoxifen Treatment in Danish Breast Cancer Patients and 5-Year Risk of Arterial Atherosclerotic Events: A Null Association. Cancer Epidemiol Biomarkers Prev 1 September 2008; 17 (9): 2509–2511. https://doi.org/10.1158/1055-9965.EPI-08-0570	The median follow-up was not reported
Jacquin JP, 2020	Jacquin JP, Uwer L, Savignoni A, et al. Safety profile of subcutaneous trastuzumab in patients with HER2-positive early breast cancer: The French HERmione non-interventional prospective study. Breast. 2020;49:1-7. doi:10.1016/j.breast.2019.10.002	The study provided outcomes that combined symptomatic and asymptomatic left ventricle dysfunction
Jacobse JN, 2021	Jacobse JN, Schaapveld M, Boekel NB, Hooning MJ, Jager A, Baaijens MHA, Hauptmann M, Russell NS, Rutgers EJT, Aleman BMP, Sonke GS, van Leeuwen FE. Risk of heart	The study was performed on the same cohort of patients that has already been included in the meta-analysis

	failure after systemic treatment for early breast cancer: results of a cohort study. <i>Breast Cancer Res Treat.</i> 2021 Jan;185(1):205-214. doi: 10.1007/s10549-020-05930-w. Epub 2020 Sep 22.	
Jakobsen M, 2021	Jakobsen M, Kolodziejczyk C, Jensen MS, et al. Cardiovascular disease in women with breast cancer - a nationwide cohort study. <i>BMC Cancer.</i> 2021;21(1):1040. Published 2021 Sep 18. doi:10.1186/s12885-021-08716-5	The median follow-up was not reported
Joensuu H, 2018	Joensuu H, Fraser J, Wildiers H, et al. Effect of Adjuvant Trastuzumab for a Duration of 9 Weeks vs 1 Year With Concomitant Chemotherapy for Early Human Epidermal Growth Factor Receptor 2-Positive Breast Cancer: The SOLD Randomized Clinical Trial. <i>JAMA Oncol.</i> 2018;4(9):1199-1206. doi:10.1001/jamaoncol.2018.1380	The study provided outcomes that combined symptomatic and asymptomatic cardiac events
Jones LW, 2016	Jones LW, Habel LA, Weltzien E, et al. Exercise and Risk of Cardiovascular Events in Women With Nonmetastatic Breast Cancer. <i>J Clin Oncol.</i> 2016 Aug 10;34(23):2743-9. doi: 10.1200/JCO.2015.65.6603. Epub 2016 May 23.	The study was performed on the same cohort of patients that has already been included in the meta-analysis
Kaboré EG, et al	Kaboré EG, Guenancia C, Vaz-Luis I, et al. Association of body mass index and cardiotoxicity related to anthracyclines and trastuzumab in early breast cancer: French CANTO cohort study. <i>PLoS Med.</i> 2019 Dec 23;16(12):e1002989. doi: 10.1371/journal.pmed.1002989.	The study provided outcomes that combined symptomatic and asymptomatic endpoints

	PMID: 31869400; PMCID: PMC6927582.	
Khosrow-Khavar F, 2020	Khosrow-Khavar F, Bouganim N, Fillion KB, Suissa S, Azoulay L. Cardiotoxicity of Use of Sequential Aromatase Inhibitors in Women With Breast Cancer. <i>Am J Epidemiol</i> . 2020 Oct 1;189(10):1086-1095. doi: 10.1093/aje/kwaa065.	The study was performed on the same cohort of patients that has already been included in the meta-analysis
Kim DY, 2019	Kim DY, Youn JC, Park MS, et al. Cardiovascular outcome of breast cancer patients with concomitant radiotherapy and chemotherapy: A 10-year multicenter cohort study. <i>J Cardiol</i> . 2019 Aug;74(2):175-181. doi: 10.1016/j.jjcc.2019.02.001. Epub 2019 Mar 1.	The study was performed on the same cohort of patients that has already been included in the meta-analysis
Lawrenson, 2018	Lawrenson R, Lao C, Ali A, Campbell I. Impact of radiotherapy on cardiovascular health of women with breast cancer. <i>J Med Imaging Radiat Oncol</i> . 2019 Apr;63(2):250-256. doi: 10.1111/1754-9485.12838. Epub 2018 Dec 17. PMID: 30556371.	Median follow-up was not reported
Lee YC, 2015	Lee YC, Chuang JP, Hsieh PC, Chiou MJ, Li CY. A higher incidence rate of acute coronary syndrome following radiation therapy in patients with breast cancer and a history of coronary artery diseases. <i>Breast Cancer Res Treat</i> . 2015 Jul;152(2):429-35. doi: 10.1007/s10549-015-3481-5. Epub 2015 Jun 25. PMID: 26109348.	The reported study outcomes combined some endpoints that were not of interest for our meta-analysis.
Martin M, 2005	Martin M, Pienkowski T, Mackey J, et al. Breast Cancer International Research Group 001 Investigators.	The study was performed on the cohort of patients that was already included in the meta-analysis.

	Adjuvant docetaxel for node-positive breast cancer. N Engl J Med. 2005 Jun 2;352(22):2302-13. doi: 10.1056/NEJMoa043681. PMID: 15930421.	
Martinello R, 2019	Martinello R, Becco P, Vici P, et al. Trastuzumab-related cardiotoxicity in patients with nonlimiting cardiac comorbidity. Breast J. 2019 May;25(3):444-449. doi: 10.1111/tbj.13240. Epub 2019 Apr 1.	
Mery B, 2020	Mery B, Fouilloux A, Rowinski E, et al. Cardiovascular disease events within 5 years after a diagnosis of breast cancer. BMC Cancer. 2020;20(1):337. Published 2020 Apr 21. doi:10.1186/s12885-020-06838-w	The median follow-up was not reported
Mouridsen H, 2007	Mouridsen H, Keshaviah A, Coates AS, et al. Cardiovascular adverse events during adjuvant endocrine therapy for early breast cancer using letrozole or tamoxifen: safety analysis of BIG 1-98 trial. J Clin Oncol. 2007 Dec 20;25(36):5715-22. doi: 10.1200/JCO.2007.12.1665. Epub 2007 Nov 12.	The study was performed on the same cohort of patients that has already been included in the meta-analysis
Nichols HB, 2009	Nichols HB, Trentham-Dietz A, Egan KM, et al. Body mass index before and after breast cancer diagnosis: associations with all-cause, breast cancer, and cardiovascular disease mortality. Cancer Epidemiol Biomarkers Prev. 2009 May;18(5):1403-9. doi: 10.1158/1055-9965.EPI-08-1094. Epub 2009 Apr 14.	The study was performed on the same cohort of patients that has already been included in the meta-analysis
Nichols HB,	Nichols HB, Trentham-Dietz A,	The study was performed on the same

2013	Newcomb PA, Egan KM, Titus LJ, Hampton JM, Visvanathan K. Pre-diagnosis oophorectomy, estrogen therapy and mortality in a cohort of women diagnosed with breast cancer. Breast Cancer Res. 2013;15(5):R99. doi: 10.1186/bcr3560.	cohort of patients that has already been included in the meta-analysis
Nilsson G, 2005	Nilsson G, Holmberg L, Garmo H, Terent A, Blomqvist C. Increased incidence of stroke in women with breast cancer. Eur J Cancer. 2005 Feb;41(3):423-9. doi: 10.1016/j.ejca.2004.11.013.	The study did not provide sufficient data for a statistical analysis.
Nixon AJ, 1998	A J Nixon, J Manola, R Gelman, B Bornstein, A Abner, S Hetelekidis, A Recht, and J R Harris Journal of Clinical Oncology 1998 16:4, 1374-1379. doi: 10.1200/JCO.1998.16.4.1374	The study participants were enrolled in a period from 1968 to 1986
Oh CM, 2020	Oh CM, Lee D, Kong HJ, Lee S, Won YJ, Jung KW, Cho H. Causes of death among cancer patients in the era of cancer survivorship in Korea: Attention to the suicide and cardiovascular mortality. Cancer Med. 2020 Mar;9(5):1741-1752. doi: 10.1002/cam4.2813. Epub 2020 Jan 20.	The study did not provide sufficient data for conducting statistical analyses
Ording AG, 2013	Ording AG, Cronin-Fenton DP, Jacobsen JB, et al. Comorbidity and survival of Danish breast cancer patients from 2000-2011: a population-based cohort study. Clin Epidemiol. 2013;5(Suppl 1):39-46. Published 2013 Nov 1. doi:10.2147/CLEP.S47152	The study reported only all-cause mortality as an endpoint
Patnaik JL, 2011	Patnaik JL, Byers T, DiGuseppi C, Dabelea D, Denberg TD.	The number of patients with events was not reported

	Cardiovascular disease competes with breast cancer as the leading cause of death for older females diagnosed with breast cancer: a retrospective cohort study. Breast Cancer Res. 2011;13(3):R64. Published 2011 Jun 20. doi:10.1186/bcr2901	
Procter M, 2010	Procter M, Suter TM, de Azambuja E, et al. Longer-term assessment of trastuzumab-related cardiac adverse events in the Herceptin Adjuvant (HERA) trial. J Clin Oncol. 2010 Jul 20;28(21):3422-8. doi: 10.1200/JCO.2009.26.0463. Epub 2010 Jun 7.	The study was performed on the same cohort of patients that has already been included in the meta-analysis
Romond EH, 2005	Romond EH, Perez EA, Bryant J, et al. Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. N Engl J Med. 2005 Oct 20;353(16):1673-84. doi: 10.1056/NEJMoa052122. PMID: 16236738.	The study was performed on the cohort of patients that was already included in the meta-analysis.
Rosell J, 2013	Rosell J, Nordenskjöld B, Bengtsson NO, et al. Effects of adjuvant tamoxifen therapy on cardiac disease: results from a randomized trial with long-term follow-up. Breast Cancer Res Treat. 2013 Apr;138(2):467-73. doi: 10.1007/s10549-013-2457-6. Epub 2013 Mar 2. PMID: 23456195.	The majority of study participants were enrolled before 1990
Russell SD, 2010	Russell SD, Blackwell KL, Lawrence J, et al. Independent adjudication of symptomatic heart failure with the use of doxorubicin and cyclophosphamide followed by trastuzumab adjuvant therapy: a combined review of cardiac data	The study was performed on the same cohort of patients that has already been included in the meta-analysis

	from the National Surgical Adjuvant breast and Bowel Project B-31 and the North Central Cancer Treatment Group N9831 clinical trials. J Clin Oncol. 2010 Jul 20;28(21):3416-21. doi: 10.1200/JCO.2009.23.6950. Epub 2010 Jun 7. PMID: 20530275.	
Russo G, 2012	Russo G, Cioffi G, Di Lenarda A, et al. Role of renal function on the development of cardiotoxicity associated with trastuzumab-based adjuvant chemotherapy for early breast cancer. Intern Emerg Med. 2012 Oct;7(5):439-46. doi: 10.1007/s11739-012-0794-9. Epub 2012 Jun 20. PMID: 22714882.	Median follow-up was not reported
Schoormans D, et al	Schoormans D, van de Poll-Franse L, Vissers P, et al. Pharmaceutically treated anxiety but not depression prior to cancer diagnosis predicts the onset of cardiovascular disease among breast cancer survivors. Breast Cancer Res Treat. 2017;166(1):259-266. doi:10.1007/s10549-017-4387-1	The study defined its primary endpoint as prescribing of cardiovascular drugs. However, it is highly likely that the study primary endpoint combined some outcomes that were of no interest for our meta-analysis.
Seferina SC, 2016	Seferina SC, de Boer M, Derksen MW, et al. Cardiotoxicity and Cardiac Monitoring During Adjuvant Trastuzumab in Daily Dutch Practice: A Study of the Southeast Netherlands Breast Cancer Consortium. Oncologist. 2016 May;21(5):555-62. doi: 10.1634/theoncologist.2015-0230. Epub 2016 Mar 23	The study was performed on the same cohort of patients that has already been included in the meta-analysis
Shaffer R, et al, 2009	Shaffer R, Tyldesley S, Rolles M, Chia S, Mohamed I. Acute cardiotoxicity with concurrent trastuzumab and radiotherapy	The study was performed on the same cohort of patients that has already been included in the meta-analysis

	including internal mammary chain nodes: a retrospective single-institution study. <i>Radiother Oncol</i> . 2009 Jan;90(1):122-6. doi: 10.1016/j.radonc.2008.09.003. Epub 2008 Oct 29.	
Stokes EL, 2011	Stokes EL, Tyldesley S, Woods R, Wai E, Olivotto IA. Effect of nodal irradiation and fraction size on cardiac and cerebrovascular mortality in women with breast cancer treated with local and locoregional radiotherapy. <i>Int J Radiat Oncol Biol Phys</i> . 2011 Jun 1;80(2):403-9. doi: 10.1016/j.ijrobp.2010.02.041. Epub 2010 Jun 26.	The study was performed on the same cohort of patients that has already been included in the meta-analysis
Stoltzfus, 2020	Stoltzfus KC, Zhang Y, Sturgeon K, et al. Fatal heart disease among cancer patients. <i>Nat Commun</i> . 2020;11(1):2011. Published 2020 Apr 24. doi:10.1038/s41467-020-15639-5	The study did not provide effect estimates with 95% CI for breast cancer population separately.
Sukel MP, 2008	Sukel MP, Breckveldt-Postma NS, et al. Incidence of cardiovascular events in breast cancer patients receiving chemotherapy in clinical practice. <i>Pharmacoepidemiol Drug Saf</i> . 2008 Feb;17(2):125-34. doi: 10.1002/pds.1528.	The study was performed on the same cohort of patients that has already been included in the meta-analysis
Suter TM, 2007	Suter TM, Procter M, van Veldhuisen DJ, et al. Trastuzumab-associated cardiac adverse effects in the herceptin adjuvant trial. <i>J Clin Oncol</i> . 2007 Sep 1;25(25):3859-65. doi: 10.1200/JCO.2006.09.1611. Epub 2007 Jul 23.	The study was performed on the same cohort of patients that has already been included in the meta-analysis
Tan CH, 2016	Tan CH, Chao TT, Liu JC, et al. Breast cancer therapy and age	The study endpoint combined ischemic heart disease with heart failure

	<p>difference in cardiovascular disease risks: A population-based cohort study in Taiwan. Taiwan J Obstet Gynecol. 2016 Feb;55(1):98-103. doi: 10.1016/j.tjog.2015.12.005.</p>	
<p>Tan-Chiu, 2005</p>	<p>Tan-Chiu E, Yothers G, Romond E, et al. Assessment of cardiac dysfunction in a randomized trial comparing doxorubicin and cyclophosphamide followed by paclitaxel, with or without trastuzumab as adjuvant therapy in node-positive, human epidermal growth factor receptor 2-overexpressing breast cancer: NSABP B-31. J Clin Oncol. 2005 Nov 1;23(31):7811-9. doi: 10.1200/JCO.2005.02.4091. PMID: 16258083.</p>	<p>The study was performed on the same cohort of patients that has already been included in the meta-analysis</p>
<p>Thavendirana than P, 2018</p>	<p>Thavendiranathan P, Abdel-Qadir H, Fischer HD, et al. Risk-Imaging Mismatch in Cardiac Imaging Practices for Women Receiving Systemic Therapy for Early-Stage Breast Cancer: A Population-Based Cohort Study. J Clin Oncol. 2018 Oct 20;36(30):2980-2987. doi: 10.1200/JCO.2018.77.9736. Epub 2018 May 23. PMID: 29791284.</p>	<p>Median follow-up was not reported</p>
<p>Thürlimann B, 2005</p>	<p>Thürlimann B, Keshaviah A, Coates AS, et al. A comparison of letrozole and tamoxifen in postmenopausal women with early breast cancer. N Engl J Med. 2005 Dec 29;353(26):2747-57. doi: 10.1056/NEJMoa052258. Erratum in: N Engl J Med. 2006 May 18;354(20):2200. Wardly, Andrew [corrected to Wardley, Andrew].</p>	<p>The study was performed on the same cohort of patients that has already been included in the meta-analysis</p>

	PMID: 16382061.	
Tolaney SM, 2015	Tolaney SM, Barry WT, Dang CT, et al. Adjuvant paclitaxel and trastuzumab for node-negative, HER2-positive breast cancer. <i>N Engl J Med.</i> 2015 Jan 8;372(2):134-41. doi: 10.1056/NEJMoa1406281. Erratum in: <i>N Engl J Med.</i> 2015 Nov 12;373(20):1989.	The study was performed on the same cohort of patients that has already been included in the meta-analysis
van den Bogaard VA, et al, 2017	van den Bogaard VA, Ta BD, van der Schaaf A, et al. Validation and Modification of a Prediction Model for Acute Cardiac Events in Patients With Breast Cancer Treated With Radiotherapy Based on Three-Dimensional Dose Distributions to Cardiac Substructures. <i>J Clin Oncol.</i> 2017 Apr 10;35(11):1171-1178. doi: 10.1200/JCO.2016.69.8480. Epub 2017 Jan 17	The study was performed on the same cohort of patients that has already been included in the meta-analysis
van den Bogaard VAB, 2021	van den Bogaard VAB, Spoor DS, van der Schaaf A, et al. The Importance of Radiation Dose to the Atherosclerotic Plaque in the Left Anterior Descending Coronary Artery for Radiation-Induced Cardiac Toxicity of Breast Cancer Patients? <i>Int J Radiat Oncol Biol Phys.</i> 2021 Aug 1;110(5):1350-1359. doi: 10.1016/j.ijrobp.2021.03.004. Epub 2021 Mar 10.	The study was performed on the same cohort of patients that has already been included in the meta-analysis
von Minckwitz, 2014	von Minckwitz, M Rezai, P A Fasching, J Huober, et al. Survival after adding capecitabine and trastuzumab to neoadjuvant anthracycline-taxane-based chemotherapy for primary breast cancer (GBG 40—GeparQuattro).	Cardiovascular events were reported as adverse events, however the grades were not provided. It is highly likely that asymptomatic and symptomatic events were combined.

	Ann Oncol. 2014 Jan;25(1):81-9. doi: 10.1093/annonc/mdt410.	
Wang D, 2021	Wang D, Yi L, Zhang L, Wang Z. Cause-specific mortality among patients with different molecular subtypes of T1-2N0M0 breast cancer: A population-based study. Medicine (Baltimore). 2021 Oct 29;100(43):e27605. doi: 10.1097/MD.00000000000027605.	The study did not provide sufficient data for conducting statistical analyses
Wang T, 2020	Wang T, Bradshaw PT, Moorman PG, et al. Menopausal hormone therapy use and long-term all-cause and cause-specific mortality in the Long Island Breast Cancer Study Project. Int J Cancer. 2020 Dec 15;147(12):3404-3415. doi: 10.1002/ijc.33174.	The study was performed on the same cohort of patients that has already been included in the meta-analysis
Weberpals J, 2018	Weberpals J, Jansen L, Müller OJ, Brenner H. Long-term heart-specific mortality among 347 476 breast cancer patients treated with radiotherapy or chemotherapy: a registry-based cohort study. Eur Heart J. 2018 Nov 14;39(43):3896-3903. doi: 10.1093/eurheartj/ehy167.	The study did not provide sufficient data for conducting statistical analyses
Weiss A, 2013	Weiss A, Noorbakhsh A, Tokin C, Chang D, Blair SL. Hormone receptor-negative breast cancer: undertreatment of patients over 80. Ann Surg Oncol. 2013 Oct;20(10):3274-8. doi: 10.1245/s10434-013-3115-2. Epub 2013 Jul 10.	Median follow-up was not reported
Zardavas D, 2017	Zardavas D, Suter TM, Van Veldhuisen DJ, et al. Role of Troponins I and T and N-Terminal Prohormone of Brain Natriuretic Peptide in Monitoring Cardiac	This is a biomarker sub-study of the study that was already included in the meta-analysis

	<p>Safety of Patients With Early-Stage Human Epidermal Growth Factor Receptor 2-Positive Breast Cancer Receiving Trastuzumab: A Herceptin Adjuvant Study Cardiac Marker Substudy. <i>J Clin Oncol</i>. 2017 Mar 10;35(8):878-884. doi: 10.1200/JCO.2015.65.7916. Epub 2016 Oct 23. PMID: 28199174.</p>	
Zheng J, 2018	<p>Zheng J, Tabung FK, Zhang J, et al. Association between Post-Cancer Diagnosis Dietary Inflammatory Potential and Mortality among Invasive Breast Cancer Survivors in the Women's Health Initiative. <i>Cancer Epidemiol Biomarkers Prev</i>. 2018 Apr;27(4):454-463. doi: 10.1158/1055-9965.EPI-17-0569. Epub 2018 Jan 22.</p>	<p>The study was performed on the same cohort of patients that has already been included in the meta-analysis</p>
Yancik R, 2001	<p>Yancik R, Wesley MN, Ries LAG, Havlik RJ, Edwards BK, Yates JW. Effect of Age and Comorbidity in Postmenopausal Breast Cancer Patients Aged 55 Years and Older. <i>JAMA</i>. 2001;285(7):885–892. doi:10.1001/jama.285.7.885</p>	<p>Median follow-up was not reported</p>
Yood MU et al, 2012	<p>Yood MU, Wells KE, Alford SH, et al. Cardiovascular outcomes in women with advanced breast cancer exposed to chemotherapy. <i>Pharmacoepidemiol Drug Saf</i>. 2012;21(8):818-827. doi:10.1002/pds.3239</p>	<p>The reported outcomes included symptomatic as well as asymptomatic events</p>

Table S3. The baseline features of the included studies that estimated the incidence rates of cardiovascular endpoints in patients with breast cancer.

Author	Year	PMID	Country	FU, y	Study design	Sample size	Mean age, y	DM, %	Hypertension, %	Dyslipidemia, %	DCI S, %	Surgery, %	Chemotherapy, %	Radiation therapy, %
Batist[1]	2001	11230490	USA	1.67	RCT	297	54				0		100	36.1
Bonneterr e[2]	2004	15284257	France	8.5	RCT	150	59	4	22	5.3				97.33
Pagani[3]	2004	15550579	Multinational	5.5	RCT	1035					0	100	86.1	
Bradbury[4]	2005	15712362	UK	2.3	retrospective cohort	3030								
Guarnieri[5]	2006	16908934	USA	2.7	retrospective cohort	173	50	5.2			0			56.4
Jagsi[6]	2007	17238178	USA	6.8	retrospective cohort	834	55.7	7	38	25	0	100	39	100
Coates[7]	2007	17200148	Multinational	4.25	RCT	4922	61					100	25	68.5
Pinder[8]	2007	17664460	USA	4.67	retrospective cohort	43338	73.2	14.4	55.3		0	98.8	20	46.6
Ejlertsen[9]	2007	17306974	Denmark	10	RCT	1224					0	100	100	49

Testore[10]	2008	18690759	Italy	2.92	retrospective cohort	318	59				0		100	89.6
Extra[11]	2010	20671105	France	12.2	retrospective cohort	623	54		17		0	88	90	82
Untch[12]	2011	21788566	Germany	3.42	prospective cohort	217	48.5				0	100	100	
Park[13]	2011	21762242	USA	8.2	retrospective cohort	129	55.3				100	100		100
Appel[14]	2012	22909389	Denmark	12	RCT	980	48.2					100		64
Seiceanu[15]	2013	23425978	USA	3.2	retrospective cohort	318	56.6	12	38.7				100	58.5
Jacob[16]	2013	23499212	France	4.33	prospective cohort	173	52				0	98.3	100	100
Henson[17]	2013	23257897	USA		retrospective cohort	397740								45.98
Rugo[18]	2013	24062208	USA	2.25	prospective cohort	919	53	7.4	5.1					
Morris[19]	2013	24037735	USA	2	prospective cohort	165	46		17		0		100	
Martin[20]	2013	23733779	Spain	5.3	RCT	1925	50				0	100	100	
Goss[21]	2013	2335897	multinatio	4.1	RCT	7576	64.1				0	100	31	

		1	nal											
Mackey [22]	2013	23246022	multinatio nal	10.3	RCT	1491	49					100	100	70.5
Obi [23]	2014	24570215	Germany	5.78	retrospective cohort	2542	62.1	6. 6	37.4		6.4		45.8	78.7
Haque [24]	2014	24512167	USA	5	retrospective cohort	1361		15 .1 4	63.63					
Boekel [25]	2014	25128694	the Netherland s		retrospective cohort	10444					100	99.3		
Wang [26]	2014	24951268	USA	4.2	retrospective cohort	585					0			62.2
Freedman [27]	2014	24756187	United States	2.8	retrospective cohort	2106					0	100	100	
von Minckwit z Gunter [28]	2014	25273342	multinatio nal	1.33	RCT	494			52				100	
Vazdar [29]	2014		Croatia	1.83		140	58						100	
Qin [30]	2015	25342090	USA	7.6	retrospective cohort	1153	52.6	9. 3	38.3	22.9	0		100	

Torres [31]	2015	26026467	Canada		retrospective cohort	8462		9.1	27.3		0	100	100	
Ye [32]	2015	25223278	USA	13.7	retrospective cohort	6515	62				0	100		42.9
Vulsteke [33]	2015	26017071	Belgium	3.62	prospective cohort	877					9.2		100	
Chan [34]	2015	25227961	Canada	14.2	retrospective cohort	5334	58	2.9	7.9		0	100	23.7	100
Lu [35]	2015	25925388	USA	9.9	retrospective cohort	4608					0	98.4	48.3	
Pivot [36]	2015	26163096	France	4.54	RCT	3380	55					100	100	
Schneider [37]	2015	26625004	multinatio nal	6.4	RCT	227	49				0	100	100	
Boekel [38]	2016	27026313	the Netherland	9	retrospective cohort	70209					0	100	25.4	66.4
Chien [39]	2016	27310478	Taiwan	5.29	retrospective cohort	23006	50.99	8.18	17.67	2.34		93.55	100	33.54
Haque [40]	2016	27100398	USA	4.5	retrospective cohort	13273		24.3	70.3		8.5	95.6	27.1	60.1
Cadoo [41]	2016	27622751	USA		retrospective cohort	244		11.5	46.7	36.5	0	100	76.6	63.9

Truong [42]	2016	2710700 2	USA	4	prospective cohort	600	48.5	3. 1	14	9			100	
Leung [43]	2016	2635970 9	Taiwan	3.5	retrospective cohort	5132	50.6		22.1	15	0	100	0	6.4
Passarelli [44]	2016	2681152 7	USA	11	prospective cohort	20691	58							
Rossi [45]	2016	2663053 3	Italy	3	retrospective cohort	681		8. 4	40.7	13.2	0	73.4		
Dang [46]	2016	2653979 3	USA	4	prospective cohort	406	55	7	29		0		100	
Thavendiranathan [47]	2016	2709170 9	Canada	2.94	retrospective cohort	18540	54.9	12 .5	35.3	1.1	0		100	78.5
McCullough [48]	2016	2764412 7	USA	9.8	retrospective cohort	4452	70.7					86.1	22.9	56
Gernaat [49]	2017	2846558 7	Singapore	6	prospective cohort	5868	52				13	89.7	47.7	46.6
von Minckwitz Gunter [50]	2017	2858135 6	multinational	3.783	RCT	4805						100	100	
Wang [51]	2017	2910830 7	China	0.92	retrospective cohort	133	65		27		0	45.9		14.3
Veal [52]	2017	2805869	USA	6.7	prospective	1925					100	97.1		44.6

		5			cohort									
Abdel-Qadir [53]	2017	2773270 2	Canada	6.6	retrospective cohort	98999	61	13 .3	43		0		45.1	46.1
Chang [54]	2017	2871785 3	South Korea	7.9	retrospective cohort	26812	48.2	5. 7	17.5			100	65.2	100
Wu [55]	2017	2928044 8	multinatio nal	10.5	RCT	746	49	2. 9	16.8	2.8		100	100	74.9
Grellier [56]	2017	2858696 1	France	5.3	retrospective cohort	796	53.2				0	100	84.7	100
Merzenic h [57]	2017	2780405 3	Germany	6.5	retrospective cohort	11982	59.2				7.7	98.8	42.7	75.6
Cespedes [58]	2017	2817617 4	USA	8.28	retrospective cohort	3109	56.86				0		57	54
Choi [59]	2018	2973747 4	South Korea	3.62	retrospective cohort	83544		18 .8	24.6	39		100	97.2	72.6
Deen [60]	2018	3012159 9	the Netherland		retrospective cohort	127714	60.4				8.9			
Boekel [61]	2018	3006525 4	the Netherland	9	retrospective cohort	4448	51	2. 9	2.9	2.9	12.8	100	37.8	81.6
Busby [62]	2018	2960854 6	UK	5.5	retrospective cohort	23669		6. 2			0	81.2	28.6	35.2

Elshof [63]	2018	2837585	the Netherlands	9.8	retrospective cohort	9799	57.4				100	100		
Gernaat [64]	2018	2949273	the Netherlands	5	prospective cohort	1103	54	2.4						
Simon [65]	2018	2933808	USA		RCT	8641		5	40	13	0			
James [66]	2018	2943617	New Zealand	10.33	retrospective cohort	501	55.5				0	100	38.3	100
Obi [67]	2018	2924887	Germany	11.9	retrospective cohort	2951	62.4	8.6	41		0	100		82.6
Banke [68]	2018	2949304	Denmark	16.9	RCT	962	47.6		0.6			100	100	38.8
Cho [69]	2018	2996311	South Korea	8.1	retrospective cohort	4333		4.6	5.9	7.7	11.8	100	60.1	100
Swain [70]	2018	2925308	multinational	1.2	Non-randomized trial	400	49				0.2	100	100	
Wildiers [71]	2018	2943396	multinational	1.73	RCT	80	76.8				0	51.9		
Nowsheen [72]	2018	3037123	USA	6.84	retrospective cohort	428	52.9	7.9	27.1	21.3	0			70.8
Lidbrink [73]	2019	3050611	multinational	5	prospective cohort	3733	55	4.7	28.3	7.5	0			35.8

Roca-Barcel [74]	2019	3053620 9	Spain	8.4	retrospective cohort	641	55.9				100	100		51.7
Banke [75]	2019	3081937 7	Denmark	5.4	retrospective cohort	8611	51.8	2. 2	7.7			100	100	81.6
Troeschel [76]	2019	3115564 4	USA	6.67	retrospective cohort	407587						93	34.3	46.9
Kamaraju [77]	2019	3044392 1	USA	2.39	retrospective cohort	5648		34 .1	85		0		14.6	56.4
Lee [78]	2019	3069068 7	Taiwan	5.2	retrospective cohort	3489		6. 3	17.7			100		100
Fogarassy [79]	2019	3090552 0	Hungary	5.89	retrospective cohort	8068		14 .4	63.5	16.6				81.8
Buddeke [80]	2019	3115202 2	the Netherlands	8.5	retrospective cohort	163881					7.6	100		
Cespedes [81]	2019	3136930 2	USA	6	retrospective cohort	2943	55.5	25	39.7	35.8	0		75.4	25.2
Kensler [82]	2019	3060400 1	USA	12.9	retrospective cohort	2073					18.5	77	28.2	51.9
Chou [83]	2020	3199669 5	Taiwan		retrospective cohort	19007		11 .7	22.8	12.9	0	100		
Rodriguez [84]	2020	3214655 3	USA	13	retrospective cohort	1358	58.6		34	29.8				

Franchi [85]	2020	32770690	Italy	5.9	retrospective cohort	18624	55	6.9	29.9			100	100	
Sung [86]	2020	32595991	South Korea	3.22	retrospective cohort	3251	50	7	16.4		0	100	69.4	100
Chung [87]	2020	32771950	South Korea	5.57	retrospective cohort	56338	50.5	7.5	22.8	23.8	0	100	60.4	69.4
Gong [88]	2020	32236828	Canada		retrospective cohort	1230	56	14.6	33.9					
Collin [89]	2020	32954254	USA	4.7	retrospective cohort	8523	58.4				0	89.8	46.9	56.4
Khosrow-Khavar [90]	2020	32065766	UK	1.3	retrospective cohort	17922	67.7	9.9			0		13.8	4.5
Offersen [91]	2020	32910709	Denmark	7.26	RCT	1854	59				13	100	43	100
Killander [92]	2020	32302682	Sweden	21.3	RCT	1187					0	100	1	54.3
Rushton [93]	2020	32343801	Canada	6.4	retrospective cohort	5547	56				0			
de Azambuja [94]	2020	31605311	multinational	11	RCT	7445		2	18.3			100	99.8	

Eiger [95]	2020	32203207	multinatio nal	6.9	RCT	4190		5. 5	21.5	8.5		100	100	71
Delaloge [96]	2020	32083990	multinatio nal	5	RCT	1301						100	100	
Tao [97]	2020	32132977	USA	13	retrospective cohort	6330								
Lee [98]	2020	31454422	USA	3.1	retrospective cohort	91227	49.1	6. 6	19.3	12.2				
Lim [99]	2021	33531527	USA	9.5	retrospective cohort	42528					100	100		100
Milo [100]	2021	33515670	Denmark	7.9	retrospective cohort	22056					0	100	44	100
Koczwar a [101]	2021	33296507	Australia	17	retrospective cohort	6259								
Rabaglio [102]	2021	33159633	multinatio nal	3.82	RCT	6144			32.3	13.3		100		
Kim [103]	2021	34369199	South Korea	4.06	retrospective cohort	1256	51.4	8. 7	16.5	27.9	1	99.9	79.5	100
Matthews [104]	2021	33177117	USA and UK		retrospective cohort	10005	10005	69	11.9	46.7	30			
Franchi [105]	2021	34066685	Italy	5.8	retrospective cohort	33946			54.6	20.2		100	15.4	44.3

Connor [106]	2021	3379396 7	USA	5.083	retrospective cohort	33099	60.9					96.3	40.8	48.5
van den Bogaard [107]	2021	3371374 1	the Netherland	9.2	retrospective cohort	910	59	7.1	30	15.5	0	100	36.7	100
Carlson [108]	2021	3460479 8	USA, Canada, Denmark	14	retrospective cohort	972	46		10	5.5	0		60	100
He [109]	2021	3411703 5	USA	9.2	retrospective cohort	2448	50	18.9	15.3	9.3	0			63.4
Kim [110]	2021	3359986 6	South Korea		retrospective cohort	39775	51.2							58
Haffadi [111]	2021	3371621 4	Morrocca	1	prospective cohort	549	50	9.5	16	0.9	0			68
Wang [112]	2021	3445657 7	China	3	prospective cohort	316	64.7	31.9	69.9			100	100	100
Leoce [113]	2021	3457976 5	USA	7.5	retrospective cohort	20462	60	13.1			0	97.2	47.1	32.4
Sund [114]	2021	3426549 6	Sweden	3.9	retrospective cohort	15815	66	7.9	60.2	24.8	0	100	30.2	70.3
Liou [115]	2021	3459300 9	UK	10.3	retrospective cohort	12413	54.6						38	71
Reding [116]	2022	3549281 0	USA	7.2	retrospective cohort	2272			75.6	26.7				

Cheng [117]	2022	3506379 3	USA	8.1	retrospective cohort	3089		11	36.8			94	24.6	38.9
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Abbreviations: DCIS, ductal carcinoma in situ; DM, diabetes mellitus; FU, follow-up; PMID, PubMed identification number; RCT. Randomized controlled trial; y, year(s).

Table S4. Risk of bias assessment of the studies that estimated the incidence rates of cardiovascular endpoints in patients with breast cancer.

First author	Year	PMID	1. Representativeness of the exposed cohort	3. Ascertainment of exposure	4. Demonstration that outcome of interest was not present at the start of the study	6. Assessment of outcome	7. Was follow-up long enough for outcomes to occur	8. Adequacy of follow up of cohorts
Batist	2001	11230490	low risk	low risk	low risk	low risk	low risk	uncertain or high risk
Bonnetterre	2004	15284257	low risk	low risk	low risk	low risk	low risk	low risk
Pagani	2004	15550579	low risk	low risk	uncertain or high risk	uncertain or high risk	low risk	uncertain or high risk
Bradbury	2005	15712362	low risk	low risk	low risk	low risk	low risk	low risk
Guarneri	2006	16908934	low risk	low risk	uncertain or high risk	low risk	low risk	uncertain or high risk
Jagsi	2007	17238178	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Coates	2007	17200148	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Pinder	2007	17664460	low risk	low risk	low risk	low risk	low risk	low risk
Ejlertsen	2007	17306974	low risk	low risk	low risk	low risk	low risk	low risk
Testore	2008	18690759	low risk	low risk	low risk	low risk	low risk	low risk
Extra	2010	20671105	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Untch	2011	21788566	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Park	2011	21762242	low risk	low risk	low risk	low risk	low risk	low risk
Appel	2012	22909389	low risk	low risk	uncertain or high risk	low risk	low risk	uncertain or high risk
Seicean	2013	23425978	low risk	low risk	low risk	low risk	low risk	low risk

Jacob	2013	23499212	low risk	uncertain or high risk	uncertain or high risk	uncertain or high risk	low risk	low risk
Henson	2013	23257897	low risk	low risk	low risk	low risk	low risk	low risk
Rugo	2013	24062208	low risk	low risk	uncertain or high risk	low risk	low risk	uncertain or high risk
Morris	2013	24037735	low risk	low risk	low risk	low risk	low risk	low risk
Martin	2013	23733779	low risk	low risk	low risk	low risk	low risk	low risk
Goss	2013	23358971	low risk	low risk	low risk	low risk	low risk	low risk
Mackey	2013	23246022	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Obi	2014	24570215	low risk	low risk	uncertain or high risk	uncertain or high risk	low risk	uncertain or high risk
Haque	2014	24512167	low risk	low risk	uncertain or high risk	low risk	low risk	uncertain or high risk
Boekel	2014	25128694	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Wang	2014	24951268	low risk	low risk	low risk	low risk	low risk	low risk
Freedman	2014	24756187	low risk	low risk	low risk	low risk	low risk	low risk
von Minckwitz Gunter	2014	25273342	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Vazdar	2014		uncertain or high risk	uncertain or high risk	uncertain or high risk	uncertain or high risk	low risk	uncertain or high risk
Qin	2015	25342090	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Torres	2015	26026467	low risk	low risk	low risk	low risk	low risk	low risk
Ye	2015	25223278	low risk	low risk	low risk	low risk	low risk	low risk
Vulsteke	2015	26017071	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Chan	2015	25227961	low risk	low risk	low risk	low risk	low risk	low risk
Lu	2015	25925388	low risk	low risk	low risk	low risk	low risk	low risk
Pivot	2015	261630	low risk	low risk	low risk	low risk	low risk	uncertain

		96						n or high risk
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Schneider	2015	26625004	low risk	low risk	low risk	low risk	low risk	low risk
Boekel	2016	27026313	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Chien	2016	27310478	low risk	low risk	low risk	low risk	low risk	low risk
Haque	2016	27100398	low risk	low risk	low risk	low risk	low risk	low risk
Cadoo	2016	27622751	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Truong	2016	27107002	uncertain or high risk	low risk	low risk	low risk	low risk	low risk
Leung	2016	26359709	low risk	low risk	low risk	low risk	low risk	low risk
Passarelli	2016	26811527	low risk	low risk	low risk	low risk	low risk	low risk
Rossi	2016	26630533	low risk	low risk	uncertain or high risk	low risk	low risk	uncertain or high risk
Dang	2016	26539793	low risk	low risk	low risk	low risk	low risk	low risk
Thavendiranathan	2016	27091709	low risk	low risk	low risk	low risk	low risk	low risk
McCullough	2016	27644127	low risk	low risk	low risk	low risk	low risk	low risk
Gernaat	2017	28465587	low risk	low risk	low risk	low risk	low risk	low risk
von Minckwitz Gunter	2017	28581356	low risk	low risk	low risk	low risk	low risk	low risk
Wang	2017	29108307	low risk	low risk	uncertain or high risk	uncertain or high risk	low risk	low risk
Veal	2017	28058695	low risk	uncertain or high risk	low risk	low risk	low risk	uncertain or high risk
Abdel-Qadir	2017	27732702	low risk	low risk	low risk	low risk	low risk	low risk
Chang	2017	28717853	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Wu	2017	29280448	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Grellier	2017	28586961	low risk	low risk	uncertain or high risk	low risk	low risk	uncertain or high risk
Merzenich	2017	278040	low risk	low risk	low risk	low risk	low risk	low risk

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Cespedes	2017	281761 74	low risk	low risk	low risk	low risk	low risk	low risk
Choi	2018	297374 74	low risk	low risk	low risk	low risk	low risk	low risk
Deen	2018	301215 99	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Boekel	2018	300652 54	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Busby	2018	296085 46	low risk	low risk	low risk	low risk	uncertain or high risk	low risk
Elshof	2018	283758 55	low risk	low risk	low risk	low risk	low risk	low risk
Gernaat	2018	294927 35	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Simon	2018	293380 86	low risk	low risk	low risk	low risk	low risk	low risk
James	2018	294361 71	low risk	low risk	uncertain or high risk	low risk	low risk	uncertain or high risk
Obi	2018	292488 76	low risk	low risk	low risk	low risk	low risk	uncertain or high risk
Banke	2018	294930 47	low risk	low risk	low risk	low risk	low risk	low risk
Cho	2018	299631 17	low risk	low risk	low risk	low risk	low risk	low risk
Swain	2018	292530 81	low risk	low risk	low risk	low risk	low risk	low risk
Wildiers	2018	294339 63	low risk	low risk	low risk	low risk	low risk	low risk
Nowsheen	2018	303712 38	low risk	low risk	uncertain or high risk	low risk	low risk	uncertain or high risk
Lidbrink	2019	305061 10	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Roca-Barcel	2019	305362 09	low risk	low risk	low risk	low risk	low risk	low risk
Banke	2019	308193 77	low risk	low risk	low risk	low risk	low risk	low risk
Troeschel	2019	311556 44	low risk	low risk	low risk	low risk	low risk	low risk
Kamaraju	2019	304439 21	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Lee	2019	306906 87	low risk	low risk	uncertain or	low risk	low risk	low risk

					high risk			
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Fogarassy	2019	30905520	low risk	low risk	low risk	low risk	low risk	low risk
Buddeke	2019	31152022	low risk	low risk	low risk	low risk	low risk	low risk
Cespedes	2019	31369302	low risk	low risk	low risk	low risk	low risk	low risk
Kensler	2019	30604001	low risk	low risk	low risk	low risk	low risk	low risk
Chou	2020	31996695	low risk	low risk	low risk	low risk	low risk	low risk
Rodriguez	2020	32146553	low risk	low risk	low risk	low risk	low risk	low risk
Franchi	2020	32770690	low risk	low risk	low risk	low risk	low risk	uncertain or high risk
Sung	2020	32595991	low risk	low risk	low risk	low risk	low risk	low risk
Chung	2020	32771950	low risk	low risk	low risk	low risk	low risk	low risk
Gong	2020	32236828	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Collin	2020	32954254	low risk	low risk	low risk	low risk	low risk	low risk
Khosrow-Khavar	2020	32065766	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Offersen	2020	32910709	low risk	low risk	low risk	low risk	low risk	low risk
Killander	2020	32302682	low risk	low risk	low risk	low risk	low risk	low risk
Rushton	2020	32343801	low risk	low risk	low risk	low risk	low risk	uncertain or high risk
de Azambuja	2020	31605311	low risk	low risk	low risk	low risk	low risk	low risk
Eiger	2020	32203207	low risk	low risk	low risk	low risk	low risk	low risk
Delaloge	2020	32083990	low risk	low risk	low risk	low risk	low risk	low risk
Tao	2020	32132977	low risk	low risk	low risk	low risk	low risk	low risk
Lim	2021	33531527	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Milo	2021	33515670	low risk	low risk	uncertain or high risk	low risk	low risk	low risk
Koczwar	2021	33296507	low risk	low risk	low risk	low risk	low risk	low risk
Rabaglio	2021	331596	low risk	low risk	uncertain	low risk	low risk	uncertain

		33			n or high risk			n or high risk
Kim	2021	343691 99	low risk	low risk	low risk	low risk	low risk	low risk
Matthews	2021	331771 17	low risk	low risk	low risk	low risk	low risk	low risk
Franchi	2021	340666 85	low risk	low risk	low risk	low risk	low risk	low risk
Connor	2021	337939 67	low risk	low risk	uncertain n or high risk	uncertain n or high risk	low risk	low risk
van den Bogaard	2021	337137 41	low risk	low risk	uncertain n or high risk	low risk	low risk	low risk
Carlson	2021	346047 98	low risk	low risk	low risk	uncertain n or high risk	low risk	low risk
He	2021	341170 35	low risk	low risk	uncertain n or high risk	low risk	low risk	low risk
Kim	2021	335998 66	low risk	low risk	low risk	low risk	low risk	low risk
Haffadi	2021	337162 14	low risk	low risk	low risk	uncertain n or high risk	low risk	uncertain n or high risk
Wang	2021	344565 77	low risk	low risk	uncertain n or high risk	low risk	low risk	low risk
Leoce	2021	345797 65	low risk	low risk	uncertain n or high risk	low risk	low risk	low risk
Sund	2021	342654 96	low risk	low risk	uncertain n or high risk	low risk	low risk	low risk
Liou	2021	345930 09	low risk	low risk	low risk	low risk	low risk	uncertain n or high risk
Reding	2022	354928 10	low risk	low risk	low risk	low risk	low risk	low risk
Cheng	2022	350637 93	low risk	low risk	low risk	low risk	low risk	low risk

Abbreviations: PMID, PubMed identification number.

Table S5. The results of leave-one-out sensitivity analyses for studies that estimated the incidence rates of cardiovascular endpoints in patients with breast cancer.

Omitting the study: First author, year	Outcomes, HR (95% CI)	
	ML	REML
	Cardiovascular death (0-5 years after breast cancer diagnosis)	
Riihimäki, 2012	1.13 (1.05-1.20)	1.13 (1.05-1.20)
Bradshaw, 2016	1.09 (1.07-1.11)	1.10 (1.07-1.13)
Staszewsky, 2020	1.09 (1.07-1.11)	1.09 (1.07-1.11)

Ramin, 2021	1.09 (1.07-1.11)	1.09 (1.07-1.12)
Park, 2017	1.09 (1.07-1.11)	1.10 (1.07-1.13)
Paterson, 2022	1.09 (1.07-1.11)	1.09 (1.07-1.11)
Heart failure (0-1 year after breast cancer diagnosis)		
Ng, 2019	1.32 (1.01-1.72)	1.35 (0.95-1.93)
Staszewsky, 2020	1.24 (1.20-1.29)	1.24 (1.20-1.29)
Abdel-Qadir, 2019	1.32 (1.01-1.73)	1.36 (0.95-1.94)
Paterson, 2022	1.31 (1.00-1.71)	1.34 (0.94-1.92)
Yang, 2022	1.19 (1.12-1.28)	1.19 (1.09-1.29)
Heart failure (1-2 years after breast cancer diagnosis)		
Ng, 2019	1.20 (1.07-1.33)	1.22 (1.03-1.44)
Staszewsky, 2020	1.24 (1.20-1.28)	1.24 (1.20-1.28)
Abdel-Qadir, 2019	1.20 (1.07-1.35)	1.23 (1.03-1.46)
Paterson, 2022	1.18 (1.07-1.30)	1.20 (1.03-1.41)
Yang, 2022	1.19 (1.12-1.28)	1.19 (1.09-1.29)
Heart failure (2-5 years after breast cancer diagnosis)		
Lee, 2020	1.19 (1.12-1.27)	1.18 (1.09-1.28)
Ng, 2019	1.21 (1.10-1.34)	1.21 (1.08-1.35)
Staszewsky, 2020	1.25 (1.21-1.29)	1.26 (1.20-1.32)
Abdel-Qadir, 2019	1.22 (1.10-1.34)	1.21 (1.08-1.36)
Paterson, 2022	1.20 (1.09-1.33)	1.20 (1.07-1.34)
Yang, 2022	1.22 (1.13-1.32)	1.22 (1.11-1.34)
Heart failure (5-10 years after breast cancer diagnosis)		
Khan, 2011	1.21 (1.16-1.26)	1.18 (1.09-1.27)
Ng, 2019	1.18 (1.08-1.30)	1.18 (1.04-1.35)
Lash, 2014	1.24 (1.19-1.28)	1.24 (1.19-1.28)
Abdel-Qadir, 2019	1.19 (1.08-1.31)	1.19 (1.04-1.36)
Paterson, 2022	1.20 (1.14-1.25)	1.17 (1.04-1.32)
Yang, 2022	1.23 (1.19-1.27)	1.21 (1.12-1.31)
Atrial fibrillation (0-3 months after breast cancer diagnosis)		
D'Souza, 2018	1.77 (1.28-2.45)	1.79 (1.22-2.61)
Saliba, 2018	1.54 (1.15-2.07)	1.54 (1.10-2.16)
Abdel-Qadir, 2019	1.48 (1.09-2.01)	1.51 (1.04-2.17)
Guha, 2022	1.54 (1.09-2.17)	1.56 (1.04-2.34)
Staszewsky, 2020	1.81 (1.38-2.38)	1.83 (1.32-2.53)
Atrial fibrillation (3 months-3 years after breast cancer diagnosis)		
D'Souza, 2018	1.09 (1.01-1.17)	1.09 (1.01-1.17)
Saliba, 2018	1.12 (1.04-1.20)	1.11 (1.02-1.21)
Abdel-Qadir, 2019	1.16 (1.09-1.24)	1.16 (1.09-1.24)
Staszewsky, 2020	1.14 (1.05-1.23)	1.14 (1.03-1.26)
Myocardial infarction (0-3 months after breast cancer diagnosis)		
Ligibel, 2012	0.92 (0.76-1.12)	0.94 (0.85-1.05)
van Herk-Sukel, 2011	0.91 (0.81-1.02)	0.91 (0.84-0.99)
Lamont, 2003	0.94 (0.85-1.03)	0.94 (0.86-1.02)
Park, 2017	0.90 (0.79-1.04)	0.91 (0.84-1.00)
Reiner, 2017	0.90 (0.80-1.00)	0.91 (0.84-0.99)
Paterson, 2022	0.87 (0.78-0.96)	0.87 (0.78-0.96)
Myocardial infarction (3-6 months after breast cancer diagnosis)		
Ligibel, 2012	0.93 (0.76-1.14)	0.95 (0.86-1.05)
van Herk-Sukel, 2011	0.91 (0.81-1.02)	0.92 (0.84-0.99)

Lamont, 2003	0.94 (0.86-1.03)	0.94 (0.86-1.02)
Park, 2017	0.91 (0.78-1.06)	0.92 (0.84-1.00)
Reiner, 2017	0.90 (0.80-1.00)	0.91 (0.84-0.99)
Paterson, 2022	0.87 (0.78-0.97)	0.87 (0.78-0.97)
Myocardial infarction (6-12 months after breast cancer diagnosis)		
Ligibel, 2012	0.95 (0.86-1.05)	0.93 (0.78-1.11)
van Herk-Sukel, 2011	0.91 (0.84-0.99)	0.90 (0.81-1.01)
Lamont, 2003	0.94 (0.87-1.02)	0.94 (0.86-1.03)
Park, 2017	0.92 (0.84-1.00)	0.91 (0.80-1.04)
Reiner, 2017	0.91 (0.84-0.99)	0.90 (0.81-1.01)
Paterson, 2022	0.87 (0.79-0.97)	0.87 (0.79-0.97)

Abbreviations: CI, confidence interval; HR, Hazard ratio; ML, maximum likelihood; REML, restricted maximum likelihood.

Table S6. The results of leave-one-out sensitivity analyses for studies that estimated the incidence rates of cardiovascular endpoints in patients with breast cancer.

# in the main analysis	CV death national			CV death regional			HF national			HF regional			CAD			MI nation			MI region			stroke			ischemic stroke		
	IR	ci.l b	ci.u b	IR	ci.l b	ci.u b	IR	ci.l b	ci.u b	IR	ci.l b	ci.u b	IR	ci.l b	ci.u b	IR	ci.l b	ci.u b	IR	ci.l b	ci.ub	IR	ci.l b	ci.u b	IR	ci.l b	ci.ub
1	1.52	0.96	2.40	1.72	1.16	2.55	4.46	3.29	6.04	4.38	3.28	5.86	4.37	3.13	6.09	2.44	1.43	4.16	2.19	1.41	3.42	4.62	3.17	6.73	3.20	2.52	4.07
2	1.50	0.95	2.38	1.71	1.15	2.53	4.61	3.40	6.23	4.52	3.39	6.04	4.31	3.08	6.05	2.16	1.19	3.92	1.97	1.20	3.23	4.14	2.79	6.15	2.78	1.72	4.49
3	1.57	0.99	2.48	1.77	1.20	2.61	4.66	3.45	6.28	4.57	3.44	6.09	4.31	3.08	6.03	2.17	1.20	3.92	1.98	1.21	3.24	3.97	2.76	5.70	2.35	1.55	3.57
4	1.56	0.98	2.46	1.73	1.17	2.55	4.45	3.29	6.04	4.38	3.27	5.85	4.34	3.10	6.09	2.22	1.22	4.01	2.02	1.23	3.31	4.25	2.84	6.35	2.51	1.55	4.08
5	1.51	0.95	2.39	1.76	1.19	2.60	4.29	3.22	5.72	4.43	3.31	5.93	4.09	2.95	5.66	1.92	1.12	3.28	1.77	1.17	2.69	4.50	3.04	6.68	2.45	1.54	3.90
6	1.47	0.93	2.33	1.72	1.16	2.54	4.51	3.32	6.12	4.35	3.25	5.81	4.37	3.12	6.12	2.26	1.26	4.03	1.92	1.17	3.16	4.53	3.08	6.68			
7	1.49	0.94	2.37	1.68	1.14	2.49	4.42	3.27	5.99	4.52	3.39	6.03	4.27	3.04	6.00	2.13	1.17	3.88	2.05	1.27	3.32	4.41	2.95	6.58			
8	1.59	1.02	2.50	1.70	1.15	2.52	4.60	3.40	6.22	4.26	3.22	5.65	4.12	2.96	5.73	2.32	1.31	4.12	1.95	1.18	3.20	4.29	2.86	6.41			

9	1.4 8	0.9 3	2.3 4	1.69	1.1 5	2.5 1	4.34	3.2 3	5.8 3	4.52	3.3 9	6.0 3	4.5 4	3.3 2	6.2 2	2.02	1.1 2	3.6 2	2.11	1.3 1	3.3 9	4.32	2.8 9	6.4 7			
10	1.4 9	0.9 4	2.3 7	1.79	1.2 2	2.6 3	4.60	3.4 0	6.2 2	4.38	3.2 7	5.8 6	4.3 8	3.1 3	6.1 3	2.10	1.1 6	3.8 0	1.85	1.1 5	2.9 8	4.80	3.3 8	6.8 0			
11	1.5 1	0.9 5	2.4 0	1.69	1.1 4	2.4 9	4.46	3.2 9	6.0 5	4.37	3.2 7	5.8 4	4.3 1	3.0 7	6.0 5	1.91	1.1 2	3.2 4	1.92	1.1 7	3.1 4	4.14	2.7 9	6.1 3			
12	1.6 1	1.0 3	2.5 2	1.68	1.1 4	2.4 7	4.45	3.2 8	6.0 3	4.66	3.5 3	6.1 4	4.5 5	3.3 2	6.2 3	2.12	1.1 6	3.8 5	1.97	1.2 0	3.2 4	4.47	3.0 0	6.6 5			
13	1.4 7	0.9 3	2.3 2	1.70	1.1 5	2.5 2	4.74	3.5 5	6.3 4	4.48	3.3 5	6.0 1	4.2 6	3.0 3	5.9 8	2.35	1.3 3	4.1 5	1.93	1.1 8	3.1 8	4.35	2.9 3	6.4 5			
14	1.7 0	1.1 3	2.5 7	1.72	1.1 6	2.5 5	4.56	3.3 6	6.2 0	4.33	3.2 5	5.7 9	4.4 2	3.1 7	6.1 7	2.37	1.3 6	4.1 3	2.14	1.3 3	3.4 2	3.92	2.7 7	5.5 3			
15	1.4 9	0.9 4	2.3 5	1.81	1.2 4	2.6 5	4.41	3.2 6	5.9 7	4.33	3.2 5	5.7 9	4.0 9	2.9 5	5.6 5	2.18	1.2 0	3.9 7	2.14	1.3 5	3.4 0	4.31	2.8 8	6.4 6			
16	1.6 0	1.0 2	2.5 1	1.71	1.1 5	2.5 3	4.41	3.2 6	5.9 7	4.58	3.4 4	6.1 0	4.0 2	2.9 6	5.4 8	1.98	1.1 2	3.4 9	1.99	1.2 1	3.2 8						
17	1.4 7	0.9 3	2.3 3	1.68	1.1 4	2.4 8	4.66	3.4 5	6.2 9	4.38	3.2 8	5.8 7	4.2 4	3.0 2	5.9 5	2.04	1.1 3	3.6 9	1.82	1.1 5	2.9 0						
18	1.5 5	0.9 8	2.4 5	1.90	1.3 4	2.6 9	4.48	3.3 0	6.0 9	4.31	3.2 4	5.7 4	4.4 3	3.1 8	6.1 7	2.29	1.2 8	4.1 1	1.87	1.1 5	3.0 5						
19	1.5 2	0.9 6	2.4 1	1.70	1.1 5	2.5 1	4.46	3.2 9	6.0 5	4.53	3.3 9	6.0 5	4.2 2	3.0 1	5.9 3				2.09	1.2 9	3.3 9						

20	1.4 6	0.9 3	2.3 0	1.80	1.2 3	2.6 4	4.39	3.2 5	5.9 3	4.43	3.3 0	5.9 4	4.3 4	3.0 9	6.0 8												
21	1.4 4	0.9 2	2.2 5	1.68	1.1 4	2.4 9	4.61	3.4 0	6.2 4	4.56	3.4 2	6.0 8	4.0 7	2.9 5	5.6 2												
22	1.5 1	0.9 5	2.3 9	1.76	1.1 9	2.5 9	4.51	3.3 2	6.1 2	4.54	3.4 1	6.0 6	4.4 0	3.1 5	6.1 5												
23	1.4 4	0.9 2	2.2 5	1.73	1.1 7	2.5 6	4.64	3.4 4	6.2 7	4.44	3.3 1	5.9 5	4.2 7	3.0 4	6.0 0												
24	1.5 0	0.9 5	2.3 8	1.67	1.1 3	2.4 6	4.62	3.4 2	6.2 5	4.42	3.2 9	5.9 2	4.3 2	3.0 8	6.0 6												
25	1.5 6	0.9 9	2.4 7	1.65	1.1 3	2.4 2	4.52	3.3 3	6.1 3	4.37	3.2 7	5.8 6	4.4 4	3.1 9	6.1 8												
26	1.5 9	1.0 1	2.5 0	1.72	1.1 6	2.5 4	4.50	3.3 1	6.1 1	4.47	3.3 4	5.9 9	4.0 8	2.9 5	5.6 3												
27	1.4 5	0.9 3	2.2 9	1.71	1.1 5	2.5 3	4.55	3.3 6	6.1 8	4.57	3.4 4	6.0 8	4.2 2	3.0 1	5.9 3												
28	1.6 3	1.0 5	2.5 4	1.77	1.2 0	2.6 1	4.66	3.4 5	6.2 8	4.57	3.4 3	6.0 9															
29	1.6 4	1.0 5	2.5 4	1.66	1.1 3	2.4 4	4.66	3.4 5	6.2 9	4.42	3.3 1	5.9 1															
30	1.5 8	1.0 0	2.4 9	1.69	1.1 4	2.4 9	4.50	3.3 3	6.0 9	4.36	3.2 6	5.8 3															

31	1.5 5	0.9 7	2.4 5	1.79	1.2 2	2.6 3	4.43	3.2 7	6.0 1	4.41	3.2 9	5.9 2															
32	1.4 7	0.9 3	2.3 2	1.67	1.1 3	2.4 5	4.49	3.3 1	6.1 0	4.52	3.3 8	6.0 5															
33	1.5 7	0.9 9	2.4 7	1.83	1.2 6	2.6 6	4.60	3.4 0	6.2 3	4.42	3.3 1	5.9 2															
34	1.5 2	0.9 6	2.4 0	1.83	1.2 6	2.6 6	4.50	3.3 2	6.1 1	4.32	3.2 4	5.7 4															
35	1.5 1	0.9 5	2.4 0	1.78	1.2 1	2.6 2	4.39	3.2 5	5.9 2	4.39	3.2 8	5.8 8															
36	1.4 4	0.9 2	2.2 5	1.75	1.1 8	2.5 9	4.47	3.2 9	6.0 7	4.35	3.2 5	5.8 1															
37				1.68	1.1 4	2.4 8	4.42	3.2 7	5.9 9	4.43	3.3 0	5.9 4															
38				1.77	1.2 0	2.6 1	4.51	3.3 2	6.1 3	4.33	3.2 4	5.7 7															
39				1.66	1.1 3	2.4 3	4.40	3.2 6	5.9 6	4.50	3.3 6	6.0 3															
40				1.67	1.1 4	2.4 6	4.58	3.3 8	6.2 2	4.48	3.3 5	6.0 1															
41				1.78	1.2 1	2.6 2	4.56	3.3 6	6.2 0	4.56	3.4 2	6.0 8															

42				1.73	1.1 7	2.5 5	4.64	3.4 3	6.2 7	4.46	3.3 3	5.9 8																
43				1.69	1.1 4	2.4 9	4.54	3.3 5	6.1 7	4.51	3.3 7	6.0 4																
44				1.72	1.1 6	2.5 5	4.59	3.3 9	6.2 3	4.47	3.3 4	5.9 9																
45							4.55	3.3 5	6.1 8	4.52	3.3 8	6.0 4																
46							4.60	3.4 0	6.2 3	4.25	3.2 2	5.6 1																
47							4.32	3.2 3	5.7 9	4.42	3.3 0	5.9 1																
48							4.49	3.3 1	6.1 0	4.32	3.2 4	5.7 7																
49							4.65	3.4 5	6.2 9	4.57	3.4 3	6.0 9																
50							4.53	3.3 3	6.1 5	4.45	3.3 2	5.9 6																
51							4.46	3.2 8	6.0 5	4.38	3.2 7	5.8 6																

Abbreviations: CAD, coronary artery disease; CV, cardiovascular; ci.lb, lower bound of a confidence interval; ci.ub, upper bound of a confidence interval; HF, heart failure; IR, incidence rate, per 1000 person-years; MI, myocardial infarction.

Table S7. Sensitivity analyses with studies conducted on the same cohorts of patients from studies that estimated the incidence rates of cardiovascular endpoints in patients with breast cancer.

First author, Year	PMID	Outcomes, IR (95% CI)
Cardiovascular death		
Boekel, 2014, 2016	25128694, 2702631	1.52 (0.99-2.33)
Deen, 2018	30121599	1.55 (0.98-2.46)
Elshof, 2018	28375855	1.50 (0.96-2.34)
Henson, 2013	23257897	1.49 (0.96-2.30)
Khosrow-Khavar, 2020	32065766	1.55 (0.99-2.45)
Leung, 2016	26359709	1.64 (1.04-2.59)
Lim, 2021	33531527	1.47 (0.95-2.27)
Rushton, 2020	32343801	1.44 (0.92-2.25)
Ye, 2015	25223278	1.50 (0.96-2.32)
Heart failure		
Wang, 2014	24951268	4.64 (3.41-6.31)
Cespedes, 2017	28176174	4.43 (3.33-5.89)
Cespedes, 2019	31369302	4.39 (3.31-5.83)
Chou, 2020	31996695	4.35 (3.20-5.91)
Chung	32771950	4.42 (3.28-5.95)
Deen	30121599	4.79 (3.56-6.45)
Gong, 2020	32236828	4.58 (3.39-6.19)
Khan, 2011	22048030	4.57 (3.39-6.17)
Lee, 2019	30690687	4.59 (3.39-6.20)
Lee, 2020	31454422	4.37 (3.24-5.89)
Leung, 2016	26359709	4.56 (3.37-6.16)
Thavendiranathan, 2016	27091709	4.49 (3.33-6.06)
Torres, 2015	26026467	4.51 (3.34-6.08)
Yang, 2022	35293856	4.61 (3.43-6.18)

Coronary artery disease		
Bradbury, 2005	15712362	4.22 (3.05-5.85)
Khan, 2011	22048030	4.38 (3.14-6.11)
Lee, 2019	30690687	4.62 (3.32-6.42)
Leung, 2016	26359709	4.65 (3.33-6.50)
Matthews, 2021	33177117	4.30 (3.10-5.96)
Myocardial infarction		
Boekel, 2018, 2014	30065254, 2512869	1.84 (1.08-3.14)
Matthews, 2021	33177117	2.18 (1.24-3.84)
Stroke		
Cespedes, 2019	31369302	4.01 (2.90-5.54)
Kim, 2021	34369199	4.51 (3.18- 6.40)

Abbreviations: CI, confidence interval; IR, incidence rate, per 1000 person-years; PMID, PubMed number; .

Table S8. The results of meta-regression analyses.

	Cardiovascular death				Heart Failure				Coronary artery disease				Myocardial infarction				Stroke			
	N	be ta	p	I2	N	be ta	p	I2	N	be ta	p	I2	N	be ta	p	I2	N	be ta	p	I2
Year of publication , %	44	0.01	0.87	.99	51	0.01	0.65	.99	27	0.04	0.35	.99	19	0.04	0.49	.99	15	0.02	0.62	.99
Median enrollment year	43	-0.06	0.05	.99	51	0.03	0.27	.99	27	0.01	0.77	.99	19	0.02	0.67	.99	15	0.01	0.63	.99
Median follow-up, y	43	0.06	0.19	.99	48	0.13	0.01	.99	24	0.09	0.18	.99	15	0.11	0.26	.98	12	0.03	0.76	.99
Mean age	27	0.14	0.00	.99	35	0.03	0.25	.99	19	0.04	0.10	.99	14	0.08	0.00	.96	11	0.05	0.06	.99
Males, %	32	-1.62	0.23	.99	39	0.93	0.14	.99	27	0.96	0.33	.99	16	0.10	0.92	.99	12			.99
Asian race, %									12	0.00	0.51	.99								
Caucasian race, %	14	0.01	0.35	.99	13	0.01	0.43	.99	12	0.01	0.47	.99								

Prior cardiac disease, %									13	0.05	0.00	99.0								
Hypertension, %	14	0.04	0.14	99.6	30	0.01	0.13	99.6	15	0.03	0.00	98.6	14	0.04	0.00	95.7				
Diabetes mellitus, %	15	0.03	0.62	99.8	25	0.07	0.02	99.7	13	0.09	0.01	99.4	14	0.06	0.02	97.2	10.0	0.03	0.26	99.5
Dyslipidemia, %					16	0.00	0.89	99.4	10	0.06	0.19	97.8								
Smoking, %	12	0.07	0.00	98.6	13	0.01	0.67	98.2	12	0.01	0.70	99.4								
Prior IHD, %					20	0.01	0.77	99.8	14	0.02	0.78	99.4								
Prior MI, %	11	0.13	0.78	99.7	21	0.18	0.46	99.5	12	0.20	0.57	99.6								
Prior heart failure, %	11	0.50	0.07	98.8	30	0.04	0.83	99.7	12	0.11	0.59	99.4								
Postmenopausal, %	14	0.03	0.03	99.5	17	0.02	0.15	99.0	27	0.20	0.79	99.6								
Estrogen positive, %	17	0.01	0.54	98.6	14	0.01	0.69	98.9												
Tumor grade 1, %	18	0.11	0.00	97.7	13	0.08	0.10	97.9												
Tumor grade 2, %	18	0.03	0.21	99.1	13	0.01	0.81	98.9												
Tumor grade 3, %	18	0.04	0.00	98.6	13	0.00	0.92	98.7												
HER2 positive, %	14	0.01	0.17	99.1	25	0.00	0.59	97.3												
Node negative, %	18	0.01	0.37	99.2	17	0.00	0.72	95.1	11	0.01	0.49	99.3								
Node positive, %	18	0.02	0.05	99.0	18	0.00	0.77	95.3												
Left-sided tumor, %	11	0.02	0.94	99.7	11	0.03	0.83	98.9	13	0.02	0.82	99.5								
Right-sided tumor, %					10	0.24	0.05	99.1	13	0.03	0.68	99.5								
Tumor size 2-5 cm	11	0.10	0.00	87.8	10	0.01	0.31	93.0												

Tumor size <2 cm, %	14	0. 08	0. 00	94 .3	11	0. 00	0. 78	92 .3											
Tumor size >5 cm, %	11	- 0. 29	0. 01	97 .6	11	0. 06	0. 00	85 .5											
Stage_0, %	31	0. 00	0. 95	99 .7	28	- 0. 01	0. 19	99 .7	15	0. 00	0. 70	99 .7	12	0. 02	0. 72	98 .8			
Stage 1, %	20	0. 01	0. 62	99 .2	22	- 0. 01	0. 32	99 .3	12	0. 01	0. 48	99 .6							
Stage 2, %	19	- 0. 03	0. 03	98 .9	20	- 0. 01	0. 64	99 .6	11	0. 00	0. 90	99 .7							
Stage 3, %	20	- 0. 06	0. 07	99 .4	21	0. 02	0. 23	99 .6	12	0. 06	0. 29	99 .6							
Stage 4, %	29	0. 02	0. 02	99 .2	29	0. 01	0. 02	99 .7	16	0. 18	0. 55	99 .7	13	0. 00	0. 68	97 .3			
Breast conserving surgery, %	21	0. 00	0. 71	99 .2	18	0. 00	0. 71	99 .6	13	0. 00	0. 79	99 .5							
Mastectom ia, %	20	0. 00	0. 90	99 .1	17	0. 01	0. 59	99 .6	12	- 0. 01	0. 05	99 .6							
Surgery, %	33	- 0. 06	0. 01	99 .7	28	- 0. 04	0. 01	99 .6	17	- 0. 34	0. 02	99 .2	10	0. 02	0. 63	97 .9			
Antracycli ne, %	11	0. 02	0. 16	89 .2	33	0. 00	0. 79	99 .6											
Endocrine treatment, %	20	0. 00	0. 84	99 .6	13	- 0. 01	0. 48	98 .8	11	- 0. 01	0. 40	99 .6							
Chemother apy, %	28	- 0. 03	0. 00	99 .6	34	0. 00	0. 74	99 .4	13	- 0. 03	0. 02	99 .5	12	- 60 .0	0. 22	97 .7			
Tamoxifen , %					10	- 0. 03	0. 01	94 .3											
Anti- HER2 treatment, %	11	- 0. 01	0. 22	99 .4	31	0. 00	0. 34	99 .4											
Trastuzum ab, %	12	- 0. 01	0. 12	99 .5	32	0. 00	0. 93	99 .7											
Radiothera py, %	26	- 0. 03	0. 01	99 .6	25	- 0. 01	0. 35	99 .7	20	- 0. 01	0. 13	99 .6	11	0. 00	0. 98	97 .0			

Abbreviations: IHD, ischemic heart disease; N, the number of studies; MI, myocardial infarction.

Table S9. Results of subgroup analyses for the studies that estimated the incidence rates of cardiovascular endpoints in patients with breast cancer.

	Cardiovascular death			Heart Failure			Coronary artery disease			Myocardial infarction			Stroke		
	N	IR (95% CI)	P for difference	N	IR (95% CI)	P for difference	N	IR (95% CI)	P for difference	N	IR (95% CI)	P for difference	N	IR (95% CI)	P for difference
Asian versus non-Asian country															
Asia	5	0.53 (0.15-1.80)	0.00	5	5.41 (3.05-9.58)	0.071	6	4.0 (1.84-8.70)	0.082	3	1.32 (0.24-7.15)	0.051	3	2.07 (1.14-3.76)	0.05
non-Asia	39	2.01 (1.38-2.92)	0.02	46	4.36 (3.19-5.95)		21	4.41 (3.11-6.26)		16	2.15 (1.36-3.38)		12	5.07 (3.45-7.45)	
RCT versus observational design															
RCT	12	0.91 (0.39-2.09)	0.00	17	2.30 (1.48-3.59)	<0.00	2	3.03 (2.42-3.80)	0.043	2	0.44 (0.20-0.99)	0.002	2	2.82 (1.38-5.76)	0.032
observational	32	2.20 (1.48-3.26)	0.04	34	6.01 (4.39-8.22)		25	4.43 (3.14-6.26)		17	2.35 (1.51-3.67)		13	4.64 (3.10-6.96)	
DCIS versus invasive breast cancer															
DCIS	3	2.48 (1.87-3.29)	0.09	1	NA	NA	3	3.55 (2.39-5.25)	0.090	0	NA	NA	0	NA	NA
Invasive	20	2.06 (1.29-3.29)	0.09	22	NA		10	4.15 (2.46-7.00)		7	NA		3	NA	
Mixed	8	2.15 (1.15-4.02)		5	NA		2	4.77 (1.40-16.32)		5	NA		3	NA	
Older versus mixed-aged study population															
Older	6	2.69 (1.78-4.03)	0.02	10	4.21 (2.18-8.14)	0.086	4	6.57 (3.35-12.87)	0.026	8	2.51 (1.22-5.16)	0.036	7	5.17 (3.15-8.50)	0.037
mixed-aged	38	1.56 (1.02-2.40)	0.01	41	4.50 (3.27-6.18)		23	3.96 (2.77-5.7)		11	1.65 (0.92-2.98)		8	3.70 (2.18-6.27)	
Person-years of follow-up > 10000 versus <10000															

<10000	4	2.33 (0.68- 7.97)	0 6	21	6.08 (3.62- 10.22)	0. 07	3	5.67 (1.94- 16.51)	0. 58	2	4.70 (1.49- 14.83)	0. 23	2	7.72 (6.29- 9.47)	0. 54
>10000	40	1.68 (1.13- 2.51)	4	30	3.70 (2.70- 5.08)		24	4.17 (2.97- 5.85)		17	1.81 (1.12- 2.95)		1 3	4.15 (2.74- 6.27)	

Abbreviations: CI, confidence interval; DCIS, ductal carcinoma in situ; IR, incidence rate, per 1000 person-years; N, the number of studies; RCT, randomized controlled study.

Supplementary Figures.

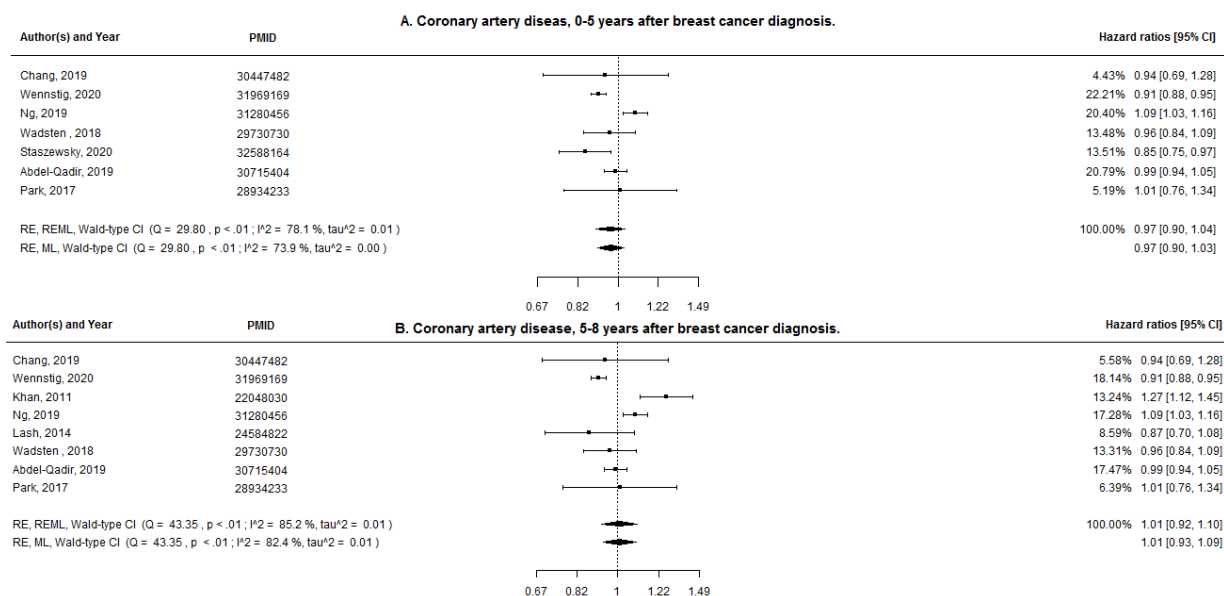


Figure S1. The risk of coronary artery disease in breast cancer patients compared to those of the general population.

Abbreviations: CI, confidence interval; ML, maximum likelihood; PMID, PubMed identification number; RE, random effects; REML, restricted maximum likelihood.

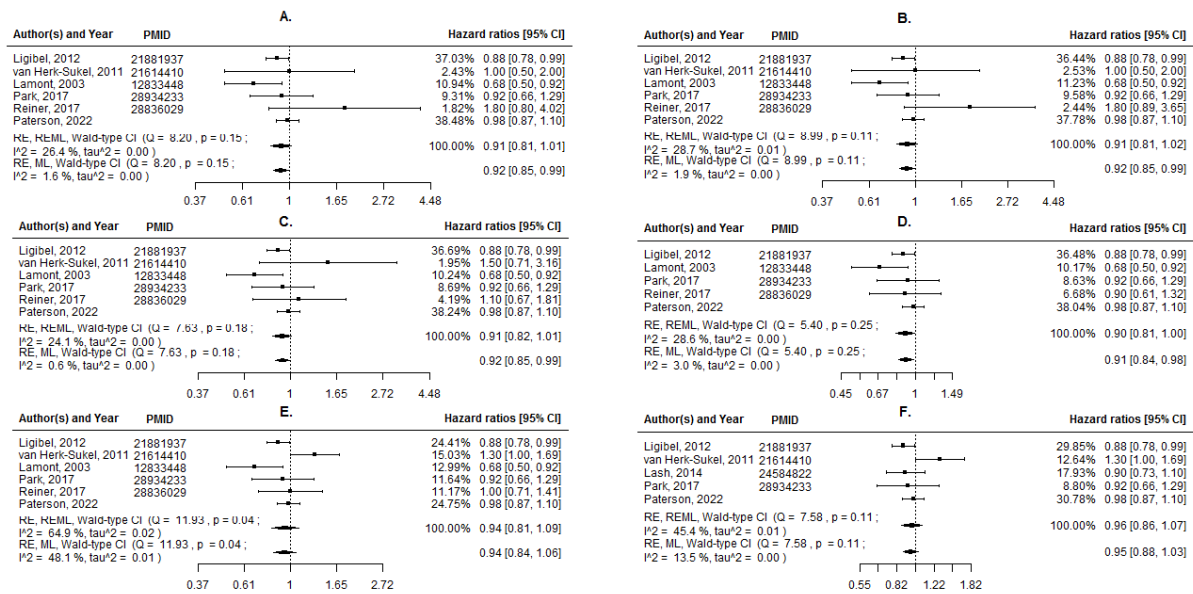


Figure S2. The risk of myocardial infarction in breast cancer patients compared to those in the general population.
Abbreviations: CI, confidence interval; ML, maximum likelihood; PMID, PubMed identification number; RE, random effects; REML, restricted maximum likelihood.

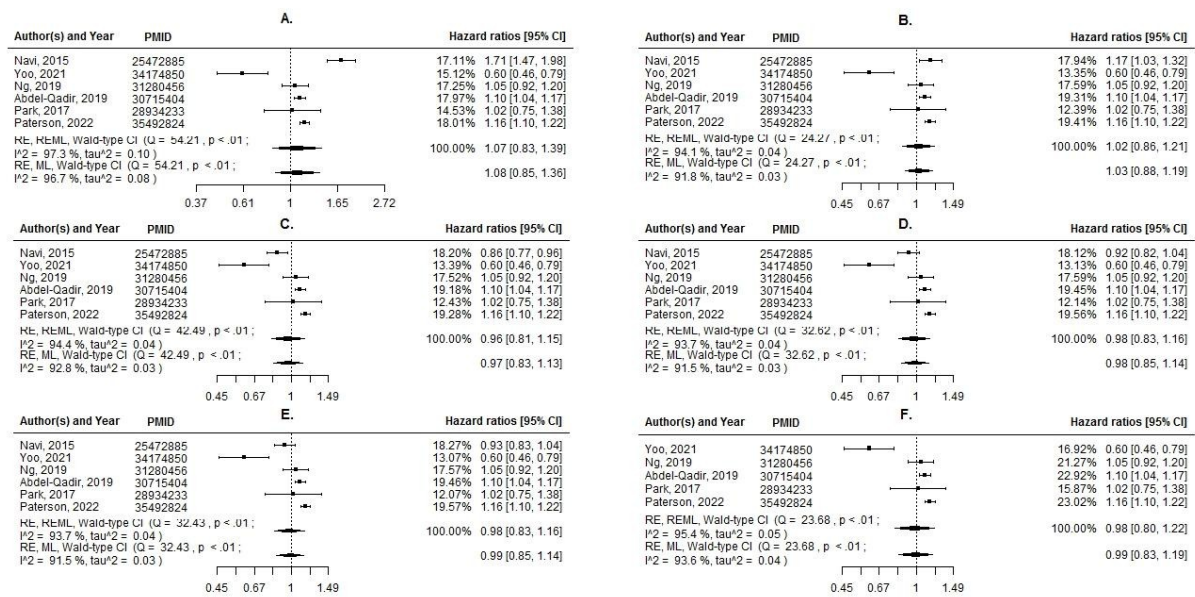


Figure S3. The risk of stroke of any type in breast cancer patients compared to those in the general population.

Abbreviations: CI, confidence interval; ML, maximum likelihood; PMID, PubMed identification number; RE, random effects; REML, restricted maximum likelihood.

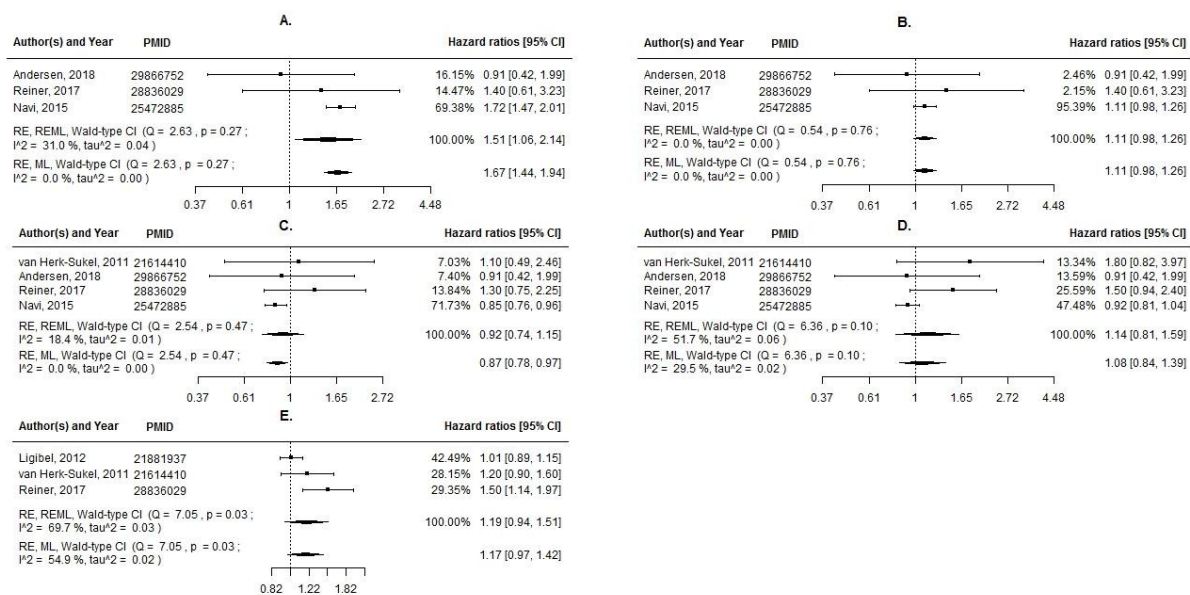


Figure S4. The risk of ischemic stroke of any type in breast cancer patients compared to those in the general population.

Abbreviations: CI, confidence interval; ML, maximum likelihood; PMID, PubMed identification number; RE, random effects; REML, restricted maximum likelihood.

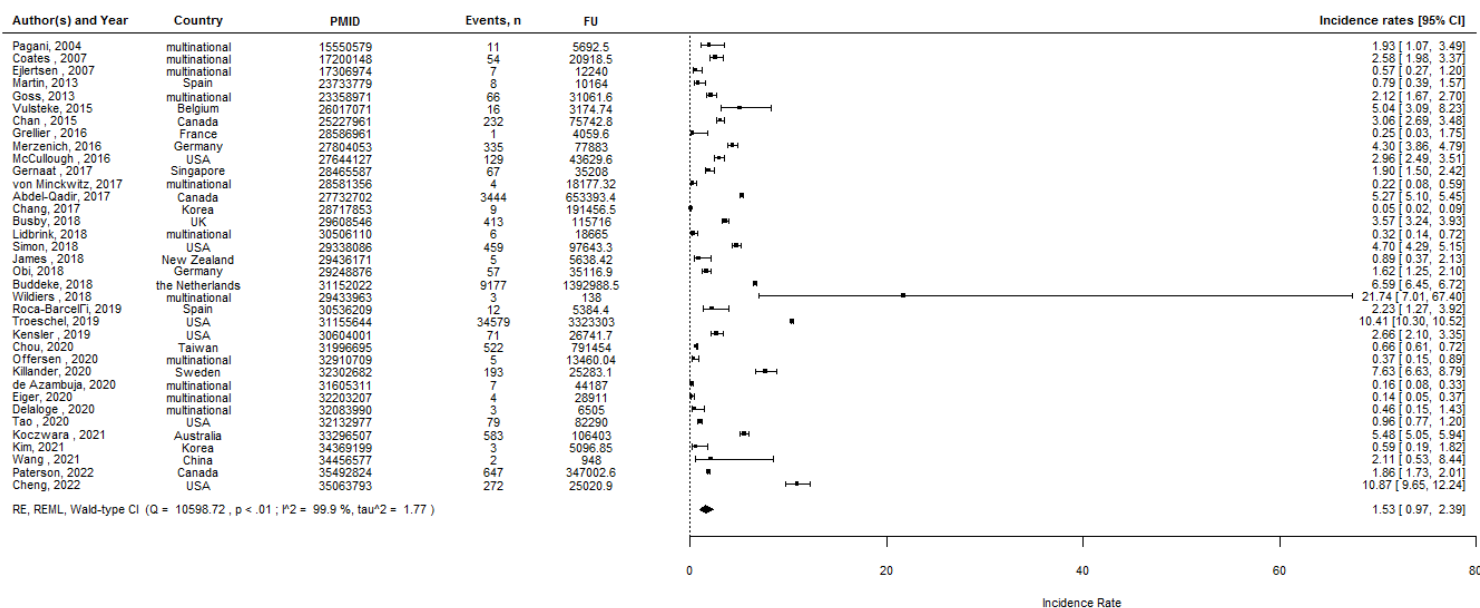


Figure S5. The incidence rate of cardiovascular death in breast cancer patients per 1000 person-years of follow-up. In this analysis, the nationwide SEER-based study with the largest person-years of follow-up was included.

Abbreviations: CI, confidence interval; FU, follow-up (person-years); PMID, PubMed identification number; RE, random effects; REML, restricted maximum likelihood.

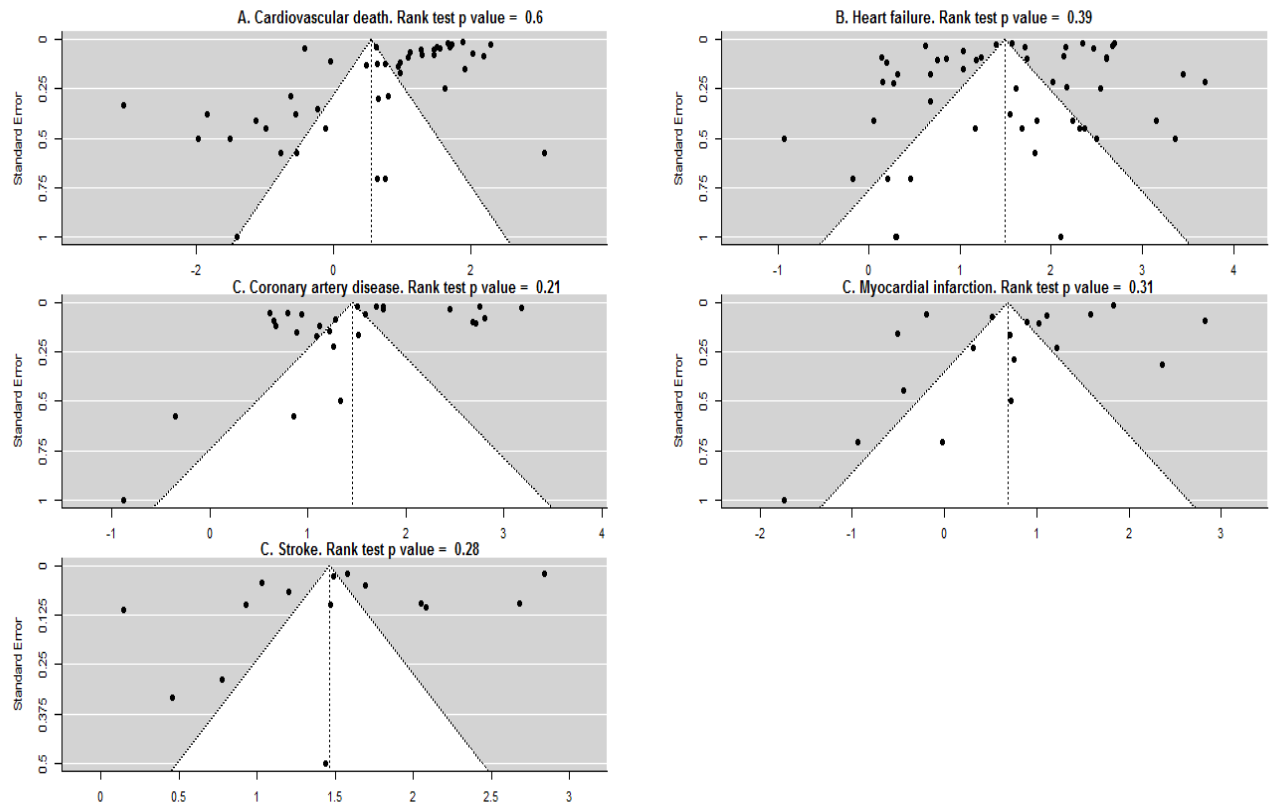


Figure S6. Publication bias assessment for studies that estimated the incidence rates of cardiovascular endpoints in patients with breast cancer.

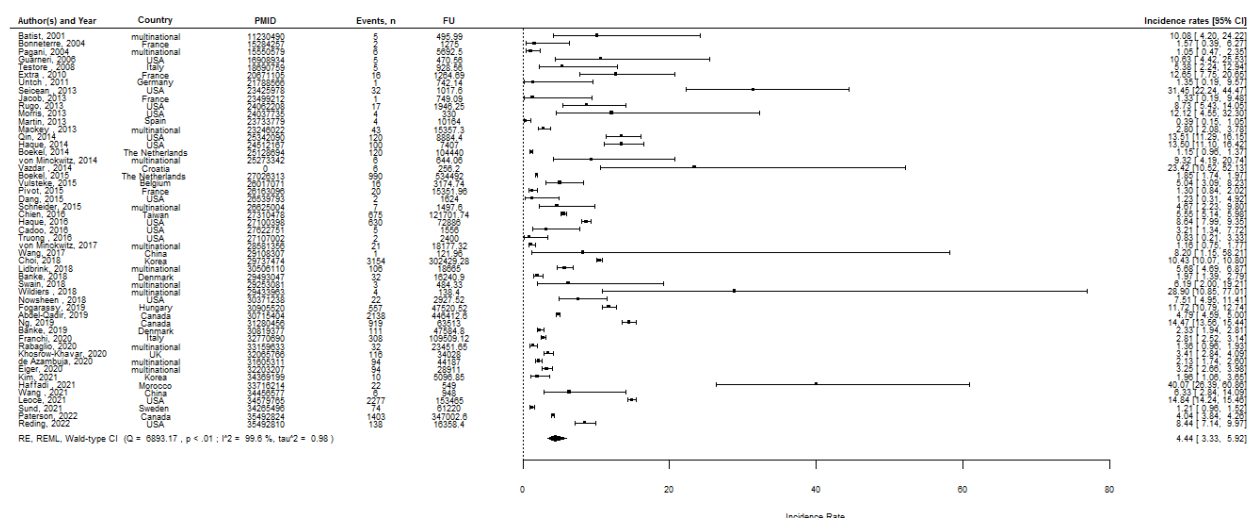


Figure S7. The incidence rate of heart failure in breast cancer patients per 1000 person-years of follow-up. In this analysis, only regional SEER-based studies were included. Abbreviations: CI, confidence interval; FU, follow-up (person-years); PMID, PubMed identification number; RE, random effects; REML, restricted maximum likelihood.

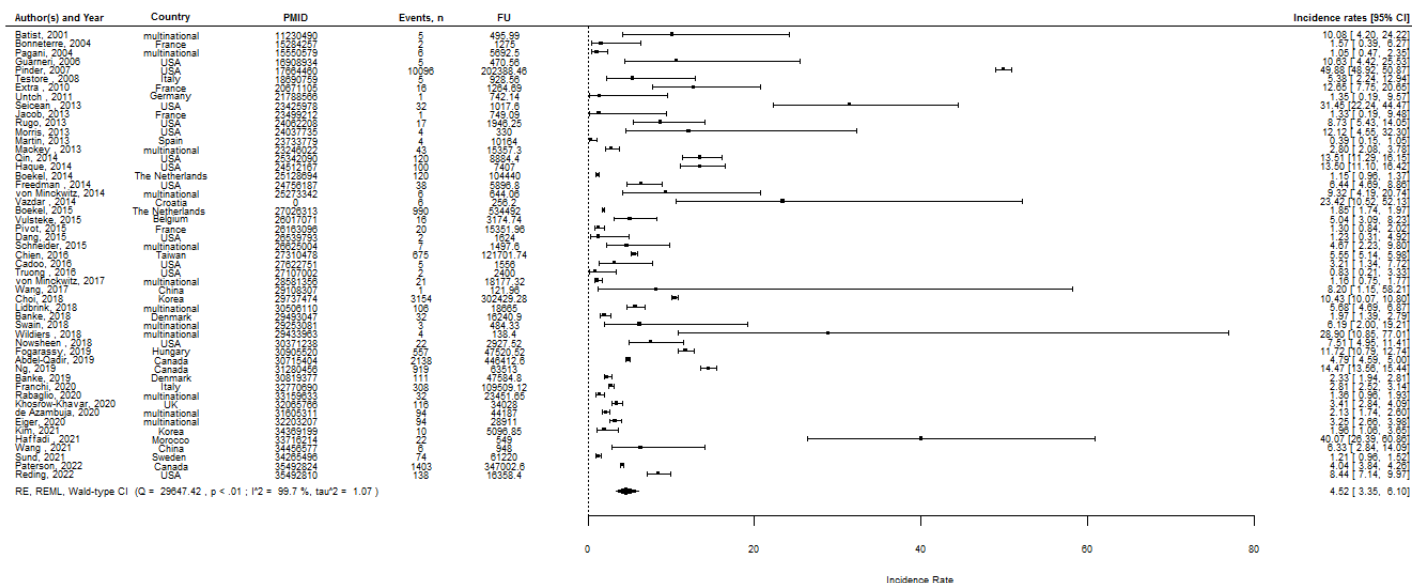


Figure S8. The incidence rate of heart failure in breast cancer patients per 1000 person-years of follow-up. In this analysis, the nationwide SEER-based study with the largest person-years of follow-up was included.

Abbreviations: CI, confidence interval; FU, follow-up (person-years); PMID, PubMed identification number; RE, random effects; REML, restricted maximum likelihood.

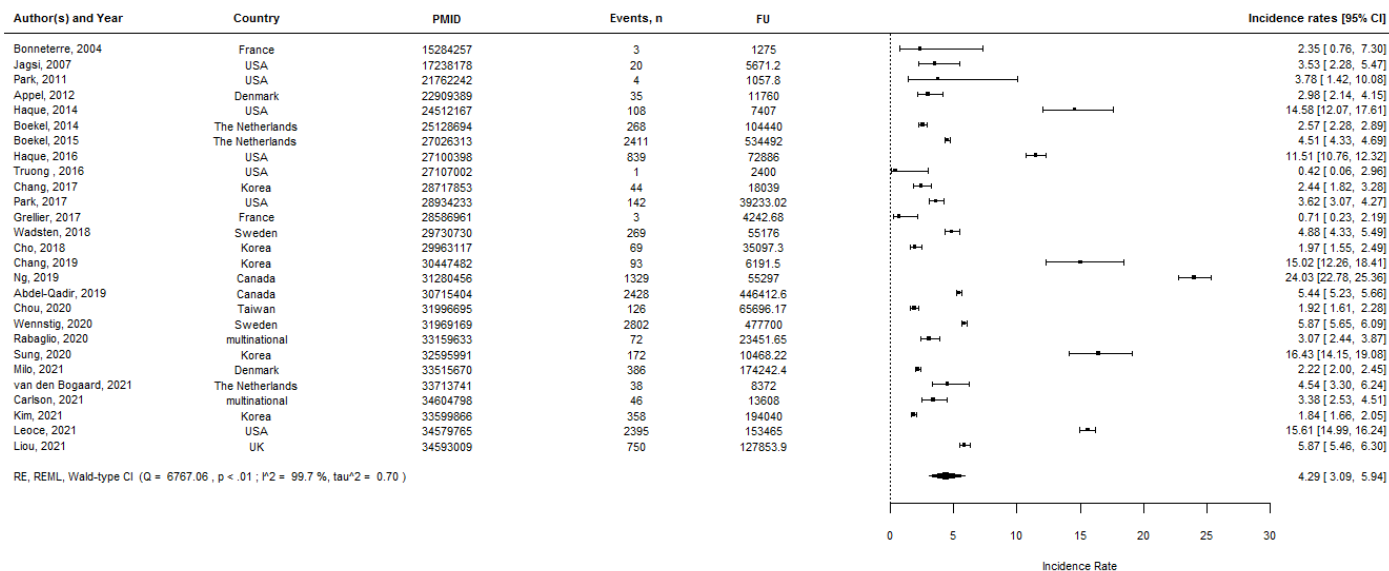


Figure S9. The incidence rate of coronary artery disease in breast cancer patients per 1000 person-years of follow-up.
Abbreviations: CI, confidence interval; FU, follow-up (person-years); PMID, PubMed identification number; RE, random effects; REML, restricted maximum likelihood.

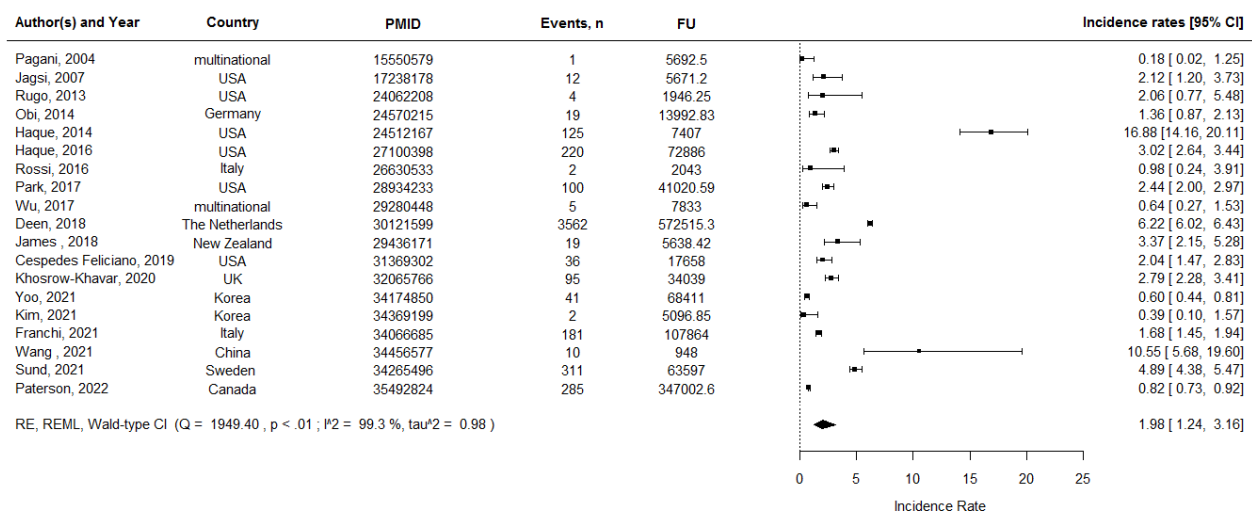


Figure S10. The incidence rate of myocardial infarction in breast cancer patients per 1000 person-years of follow-up. In this analysis, only regional SEER-based studies were included. Abbreviations: CI, confidence interval; FU, follow-up (person-years); PMID, PubMed identification number; RE, random effects; REML, restricted maximum likelihood.

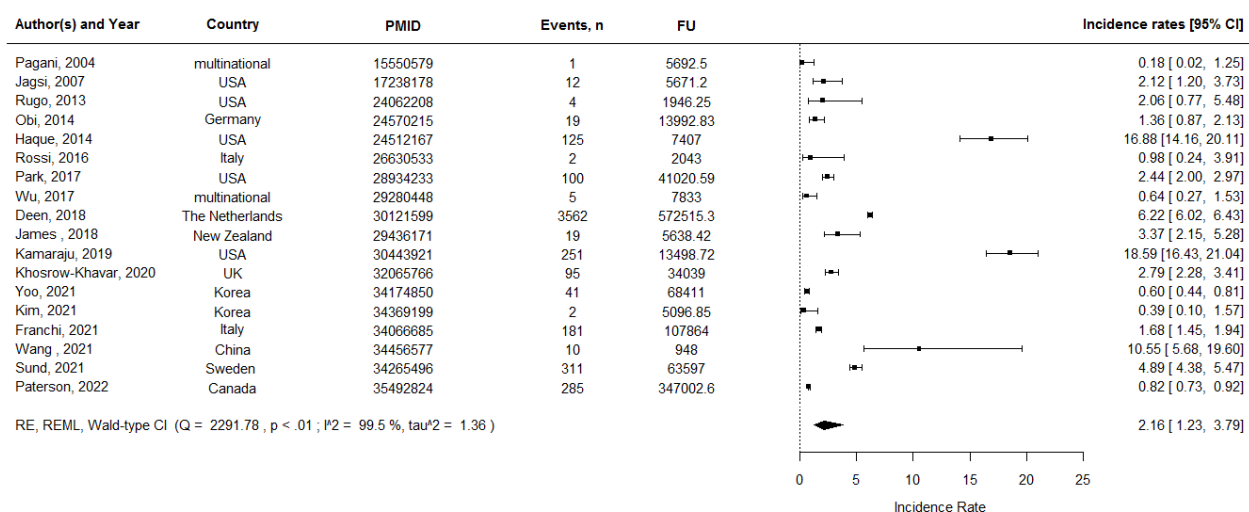


Figure S11. The incidence rate of myocardial infarction in breast cancer patients per 1000 person-years of follow-up. In this analysis, the nationwide SEER-based study with the largest person-years of follow-up was included.

Abbreviations: CI, confidence interval; FU, follow-up (person-years); PMID, PubMed identification number; RE, random effects; REML, restricted maximum likelihood.

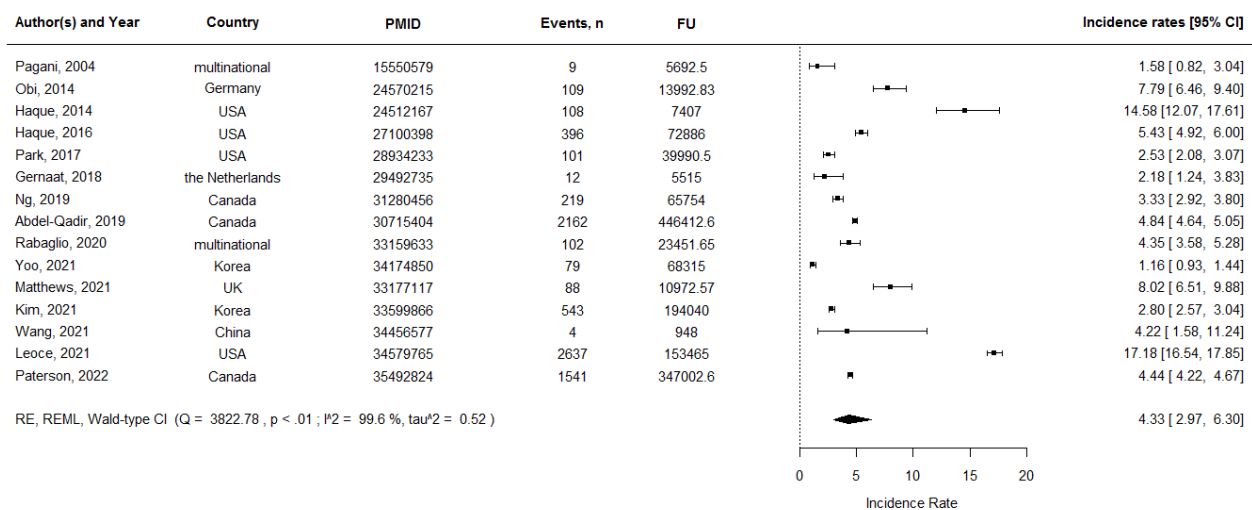


Figure S12. The incidence rate of stroke of any type in breast cancer patients per 1000 person-years of follow-up.

Abbreviations: CI, confidence interval;FU, follow-up (person-years); PMID, PubMed identification number; RE, random effects; REML, restricted maximum likelihood.

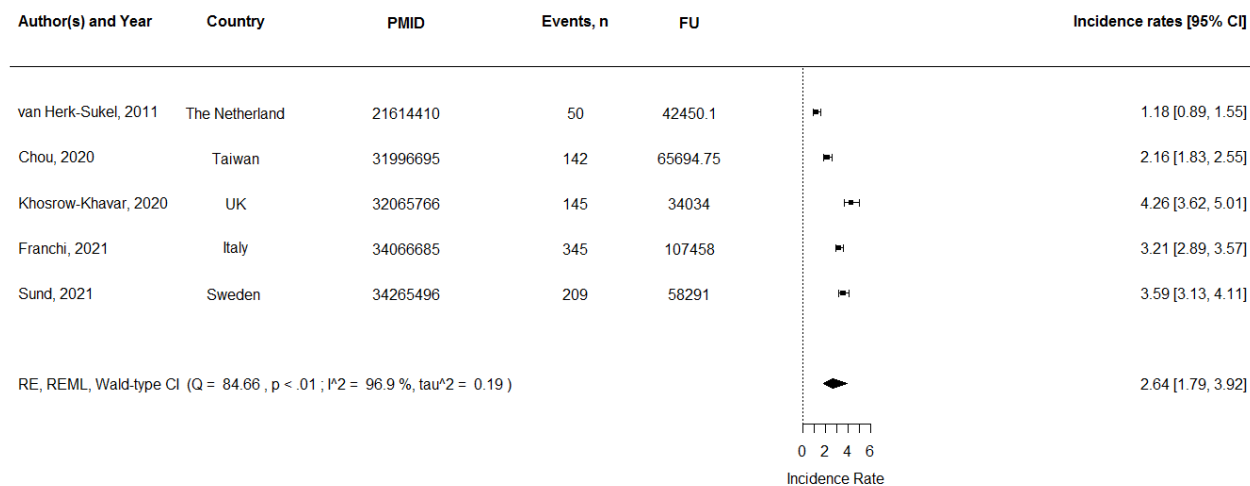


Figure S13. The incidence rate of ischemic stroke of any type in breast cancer patients per 1000 person-years of follow-up.

Abbreviations: CI, confidence interval; FU, follow-up (person-years); PMID, PubMed identification number; RE, random effects; REML, restricted maximum likelihood.

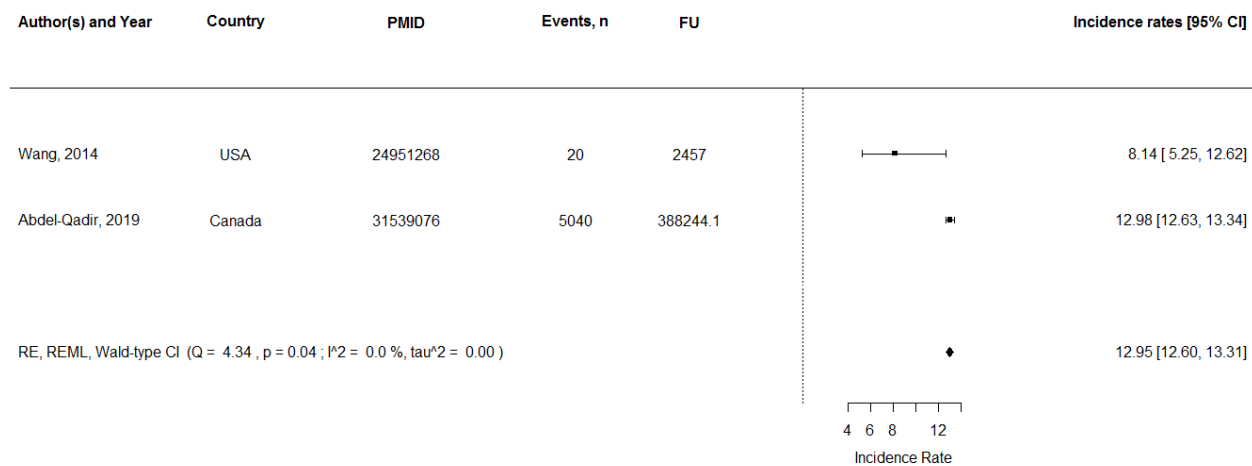


Figure S14. The incidence rate of atrial fibrillation in breast cancer patients per 1000 person-years of follow-up.

Abbreviations: CI, confidence interval; FU, follow-up (person-years); PMID, PubMed identification number; RE, random effects; REML, restricted maximum likelihood.

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