

Breastfeeding after breast cancer in young BRCA carriers

Eva Blondeaux , MD¹, Virginia Delucchi, MSc¹, Elene Mariamidze , MD², Rinat Bernstein-Molho , MD³, Sophie Frank , MD⁴, Alberta Ferrari , MD^{5,6}, Sabine Linn , MD⁷, Hee Jeong Kim , MD⁸, Elisa Agostinetti , MD⁹, Shani Paluch-Shimon , MD^{10,11}, Laura Cortesi , MD¹², Antonio Di Meglio , MD, PhD¹³, Judith Balmana , MD^{14,15}, Rinat Yerushalmi , MD¹⁶, Kenny A. Rodriguez-Wallberg , MD¹⁷, Tiphaine Renaud, MD¹⁸, Wanda Cui , MD^{19,20}, Halle C.F. Moore , MD²¹, Stephanie M. Wong , MD²², Katarzyna Pogoda , MD²³, Maryam Lustberg, MD, MPH²⁴, Kelly-Anne Phillips , MD^{19,20,25}, Sileny Han , MD²⁶, Fabio Puglisi , MD^{27,28}, Claudio Vernieri , MD^{29,30}, Jyoti Bajpai, MD³¹, Amir Sonnenblick , MD³², Christine Rousset-Jablonski , MD^{33,34}, Laura De Marchis , MD^{35,36}, Ugo De Giorgi , MD³⁷, Giampaolo Bianchini , MD^{38,39}, Luis Texeira , MD⁴⁰, Francois P. Duhoux , MD, PhD⁴¹, Cynthia Villarreal-Garza , MD⁴², Valentina Sini, MD⁴³, Robert Fruscio , MD^{44,45}, Lucia Del Mastro , MD^{46,47}, Isabelle Demeestere , MD^{48,49}, Hatem A. Azim Jr, MD, PhD⁵⁰, Fedro A. Peccatori , MD⁵¹, Ann H. Partridge , MD, MPH⁵², Matteo Lambertini , MD, PhD^{*,46,47}

¹U.O. Epidemiologia Clinica, IRCCS Ospedale Policlinico San Martino, Genova, Italy

²Department of Oncology and Haematology, Todua Clinic, Tbilisi, Georgia

³Susanne Levy Gertner Oncogenetics Unit, Danek Gertner Institute of Human Genetics, Chaim Sheba Medical Centre affiliated to Tel Aviv University, Tel Hashomer, Israel

⁴Department of Medical Oncology, Institut Curie, Paris, France

⁵Hereditary Breast and Ovarian Cancer (HBOC) Unit and General Surgery 3—Senology, Surgical Department, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

⁶Department of General Surgery, University of Pavia, Pavia, Italy

⁷Department of Molecular Pathology, Netherlands Cancer Institute (NKI), Amsterdam, The Netherlands

⁸Division of Breast Surgery, Department of Surgery, Asan Medical Centre, University of Ulsan College of Medicine, Seoul, South Korea

⁹Academic Trials Promoting Team, Institut Jules Bordet, Université libre de Bruxelles (ULB), Hôpital Universitaire de Bruxelles (H.U.B.), Bruxelles, Belgium

¹⁰Breast Oncology Unit, Sharett Institute of Oncology, Hadassah University Hospital, Jerusalem, Israel

¹¹Faculty of Medicine, Hebrew University, Jerusalem, Israel

¹²Department of Oncology and Haematology, Azienda Ospedaliero—Universitaria di Modena, Modena, Italy

¹³Cancer Survivorship Program—Molecular Predictors and New Targets in Oncology, INSERM Unit 981, Gustave Roussy, Villejuif, France

¹⁴Hereditary Cancer Genetics Unit, Medical Oncology Department, Vall d'Hebron University Hospital, Barcelona, Spain

¹⁵Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain

¹⁶Davidoff Centre, Rabin Medical Centre, Tel Aviv University, Tel Aviv, Israel

¹⁷Department of Oncology/Pathology, Karolinska Institute and Reproductive Medicine, Karolinska University Hospital, Stockholm, Sweden

¹⁸Cancer Genetics Unit, Bergonie Institute, Bordeaux, France

¹⁹Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia

²⁰Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, VIC, Australia

²¹Department of Haematology and Medical Oncology, Cleveland Clinic Taussig Cancer Institute, Cleveland, OH, United States

²²Stroll Cancer Prevention Centre, Jewish General Hospital, and McGill University Medical School, Montreal, QC, Canada

²³Department of Breast Cancer and Reconstructive Surgery, Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw, Poland

²⁴Center for Breast Cancer, Smilow Cancer Hospital and Yale Cancer Center, New Haven, CT, United States

²⁵Centre for Epidemiology and Biostatistics, School of Population and Global Health, The University of Melbourne, Melbourne, VIC, Australia

²⁶Department of General Medical Oncology and Multidisciplinary Breast Centre, Leuven Cancer Institute, University Hospitals Leuven, Leuven, Belgium

²⁷Department of Medical Oncology, Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, Aviano, Italy

²⁸Department of Medicine, University of Udine, Udine, Italy

²⁹Medical Oncology Department, Breast Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

³⁰Oncology and Haematology-Oncology Department, University of Milan, Milan, Italy

³¹Tata Memorial Centre, Homi Bhabha National Institute (HBNI), Mumbai, India

³²Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

³³Department of Surgery, Leon Berard Cancer Centre, Lyon, France

³⁴The RESHAPE (RESearch on HealthcAre PErformance) Research Laboratory, INSERM U 1290, Lyon, France

³⁵Division of Medical Oncology, Department of Radiological, Oncological and Pathological Sciences, Sapienza University of Rome, Rome, Italy

³⁶Medical Oncology, Unit Department of Hematology, Oncology, Dermatology, Umberto I University Hospital, Rome, Italy

³⁷Department of Medical Oncology, IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) Dino Amadori, Meldola, Italy

³⁸Department of Medical Oncology, IRCCS Ospedale San Raffaele, Milan, Italy

³⁹Facoltà Medicina e Chirurgia, Università Vita-Salute San Raffaele, Milan, Italy

⁴⁰Breast Disease Centre, Hôpital Saint-Louis, Paris, France

⁴¹Cliniques Universitaires Saint-Luc, UCLouvain, Brussels, Belgium

⁴²Breast Cancer Center, Hospital Zambrano Hellion TecSalud, Tecnológico de Monterrey, San Pedro Garza Garcia, Mexico

⁴³Medical Oncology, Centro Oncologico Santo Spirito-Nuovo Regina Margherita, Rome, Italy

⁴⁴UO Gynecology, IRCCS San Gerardo dei Tintori, Monza, Italy

⁴⁵Department of Medicine and Surgery, University of Milan-Bicocca, Milan, Italy

⁴⁶Medical Oncology Department, U.O.C. Clinica di Oncologia Medica, IRCCS Ospedale Policlinico San Martino, Genoa, Italy

⁴⁷Department of Internal Medicine and Medical Specialties (DIMI), School of Medicine, University of Genova, Genoa, Italy

Received: March 24, 2025. Revised: May 28, 2025. Accepted: June 18, 2025

© The Author(s) 2025. Published by Oxford University Press.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (<https://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.

⁴⁸Department of Obstetrics and Gynaecology, Fertility Clinic HUB Erasme (U.L.B), Brussels, Belgium⁴⁹Research Laboratory on Human Reproduction, Université Libre de Bruxelles (U.L.B), Brussels, Belgium⁵⁰Cairo Cure Oncology Centre, Cairo, Egypt⁵¹Gynaecology Oncology Program, European Institute of Oncology (IRCCS), Milan, Italy⁵²Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, United States

*Corresponding author: Matteo Lambertini, MD, PhD, Medical Oncology Department, U.O.C. Clinica di Oncologia Medica, IRCCS Ospedale Policlinico San Martino—University of Genova, Largo Rosanna Benzi 10, 16132 Genova, Italy (matteo.lambertini@unige.it)

Abstract

Background: We investigated safety of breastfeeding after breast cancer in patients carrying germline BRCA pathogenic or likely pathogenic variants.

Methods: This was an international, multicenter, hospital-based, retrospective cohort study including BRCA carriers diagnosed with stage I–III invasive breast cancer at age 40 years or younger between January 2000 and December 2020 (NCT03673306). Locoregional recurrences and/or contralateral breast cancers, disease-free survival (DFS), and overall survival (OS) were compared between patients who breastfed after delivery and those who did not.

Results: Among 4732 patients included from 78 centers worldwide, 659 had a pregnancy after breast cancer diagnosis, of whom 474 delivered a child. After excluding patients with uptake of bilateral risk-reducing mastectomy prior to delivery ($n = 225$) or unknown breastfeeding status ($n = 71$), 110 (61.8%) breastfed (median duration 5 months) and 68 (38.2%) did not breastfeed. Compared to patients in the no breastfeeding group, those who breastfed were more frequently nulliparous at breast cancer diagnosis (61.8% vs 45.6%) and did not report prior smoking habit (71.8% vs 57.4%). After a median follow-up of 7.0 years following delivery, 7-year cumulative incidence of locoregional recurrences and/or contralateral breast cancers was 29% in the breastfeeding group and 36% in the no breastfeeding group (adjusted subdistribution hazard ratio [HR] = 1.08, 95% CI = 0.57 to 2.06). No difference in DFS (adjusted hazard ratio [aHR] = 0.83, 95% CI = 0.49 to 1.41) nor in OS (aHR = 1.32, 95% CI = 0.31 to 5.66) was observed.

Conclusions: Breastfeeding did not appear to be associated with a higher risk of developing locoregional recurrences or contralateral breast cancers, emphasizing the possibility of achieving a balance between maternal and infant needs without compromising oncological safety.

Introduction

Breast cancer is the most common malignancy affecting young women during their reproductive years.¹ Germline BRCA genetic testing is recommended for all young patients, regardless of family history or tumor biology,² given more than 12% of young patients with breast cancer are expected to carry a germline pathogenic or likely pathogenic variant (PV) in the BRCA1 and/or BRCA2 genes.³ In this patient population, additional reproductive considerations apply.⁴ Several studies demonstrated that pregnancy after diagnosis and treatment for breast cancer is safe with no associated increased risk of breast cancer recurrence,⁵ including among BRCA carriers.⁶

For women with prior history of breast cancer who become pregnant and have a live birth, breastfeeding can be a complex and emotional decision. Breast cancer treatment, especially surgery and radiotherapy, can impact a woman's ability to breastfeed.^{7,8} Approximately 80% of patients undergoing breast conserving surgery combined with radiotherapy experience reduced breast enlargement during pregnancy, with around 50% of them experiencing limited postnatal milk production from the ipsilateral breast.^{9–11}

In the general population, several studies suggested a protective effect of breastfeeding on the risk of developing breast cancer,¹² including the most aggressive form of triple-negative disease.¹³ A similar protective effect of breastfeeding on the risk of breast cancer development was observed for BRCA1 carriers but not for BRCA2 carriers.¹⁴ Very limited evidence is available regarding the potential benefits or risks of breastfeeding in young breast cancer survivors.^{15,16} For survivors who carry a BRCA1 or BRCA2 PV, the decision to breastfeed after breast cancer is even more complex considering their higher risk of new primary breast cancer in the remaining breast tissue and the indication for consideration of risk-reducing mastectomy.¹⁷

The BRCA BCY collaboration (NCT03673306) is the largest network of BRCA carriers with a history of breast cancer diagnosed at the age of 40 years or younger. Out of 4732 included patients, 659 had at least 1 pregnancy after breast cancer,⁶ representing a unique opportunity to evaluate the safety of breastfeeding in this special population.

Methods

Study design, setting, and patients

This was an international, multicenter, hospital-based, retrospective cohort study including young BRCA carriers with a history of breast cancer. As previously reported,⁶ eligible patients were women diagnosed at the age of 40 years or younger with invasive breast cancer between January 2000 and December 2020 and known to carry a germline PV in the BRCA1 and/or BRCA2 genes. For this analysis, only patients with a live birth after breast cancer were included.

Data collection and study oversight

Collected data included breast cancer history and treatment, BRCA PV, risk-reducing surgeries, reproductive outcomes, recurrences and survival. Diagnostic, treatment, and follow-up procedures were conducted according to the clinical practice of each center. Pregnancy status, its outcomes and breastfeeding were determined using medical records or through patient self-reports collected during follow-up visits or surveys, depending on the center.

The Institut Jules Bordet (Brussels, Belgium) was the coordinating center and served as the central ethics committee. The study received ethics approval by the local, regional, or national institutional review boards of participating centers whenever required by local regulatory authorities. Written informed

consent was obtained from participants before inclusion in centers with this requirement.

Reporting of the present work followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.¹⁸

Study objectives

The primary objective of the present analysis was to evaluate the association between breastfeeding and the development of locoregional recurrences and/or contralateral breast cancers. Secondary objectives were to evaluate the association between pregnancy, fetal, and obstetric outcomes and breastfeeding status as well as the association between breastfeeding and survival outcomes.

The primary endpoint was locoregional recurrences and/or contralateral breast cancers. Secondary endpoints included pregnancy, fetal, and obstetric outcomes, disease-free survival (DFS) and overall survival (OS). Disease-free survival and OS were computed according to Standardized Definitions for Efficacy End Points (STEEP) criteria.¹⁹

Young BRCA carriers with a live birth after breast cancer were divided into 4 groups: women who breastfed (breastfeeding group), women who did not breastfeed (no breastfeeding group), women who underwent risk-reducing mastectomy before delivery (not able to breastfeed), and women with unknown breastfeeding status.

Women who underwent bilateral risk-reducing mastectomy before delivery and women with unknown breastfeeding status were included only in descriptive analysis. To evaluate the safety of breastfeeding, only patients in the breastfeeding and no breastfeeding groups were included.

Statistical analysis

Cumulative incidence of locoregional recurrences and/or contralateral breast cancers was estimated using a competing risk model. Distant recurrences, second primary malignancies, and death without recurrence were considered competing events. The Fine and Gray model was used to estimate the corresponding subdistribution hazard ratio (sHR) and to adjust for covariates.²⁰ Adjustment was made for patient or tumor characteristics unbalanced between the groups as well as for known prognostic factors. Final adjustment was made for country, smoking habit, tumor grading, nodal status, hormone receptor status, and uptake of risk-reducing surgeries. Risk-reducing mastectomy after delivery and risk-reducing salpingo-oophorectomy were included in the model as time-dependent covariates.

The Kaplan-Meier method was used to estimate DFS and OS. Unadjusted and adjusted Cox models were used to compare DFS and OS according to breastfeeding status. All survival endpoints were computed from the date of delivery. Patients without the events of interest were censored at the time of last follow-up.

Subgroup analyses were performed according to specific BRCA gene, time from breast cancer diagnosis to conception (ie, pregnancy interval), hormone receptor status, and use of prior chemotherapy.

The following parameters about pregnancy, fetal, and obstetric outcomes were compared between patients in the breastfeeding and no breastfeeding groups: patient age at delivery, time from breast cancer diagnosis to delivery (ie, pregnancy interval), type of conception, number of live births at the first pregnancy after breast cancer, number of preterm (<37 weeks) or full-term (≥37 weeks) pregnancies, congenital malformations, pregnancy, and/or obstetric complications.

All statistical analyses were 2-sided with $P < .05$ considered statistically significant. No adjustment for multiple comparison was made. Analyses were performed using SAS version 9.4 (SAS Institute Inc.).

Results

Among the 4732 patients eligible for the study from 78 centers worldwide, 659 had a pregnancy after breast cancer diagnosis. After excluding patients with ongoing pregnancy, women that experienced abortions or miscarriages and those with a DFS event before delivery, 474 patients delivered a child (Figure 1).

Among the included patients, 110 breastfed their child, 68 did not breastfeed, 225 underwent bilateral risk-reducing mastectomy before delivery (thus were not able to breastfeed), and 71 had unknown breastfeeding status. Patient and tumor characteristics in the 4 groups are reported in Table S1.

After exclusion of patients with uptake of bilateral risk-reducing mastectomy and patients with unknown breastfeeding status, 178 patients were included in the primary analysis, of whom 110 (61.8%) breastfed and 68 (38.2%) did not breastfeed. Compared to patients in the no breastfeeding group, those in the breastfeeding group were more frequently nulliparous at the time of breast cancer diagnosis (61.8% vs 45.6%, $P = .026$) and did not report prior smoking habit (71.8% vs 57.4%, $P = .019$) (Table 1). Overall, 114 (64.0%) patients had undergone breast conserving surgery with radiotherapy and 164 (92.1%) had received (neo) adjuvant chemotherapy (Table 1). Among patients that breastfed, median duration of breastfeeding was 5 months (IQR 2-6 months).

Compared to patients in the no breastfeeding group, those in the breastfeeding group more frequently had a singleton pregnancy (90.9% vs 79.4%, $P = .029$; Table 2). Otherwise, no difference in pregnancy, fetal, or obstetrical outcomes was observed between the two groups. Among patients that breastfed, median age at delivery was 35.4 years (IQR 31.7-37.7 years) and median time from breast cancer diagnosis to delivery was 4.1 years (IQR 2.9-6.0 years). The majority of pregnancies occurred through spontaneous conception (80.0%) and were at term (80.0%) with no complications (73.6%).

Patient and tumor characteristics between patients in the breastfeeding and no breastfeeding groups according to specific BRCA gene are reported in Table S2.

After a median follow-up of 7.0 years (IQR 3.6-10.5 years) following delivery, 55 (30.9%) patients experienced locoregional recurrences or a contralateral breast cancer and 16 (9.0%) experienced a competing event (Table S3). No difference in cumulative incidence of locoregional recurrences and/or contralateral breast cancer events between the breastfeeding and no breastfeeding groups was observed (Figure 2). The 7-year cumulative incidence of locoregional recurrences and/or contralateral breast cancers was 29% (95% CI = 20 to 40) in the breastfeeding group and 36% (95% CI = 23 to 49) in the no breastfeeding group (unadjusted sHR = 0.84, 95% CI = 0.49 to 1.44, $P = .531$; adjusted sHR = 1.08, 95% CI = 0.57 to 2.06, $P = .518$).

Results of the subgroups analyses are reported in Table 3. No statistically significant interaction in the analysis of cumulative incidence of locoregional recurrences and/or contralateral breast cancer events was observed between the explored subgroups (specific BRCA gene, pregnancy interval, hormone receptor status, and chemotherapy use) and breastfeeding status.

Overall, 71 DFS events were observed, 42 (38.2%) in patients that breastfed and 29 (42.7%) in patients that did not breastfeed

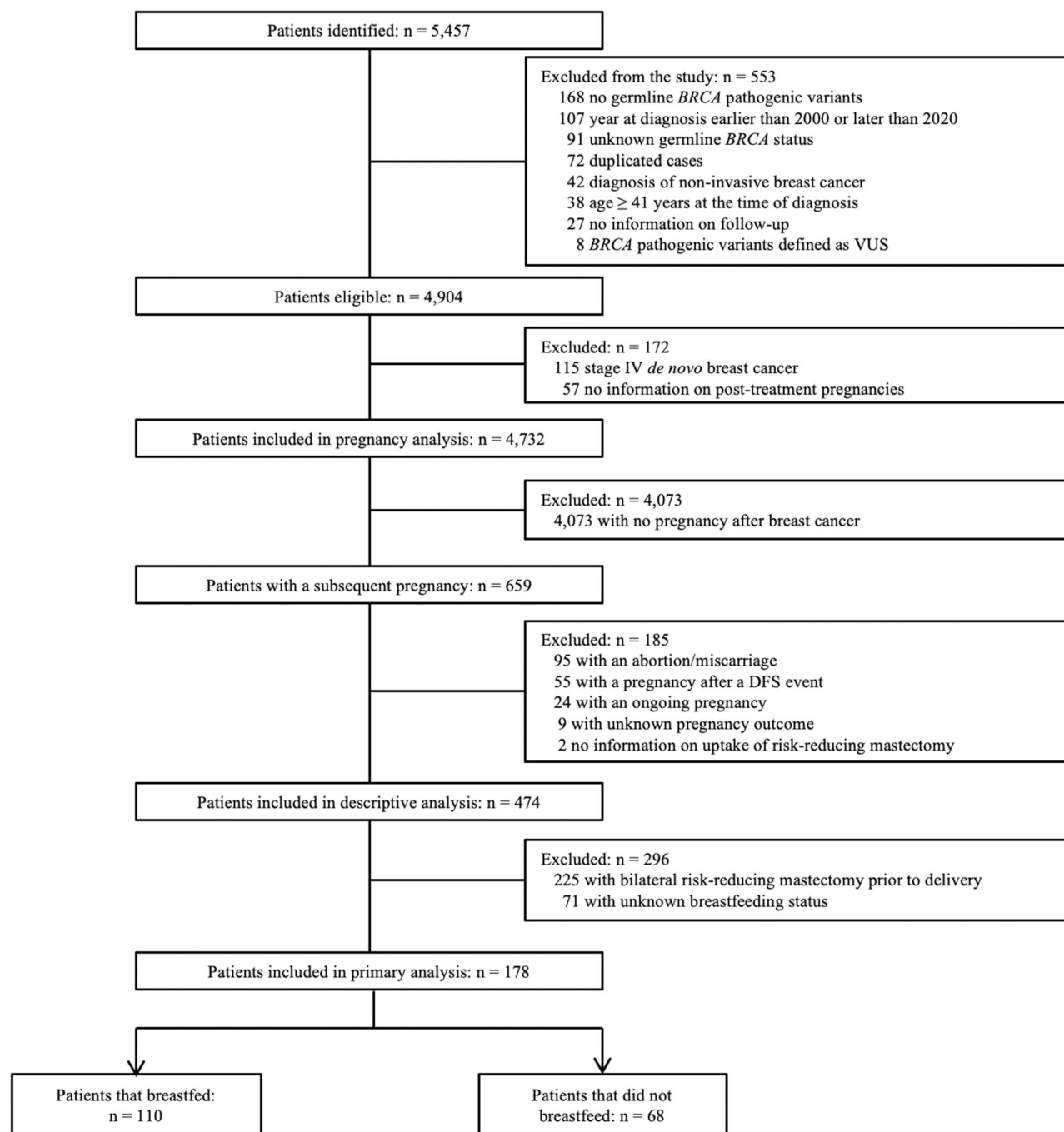


Figure 1. Study flow chart. Abbreviation: VUS = variant of unknown significance.

(Table S3). Seven-year DFS was 62% (95% CI = 50 to 71) and 54% (95% CI = 40 to 66) in patients that breastfed and that did not breastfeed, respectively (unadjusted HR = 0.79, 95% CI = 0.49 to 1.27, $P = .333$; adjusted HR [aHR] = 0.83, 95% CI = 0.49 to 1.41, $P = .096$) (Figure 3, A). The pattern of first DFS event in the breast-feeding and no breast-feeding groups according to specific BRCA gene is reported in Table S4.

Overall, 12 OS events were observed, 9 (8.2%) in patients that breastfed and 3 (4.4%) in patients that did not breastfeed. Seven-year OS was 92% (95% CI = 84 to 97) and 93% (95% CI = 79 to 98)

in patients that breastfed and that did not breastfeed, respectively (unadjusted HR = 1.78, 95% CI = 0.48 to 6.59, $P = .365$; aHR = 1.32, 95% CI = 0.31 to 5.66, $P = .117$) (Figure 3, B).

Discussion

In this large global study of young BRCA carriers with a subsequent live birth after prior breast cancer, nearly two thirds (61.8%) of patients breastfed after delivery. Patients who breastfed were more frequently nulliparous at the time of breast

Table 1. Patient and tumor characteristics at breast cancer diagnosis between patients who breastfed after delivery and those who did not.

	Breastfeeding group n = 110 (%)	No breastfeeding group n = 68 (%)	P
Region			.027
Latin/South America	3 (2.7)	0 (0.0)	
Australia/Oceania	7 (6.4)	1 (1.5)	
Northern Europe	15 (13.6)	5 (7.4)	
Eastern Europe	6 (5.5)	0 (0.0)	
North America	6 (5.5)	1 (1.5)	
Southern Europe	51 (46.4)	45 (66.2)	
Asia	22 (20.0)	16 (23.5)	
Children before diagnosis			.026
No	68 (61.8)	31 (45.6)	
Yes	33 (30.0)	34 (50.0)	
Unknown	9 (8.2)	3 (4.4)	
Smoking habit			.019
Never smoker	79 (71.8)	39 (57.4)	
Ever smoker	16 (14.6)	22 (32.4)	
Unknown	15 (13.6)	7 (10.3)	
Year at diagnosis			.477
2000-2004	24 (21.8)	14 (20.6)	
2005-2008	26 (23.6)	19 (27.9)	
2009-2012	35 (31.8)	14 (20.6)	
2013-2016	18 (16.4)	14 (20.6)	
2017-2020	7 (6.4)	7 (10.3)	
Age at diagnosis, median (IQR) years	30 (28-33)	30 (29-32)	.882
Age at diagnosis			.506
≤30 years	58 (52.7)	38 (55.9)	
31-35 years	42 (38.2)	27 (39.7)	
36-40 years	10 (9.1)	3 (4.4)	
Specific BRCA gene			.653
BRCA1	80 (72.7)	53 (77.9)	
BRCA2	29 (26.4)	14 (20.6)	
BRCA1 & BRCA2	1 (0.9)	1 (1.5)	
BRCA mutated, unknown if BRCA1 or BRCA2	0 (0.0)	0 (0.0)	
Tumor grade			.964
G1	1 (0.9)	1 (1.5)	
G2	17 (15.5)	11 (16.2)	
G3	75 (68.2)	47 (69.1)	
Unknown	17 (15.5)	9 (13.2)	
Tumor size			.185
T1 (≤2 cm)	53 (48.2)	25 (36.8)	
T2 (>2 to ≤5 cm)	43 (39.1)	31 (45.6)	
T3 (>5 cm) or T4	11 (10.0)	6 (8.8)	
Missing	3 (2.7)	6 (8.8)	
Nodal status			.448
N0	68 (61.8)	40 (58.8)	
N1	34 (30.9)	18 (26.5)	
N2 or N3	5 (4.6)	6 (8.8)	
Unknown	3 (2.7)	4 (5.9)	
Hormone receptor status			.595
ER and PR negative	72 (65.5)	43 (63.2)	
ER and/or PR positive	36 (32.7)	22 (32.4)	
Unknown	2 (1.8)	3 (4.4)	
HER2 status			.282
HER2 negative	98 (89.1)	63 (92.6)	
HER2 positive	4 (3.6)	0 (0.0)	
Unknown	8 (7.3)	5 (7.4)	
Locoregional treatment			.816
Breast conserving surgery with radiotherapy	73 (66.4)	41 (60.3)	
Breast conserving surgery without radiotherapy	2 (1.8)	2 (2.9)	
Radical surgery with radiotherapy	17 (15.5)	11 (16.2)	
Radical surgery without radiotherapy	15 (13.6)	12 (17.7)	
Unknown	3 (2.7)	2 (2.9)	
Use of chemotherapy			.709
No	8 (7.3)	6 (8.8)	
Yes	102 (92.7)	62 (91.2)	
Use of endocrine therapy ^a			.806
No	4 (11.1)	2 (9.1)	
Yes	32 (88.9)	20 (90.9)	

Abbreviations: ER = estrogen receptor; G = tumor grade; IQR = interquartile range; N = nodal status; PR = progesterone receptor; T = tumor size.

^a Calculated among patients with hormone receptor-positive breast cancer.

Table 2. Pregnancy, fetal, and obstetric outcomes between patients who breastfed after delivery and those who did not.

	Breastfeeding group, n = 110 (%)	No breastfeeding group, n = 68 (%)	P
Age at the time of delivery, median (IQR) years	35.4 (31.7-37.7)	35.1 (32.6-36.7)	.527
Time from breast cancer diagnosis to delivery, median (IQR) years	4.1 (2.9-6.0)	3.8 (3.0-5.9)	.682
Pregnancy interval			.672
≤5 years from diagnosis	71 (64.5)	46 (67.6)	
>5 years from diagnosis	39 (35.5)	22 (32.4)	
Type of conception			.794
Spontaneous pregnancy	88 (80.0)	52 (76.5)	
Use of assisted reproductive technology	11 (10.0)	9 (13.2)	
Unknown	11 (10.0)	7 (10.3)	
Number of live births at the first pregnancy after breast cancer			.029
1	100 (90.9)	54 (79.4)	
≥2	10 (9.1)	14 (20.6)	
Timing of delivery			.608
At term (≥37 weeks)	88 (80.0)	56 (82.4)	
Preterm (<37 weeks)	11 (10.0)	8 (11.8)	
Unknown	11 (10.0)	4 (5.9)	
Pregnancy complications			.619
None	81 (73.6)	53 (77.9)	
Delivery complications	6 (5.5)	1 (1.5)	
Pregnancy complications	7 (6.4)	6 (8.8)	
Congenital abnormalities	0 (0.0)	0 (0.0)	
Fetal complications	1 (0.9)	1 (1.5)	
Other complications	0 (0.0)	0 (0.0)	
Missing	15 (13.6)	7 (10.3)	

Abbreviation: IQR = interquartile range.

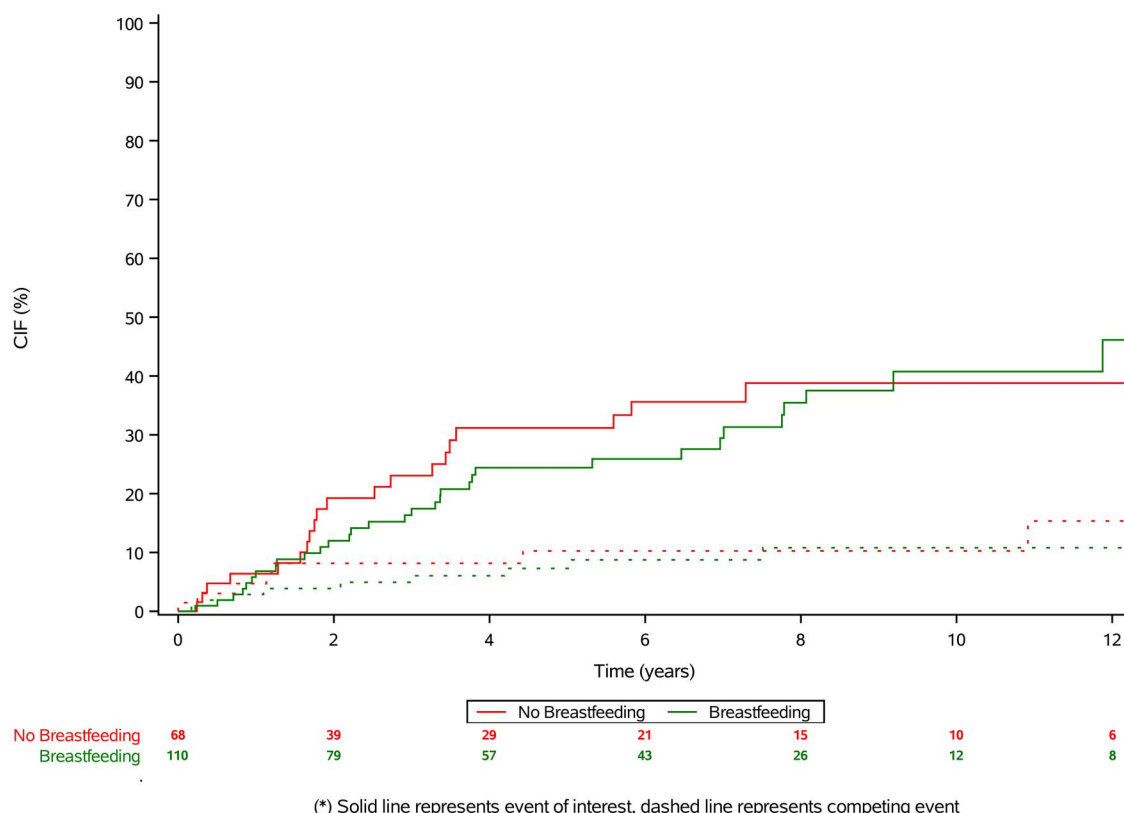
**Figure 2.** Cumulative incidence of locoregional recurrences and/or contralateral breast cancers between patients who breastfed after delivery and those who did not. CIF = cumulative incidence function.

Table 3. Subgroup analyses of cumulative incidence of locoregional recurrences and contralateral breast cancers.

Variable	Patients/Events/ Competing events	Univariate sHR (95% CI)	P ^a	Multivariate sHR (95% CI)	P ^a
Specific BRCA gene			.998		.840
BRCA1	133/38/9	0.88 (0.46 to 1.68)		1.20 (0.56 to 2.59)	
BRCA2	43/16/7	0.88 (0.34 to 2.52)		1.03 (0.29 to 3.67)	
Pregnancy interval			.141		.116
≤5 years	117/35/11	0.62 (0.33 to 1.19)		0.73 (0.35 to 1.55)	
>5 years	61/20/5	1.52 (0.56 to 4.11)		2.15 (0.68 to 6.79)	
Hormone receptor status			.728		.768
ER and PR negative	115/35/12	0.76 (0.39 to 1.49)		0.98 (0.45 to 2.14)	
ER and/or PR positive	58/19/4	0.93 (0.38 to 2.25)		1.22 (0.37 to 4.00)	
Use of chemotherapy			.184		.284
No	14/5/1	1.88 (0.58 to 6.11)		2.23 (0.56 to 8.89)	
Yes	164/50/15	0.78 (0.44 to 1.39)		0.97 (0.49 to 1.93)	

Abbreviations: CI = confidence intervals; ER = estrogen receptor; PR = progesterone receptor; sHR = hazard ratio.

^a P-value for interaction.

cancer diagnosis, did not report prior smoking habit and had a singleton pregnancy. Breastfeeding did not appear to be associated with a higher risk of locoregional recurrences and/or contralateral breast cancers. These are the first results detailing the frequency and safety of breastfeeding in young breast cancer survivors who harbor germline BRCA PVs, and provide valuable insights for counseling this special patient population.

While limited available evidence suggests that breastfeeding after breast cancer is feasible,^{11,15,21} to our knowledge, no prior study has tried to identify factors associated with breastfeeding, especially in BRCA carriers. In our study, as compared to patients that did not breastfeed, nulliparous women were more likely to breastfeed, suggesting that first-time mothers might be more motivated to breastfeed. Additionally, women who breastfed were more likely never smokers, indicating that lifestyle factors may be associated with the decision to breastfeed after breast cancer treatment.

Regarding maternal safety, prior evidence suggested that breastfeeding after breast cancer treatment did not appear to impact oncological outcomes; however, the sample size of these studies was very limited and no information on BRCA status was provided.^{15,16} In our study, breastfeeding in BRCA carriers was not associated with a higher risk of locoregional recurrences and/or contralateral breast cancers. In BRCA carriers, young age at diagnosis of breast cancer is known to be associated with an increased risk of developing second primary breast cancers.^{22,23} In our cohort, which included BRCA carriers with breast cancer diagnosis at a young age, 7-year cumulative incidence of locoregional recurrences and/or contralateral breast cancers was relatively high, being 29% in the breastfeeding group and 37% in the no breastfeeding group, with the majority of these events being second primary breast cancers (43 out of 55). Notably, for BRCA carriers, the increased risk of contralateral breast cancer and the beneficial effect of risk-reducing mastectomy in this special clinical setting should be considered during counseling and may play a crucial role in deciding to delay this surgical intervention in order to breastfeed.²⁴ With no increase in locoregional recurrences or contralateral breast cancers observed in either BRCA1 or BRCA2 carriers who breastfed, considering that pregnancies occurred a few years after breast cancer diagnosis, these results

are encouraging, although further studies are needed to confirm these data.

Despite the known limited postnatal milk production from the irradiated breast,¹⁵ patients and physicians should be informed that milk produced by the untreated breast may be sufficient for the nutritional needs of the newborn.²⁵ Guidelines recommend that women with prior history of breast cancer should be encouraged to breastfeed their children and that they should receive proper counseling in order to support unilateral breastfeeding, since misinformation is a major cause for avoiding breastfeeding.²⁶ However, no recommendation exists specifically for BRCA carriers with a history of breast cancer. Given that breastfeeding provides important nutritional and developmental benefits for infants,²⁷ our findings are helpful for informing these patients about their breastfeeding options.

In the interpretation of our results, some limitations should be acknowledged. This was a retrospective observational study. Information on breastfeeding was collected from oncological records and no information on breast side used for breastfeeding or the amount of milk production from the treated breast were collected. Furthermore, imbalances in patient and tumor characteristics between patients who breastfed after delivery and those who did not might have influenced long-term outcome results; however, survival models were adjusted for patient and tumor characteristics unbalanced between the groups as well as for known prognostic factors. Moreover, despite specific data quality control and data queries on this variable, 15% of the patients had missing information on breastfeeding uptake. Finally, given the frequency of bilateral mastectomy in this population, sample size was small precluding definitive conclusions. Despite these limitations, this is a unique cohort of young BRCA carriers, a relatively rare patient population, and it evaluated for the first time the safety of breastfeeding after breast cancer in this setting.

In conclusion, the decision to breastfeed after breast cancer among young BRCA carriers appears to be influenced by various factors, including parity and lifestyle factors. Nearly two thirds of patients who had a live birth after breast cancer opted to breastfeed without an apparent increase in the risk of developing locoregional recurrences or contralateral breast cancers. Our results provide novel information to guide health-care providers in the counseling of young BRCA carriers with breast cancer

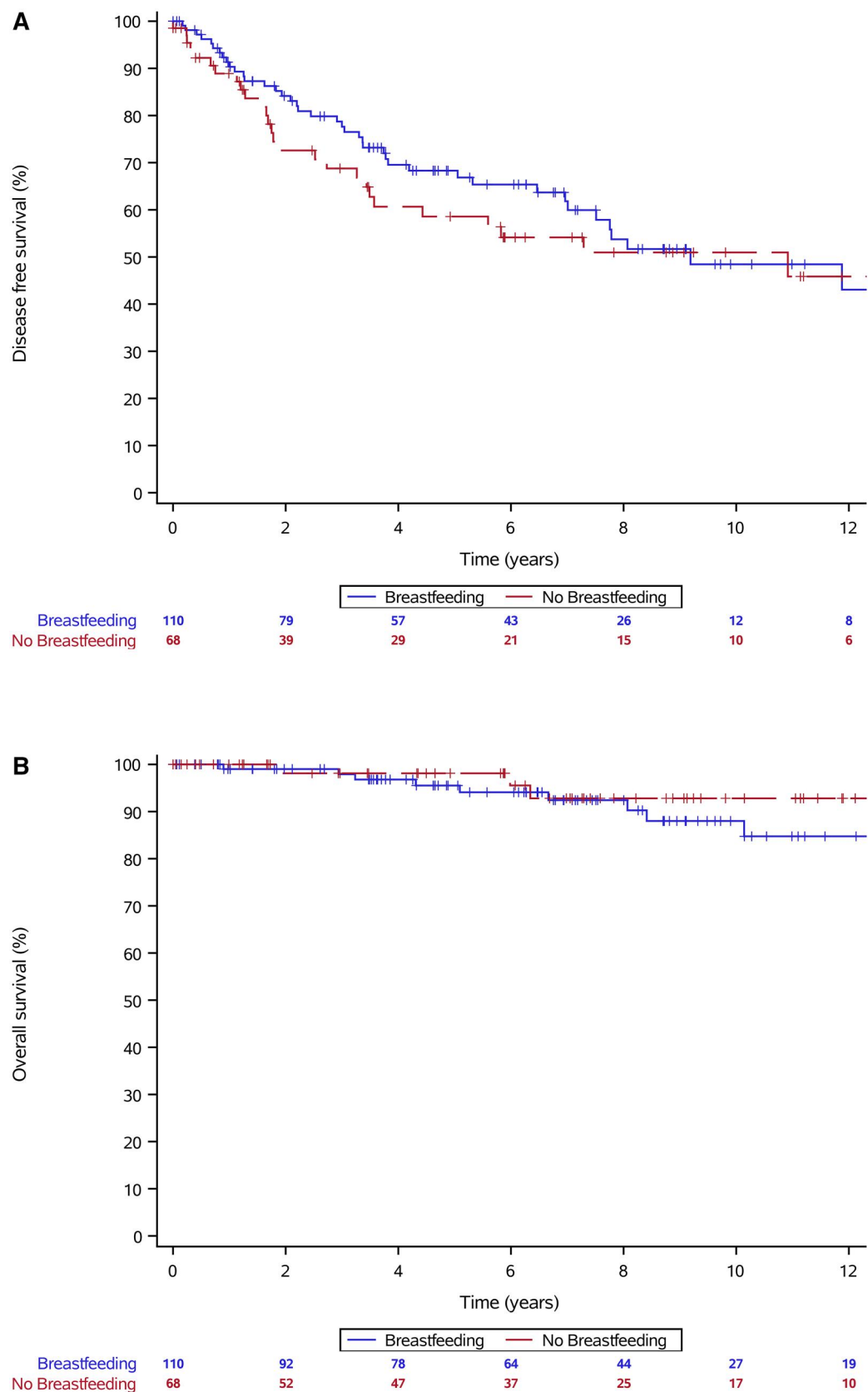


Figure 3. Survival outcomes between patients who breastfed after delivery and those who did not: (A) disease-free survival and (B) overall survival.

history who desire to breastfeed, emphasizing the possibility to achieve a balance between maternal and infant needs without compromising oncological safety. Further research is warranted to enhance our understanding of patients' needs and the implications of breastfeeding after breast cancer overall and particularly among BRCA carriers in order to further optimize their survivorship care.

Acknowledgments

An oral presentation of the study was given at the ESMO Congress 2024 (Barcelona, Spain) on September 14, 2024.

Author contributions

Eva Blondeaux (Conceptualization, Data curation, Formal analysis, Writing—original draft), Virginia Delucchi (Formal analysis, Writing—review & editing), Elene Mariamidze (Formal analysis, Writing—review & editing), Rinat Bernstein-Molho (Formal analysis, Writing—review & editing), Sophie Frank (Formal analysis, Writing—review & editing), Alberta Ferrari (Formal analysis, Writing—review & editing), Sabine Linn (Formal analysis, Writing—review & editing), Hee Jeong Kim (Formal analysis, Writing—review & editing), Elisa Agostinetti (Formal analysis, Project administration, Writing—review & editing), Shani Paluch-Shimon (Formal analysis, Writing—review & editing), Laura Cortesi (Formal analysis, Writing—review & editing), Antonio Di Meglio (Formal analysis, Writing—review & editing), Judith Balmana (Formal analysis, Writing—review & editing), Rinat Yerushalmi (Formal analysis, Writing—review & editing), Kenny A. Rodriguez-Wallberg (Formal analysis, Writing—review & editing), Tiphaine Renaud (Formal analysis, Writing—review & editing), Wanda Cui (Formal analysis, Writing—review & editing), Halle C.F. Moore (Formal analysis, Writing—review & editing), Stephanie M. Wong (Formal analysis, Writing—review & editing), Katarzyna Pogoda (Formal analysis, Writing—review & editing), Maryam Lustberg (Formal analysis, Writing—review & editing), Kelly-Anne Phillips (Formal analysis, Writing—review & editing), Sileny Han (Formal analysis, Writing—review & editing), Fabio Puglisi (Formal analysis, Writing—review & editing), Claudio Vernieri (Formal analysis, Writing—review & editing), Jyoti Bajpai (Formal analysis, Writing—review & editing), Amir Sonnenblick (Formal analysis, Writing—review & editing), Christine Rousset-Jablonski (Formal analysis, Writing—review & editing), Laura De Marchis (Formal analysis, Writing—review & editing), Ugo De Giorgi (Formal analysis, Writing—review & editing), Giampaolo Bianchini (Formal analysis, Writing—review & editing), Luis Texeira (Formal analysis, Writing—review & editing), Francois P. Duhoux (Formal analysis, Writing—review & editing), Cynthia Villarreal-Garza (Formal analysis, Writing—review & editing), Valentina Sini (Formal analysis, Writing—review & editing), Robert Fruscio (Formal analysis, Writing—review & editing), Lucia Del Mastro (Formal analysis, Writing—review & editing), Isabelle Demeestere (Formal analysis, Writing—review & editing), Hatem A. Azim (Formal analysis, Supervision, Writing—review & editing), Fedro A. Peccatori (Formal analysis, Supervision, Writing—review & editing), Ann H. Partridge (Formal analysis, Supervision, Writing—review & editing), and Matteo Lambertini (Conceptualization, Data curation, Formal analysis, Funding acquisition, Writing—original draft).

Supplementary material

Supplementary material is available at *JNCI: Journal of the National Cancer Institute* online.

Funding

The study was partly supported by the Italian Association for Cancer Research ("Associazione Italiana per la Ricerca sul Cancro", AIRC; MFAG 2020 ID 24698) and the 2022 Gilead Research Scholars Program in Solid Tumors with a focus on breast cancer. The funders of the study had no role in study design, data collection, analysis, interpretation, writing of the report, or decision to publish the manuscript and they had no access to the data. M.L. received support from the European Society for Medical Oncology (ESMO) for a translational research fellowship at the Institut Jules Bordet in Brussels, Belgium, at the time this study was initiated. H.J.K. receives support from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health and Welfare, Republic of Korea (grant HC20C0135). A.H. P. receives support from the Breast Cancer Research Foundation and Susan G. Komen. K.A.P. is an Australian National Health and Medical Research Council leadership fellow. Data collection for most Australian participants was through the kConFab Follow-Up Study with support from Cancer Australia and the National Breast Cancer Foundation (PdCCRS 1100868), Cancer Australia (809195), the Australian National Breast Cancer Foundation (IF 17), the Australian National Health and Medical Research Council (454508, 288704, and 145684), the US National Institutes of Health (1R01CA159868), the Queensland Cancer Fund, the Cancer Councils of New South Wales, Victoria, Tasmania, and South Australia, and the Cancer Foundation of Western Australia.

Conflicts of interest

E.B. reports speaker's fee from Eli Lilly, research funding (to the institution) from Gilead, all outside the submitted work. R.B.-M. reports honoraria for lectures from AstraZeneca, Roche, Pfizer; support for attending meetings from Pfizer (to the institution), AstraZeneca (to the institution), Gilead (to the institution), all outside the submitted work. E.A. reports speaker honoraria from Eli Lilly, AstraZeneca, Abiscint, Bayer; advisory role for AstraZeneca; research grant to institution from Gilead; meeting/travel grants from Eli Lilly, AstraZeneca, Daiichi Sankyo, Abiscint, Menarini, all outside the submitted work. A.D.M. reports speaker honoraria from Kephren and Techspert, all outside the submitted work. J.B. reports speaker honoraria and research at institution, AstraZeneca, all outside the submitted work. S.M.W. reports advisory role for Merck, AstraZeneca, all outside the submitted work. K.P. reports consultations/lectures/training/clinical trials and payment of conference fees from AstraZeneca, Gilead, Roche, Novartis, Eli Lilly, Pfizer, MSD, Swixx, all outside the submitted work. K.A.P. reports research funding to institution from AstraZeneca, all outside the submitted work. F.P. reports honoraria for advisory boards, activities as a speaker, travel grants from AstraZeneca, Daiichi Sankyo, Eisai, Eli Lilly, Exact Sciences, Gilead, Italfarmaco, Menarini, MSD, Novartis, Pfizer, Roche, and Seagen; research funding from AstraZeneca, Eisai, and Roche, all outside the submitted work. C.V. reports advisory role for Eli Lilly, Novartis, Pfizer, Menarini Stemline, Daiichi Sankyo; speaker honoraria from Eli Lilly, Menarini Stemline, MSD, Novartis,

Pfizer, Istituto Gentili, Accademia Nazionale di Medicina; research funding (to the institution) from Roche, all outside the submitted work. A.S. reports consulting or advisory role from Eli Lilly, Pfizer, Novartis, Roche, Gilead, MSD, AstraZeneca, Progenetics, Rhenium, Stemline; travel, accommodation, expenses from Neopharm, Celgene, Medison, Roche, MSD, Gilead, Pfizer; speakers' bureau from Teva, Roche, Pfizer, Novartis, Eli Lilly and grant support from Novartis, Roche, all outside the submitted work. U.D.G. reports advisory role/speaker's fee for AstraZeneca, MSD, Bristol Myers Squibb, Janssen, Astellas, Sanofi, Bayer, Pfizer, Ipsen, Novartis, and Merck; research funding (to the institution) from AstraZeneca, Sanofi, and Roche, all outside the submitted work. F.P.D. reports a post-doctoral research grant from Fondation Belge contre le Cancer; consulting fees from Amgen, AstraZeneca, Daiichi Sankyo, Eli Lilly, Gilead Sciences, MSD, Novartis, Pfizer, Pierre Fabre, Roche, and Seagen; and travel support from Amgen, AstraZeneca, Daiichi Sankyo, Gilead Sciences, Pfizer, Roche, and Teva, all outside the submitted work. V.S. reports speaker honoraria from Novartis, Daiichi Sankyo, Istituto Gentili, Accord; travel grants from Pfizer, Novartis, all outside the submitted work. I.D. reports research grants from Roche, speaker honoraria from Ferring, Novartis and travel grant from Theramex, Ferring, Gedeon Richter, all outside the submitted work. H.A.A. reports honoraria from AstraZeneca, consultant for LinKinVax and PEP Therapy, all outside the submitted work. M.L. reports advisory role for Roche, Lilly, Novartis, AstraZeneca, Pfizer, Seagen, Gilead, MSD, Exact Sciences, Pierre Fabre, Menarini, Nordic Pharma; speaker honoraria from Roche, Lilly, Novartis, Pfizer, Sandoz, Libbs, Daiichi Sankyo, Takeda, Menarini, AstraZeneca; travel grants from Gilead, Daiichi Sankyo, Roche, all outside the submitted work. Research funding (to the institution) from Gilead. M.L., who is a JNCI Associate Editor and co-author on this paper, was not involved in the editorial review or decision to publish the manuscript. All the other authors declare no conflict of interest.

Data availability

Data will be available upon reasonable request to the corresponding author, after proper review of the data transfer agreement of each participating center and if ultimately allowed by local Ethics Committees.

References

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA: Cancer J Clin*. 2023;73:17-48. <https://doi.org/10.3322/caac.21763>
2. Bedrosian I, Somerfield MR, Achatz MI, et al. Germline testing in patients with breast cancer: ASCO-Society of Surgical Oncology Guideline. *J Clin Oncol*. 2024;42:584-604. <https://doi.org/10.1200/JCO.23.02225>
3. Copson ER, Maishman TC, Tapper WJ, et al. Germline BRCA mutation and outcome in young-onset breast cancer (POSH): a prospective cohort study. *Lancet Oncol*. 2018;19:169-180. [https://doi.org/10.1016/S1470-2045\(17\)30891-4](https://doi.org/10.1016/S1470-2045(17)30891-4)
4. Buonomo B, Massarotti C, Dellino M, et al. Reproductive issues in carriers of germline pathogenic variants in the BRCA1/2 genes: an expert meeting. *BMC Med*. 2021;19:205. <https://doi.org/10.1186/s12916-021-02081-7>
5. Lambertini M, Blondeaux E, Bruzzone M, et al. Pregnancy after breast cancer: a systematic review and meta-analysis. *J Clin Oncol*. 2021;39:3293-3305. <https://doi.org/10.1200/JCO.21.00535>
6. Lambertini M, Blondeaux E, Agostinetto E, et al.; BRCA BCY Collaboration. Pregnancy after breast cancer in young BRCA carriers: an international hospital-based cohort study. *JAMA*. 2024;331:49-59. <https://doi.org/10.1001/jama.2023.25463>
7. Bhurosy T, Niu Z, Heckman CJ. Breastfeeding is possible: a systematic review on the feasibility and challenges of breastfeeding among breast cancer survivors of reproductive age. *Ann Surg Oncol*. 2021;28:3723-3735. <https://doi.org/10.1245/s10434-020-09094-1>
8. Lambertini M, Di Maio M, Poggio F, et al. Knowledge, attitudes and practice of physicians towards fertility and pregnancy-related issues in young BRCA-mutated breast cancer patients. *Reprod Biomed Online*. 2019;38:835-844. <https://doi.org/10.1016/j.rbmo.2018.11.031>
9. Tralins AH. Lactation after conservative breast surgery combined with radiation therapy. *Am J Clin Oncol*. 1995;18:40-43. <https://doi.org/10.1097/00000421-199502000-00008>
10. Moran MS, Colasanto JM, Haffty BG, Wilson LD, Lund MW, Higgins SA. Effects of breast-conserving therapy on lactation after pregnancy. *Cancer J*. 2005;11:399-403. <https://doi.org/10.1097/00130404-200509000-00007>
11. Sella T, Sorouri K, Rosenberg SM, et al. Breastfeeding experiences among young breast cancer survivors: a survey study. *Cancer*. 2025;131:e35585. <https://doi.org/10.1002/cncr.35585>
12. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. *Lancet*. 2002;360:187-195. [https://doi.org/10.1016/S0140-6736\(02\)09454-0](https://doi.org/10.1016/S0140-6736(02)09454-0)
13. Lambertini M, Santoro L, Del Mastro L, et al. Reproductive behaviors and risk of developing breast cancer according to tumor subtype: a systematic review and meta-analysis of epidemiological studies. *Cancer Treat Rev*. 2016;49:65-76. <https://doi.org/10.1016/j.ctrv.2016.07.006>
14. Kotsopoulos J, Lubinski J, Salmena L, et al.; Hereditary Breast Cancer Clinical Study Group. Breastfeeding and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers. *Breast Cancer Res*. 2012;14:R42. <https://doi.org/10.1186/bcr3138>
15. Azim HA, Bellettini G, Liptrott SJ, et al. Breastfeeding in breast cancer survivors: pattern, behaviour and effect on breast cancer outcome. *Breast*. 2010;19:527-531. <https://doi.org/10.1016/j.breast.2010.05.018>
16. Lambertini M, Kroman N, Ameye L, et al. Long-term safety of pregnancy following breast cancer according to estrogen receptor status. *J Natl Cancer Inst*. 2018;110:426-429. <https://doi.org/10.1093/jnci/djx206>
17. Sessa C, Balmaña J, Bober SL, et al.; ESMO Guidelines Committee. Risk reduction and screening of cancer in hereditary breast-ovarian cancer syndromes: ESMO Clinical Practice Guideline. *Ann Oncol*. 2023;34:33-47. <https://doi.org/10.1016/jannonc.2022.10.004>
18. von Elm E, Altman DG, Egger M, et al.; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007;370:1453-1457. [https://doi.org/10.1016/S0140-6736\(07\)61602-X](https://doi.org/10.1016/S0140-6736(07)61602-X)
19. Tolaney SM, Garrett-Mayer E, White J, et al. Updated standardized definitions for efficacy end points (STEEP) in adjuvant

- breast cancer clinical trials: STEEP version 2.0. *J Clin Oncol*. 2021;39:2720-2731. <https://doi.org/10.1200/JCO.20.03613>
20. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. *J Am Stat Assoc*. 1999;94:496-509. <https://doi.org/10.1080/01621459.1999.10474144>
 21. Gorman JR, Usita PM, Madlensky L, Pierce JP. A qualitative investigation of breast cancer survivors' experiences with breastfeeding. *J Cancer Surviv*. 2009;3:181-191. <https://doi.org/10.1007/s11764-009-0089-y>
 22. Graeser MK, Engel C, Rhiem K, et al. Contralateral breast cancer risk in BRCA1 and BRCA2 mutation carriers. *J Clin Oncol*. 2009;27:5887-5892. <https://doi.org/10.1200/JCO.2008.19.9430>
 23. Tung NM, Boughey JC, Pierce LJ, et al. Management of hereditary breast cancer: American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Guideline. *J Clin Oncol*. 2020;38:2080-2106. <https://doi.org/10.1200/JCO.20.00299>
 24. Blondeaux EVA, Sonnenblick A, Agostinetto E, et al. Association between risk-reducing surgeries and survival in young BRCA carriers with breast cancer: an international cohort study. *Lancet Oncol*. 2025;26:759-770. [https://doi.org/10.1016/S1470-2045\(25\)00152-4](https://doi.org/10.1016/S1470-2045(25)00152-4)
 25. Johnson HM, Mitchell KB. Breastfeeding and breast cancer: managing lactation in survivors and women with a new diagnosis. *Ann Surg Oncol*. 2019;26:3032-3039. <https://doi.org/10.1245/s10434-019-07596-1>
 26. Helewa M, Lévesque P, Provencher D, et al.; Breast Disease Committee and Executive Committee and Council, Society of Obstetricians and Gynaecologists of Canada. Breast cancer, pregnancy, and breastfeeding. *J Obstet Gynaecol Can*. 2002;24:164-180; quiz 181-184.
 27. Victora CG, Bahl R, Barros AJD, et al.; Lancet Breastfeeding Series Group. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *Lancet*. 2016;387:475-490. [https://doi.org/10.1016/S0140-6736\(15\)01024-7](https://doi.org/10.1016/S0140-6736(15)01024-7)