Breast Cancer Surveillance Consortium

BCSC

BREAST CANCER SURVEILLANCE CONSORTIUM MANUSCRIPT AND GRANT PROPOSAL FORM

ADMINISTRATIVE

1. General information about the proposal

Date proposal submitted to the BCSC:	June 1, 2001
Project title:	The Effect of Breast Augmentation on Mammographic Screening and Cancer Severity
Short title (5 words or less):	Augmentation Paper
Project leader name:	Diana Miglioretti
Project leader affiliation/ organization:	Group Health Cooperative
Project leader address:	1730 Minor Avenue, Suite 1600 Seattle, WA 98101
Project leader email address:	miglioretti.d@ghc.org
Project leader phone number:	(206) 287-4266

2. List all collaborators associated with this proposal (add rows if more than 8):

Name	Affiliation	Email Address	Will this person be part of the small working group?** (**YES, NO, or N/A**)
Carolyn Rutter	Group Health Cooperative	rutter.c@ghc.org	Yes
Karla Kerlikowske	UCSF	kerliko@itsa.ucsf.edu	Yes
Gary Cutter	Colorado	cutterg@prodigy.net	Yes

***Only applicable for a** manuscript that arises from the use of pooled BCSC data from one or more consortium sites that use the SCC to conduct analyses (or the lead investigator is a member of the BCSC).*

3. Proposed Timetable:

Date of proposed initiation: July 1, 2001

Proposed completion dates: January 2004

Anticipated deadlines (if applicable): none

4. Purpose of this request (Double-click boxes to mark all that apply):

☒ Data analysis for manuscript Target journal: _____JAMA_____

☐ Preliminary data for grant proposal

☐ Inputs/calibration data for simulation, decision analysis, or cost-effectiveness model

☐ Development of statistical methods for publication: Target journal: _____

☐ Development of statistical methods – Other: Please specify: _____

☐ Other: Please describe: _____

5. Which registries will be included in this study? (Double-click boxes to mark all that apply):

☒ Colorado (Denver) ☒ San Francisco

☒ New Hampshire ☒ Vermont

☒ North Carolina ☒ Western Washington (Group Health)

☒ New Mexico

6. Would you prefer an analyst from the SCC do the analysis? (Double-click appropriate box):

☒ **YES** (please skip to question #8)

☐ **NO, I would like a dataset sent to me, but will perform the analysis** in collaboration with the Statistical Coordinating Center

☐ **NO, I would like a dataset sent to me with** minimal consultation with the Statistical Coordinating Center

☒ Other (please describe): Project Lead from SCC to do analysis
_____

7. If you would like a dataset sent to you, please indicate the type of data request. *Note that any data request that includes dates, zip codes, specific ages >89 years or masked BCSC site identifiers will require completion of a HIPAA data use agreement following approval of your proposal.* (Double-click boxes to mark all that apply)**.**

☐ De-identified data/ **aggregate** data

☐ De-identified **individual level** data (without dates, zip codes, specific ages >89 or BCSC site IDs)

☐ **Limited dataset:** De-identified individual level data with: (**mark all that apply**):
- ☐ Dates
- ☐ Specific age >89 years
- ☐ Zip codes (*will generally not be released without careful consideration & protection in place)*

☐ Other (please describe) _____

FUNDING *(Only applicable for projects not directly funded by the BCSC)*

8. Do you have funding to support BCSC efforts for this project? *Lack of funding will not influence whether or not a project is approved. However, priority in the queue (for starting the project) is given to projects that can fund BCSC efforts.* (Double-click boxes to mark all that apply)**.**

☐ Yes, I have sources of funding (please state all sources):

Source: _____ **Start & end dates** (month/yr - month/yr) _____

Source: _____ **Start & end dates** (month/yr - month/yr) _____

☐ No

☒ Not needed

☐ Other (please describe): _____

RESEARCH OBJECTIVE/MAJOR HYPOTHESES:

9. Please fill out the content areas of your proposed research below.
Abstract (Provide a brief abstract of 300 words or less)

Specific Aims: To examine the effect of breast augmentation on accuracy of screening mammography and severity of cancer at diagnosis. We will compare sensitivity of screening mammography, mode of diagnosis (screening mammogram, diagnostic mammogram, or interval cancer), % of invasive cancer (compared to DCIS), tumor stage, tumor size, tumor grade, nodal status, and ER status for augmented and non-augmented women. This project proposes to answer the following research question: Does the distribution of characteristics associated with cancer severity (e.g., stage, grade, tumor size) differ for women with breast augmentation mammoplasty compared to those without breast augmentation? Does the sensitivity of screening mammography vary among women with breast augmentation mammoplasty compared to those without breast augmentation?

Background: Although many studies have shown that breast implants do not increase the risk of breast cancer (1), women with breast implants may be more likely to be diagnosed with more advanced disease than women without implants since breast augmentation interferes with routine mammographic evaluation (2-8). Previous studies on breast cancer following breast augmentation give contradictory results (1-3, 9-13); however, most of these studies were limited by very small sample sizes. In addition, all studies included cases that were diagnosed prior to 1989 when radiologists' began using implant displacement views, which improve visualization of breast tissue in women with implants (7).

Two larger studies on breast cancer following augmentation mammoplasty were recently published by Brinton and colleagues (1) and Skinner and colleagues (2). The Brinton et al. study concentrated on risk of breast cancer, but also compared stage of cancer in 116 augmented women to 52 non-augmented women who had undergone other types of plastic surgery. Although they found women with breast implants tended to have later stage disease (35% versus 17% with regional or distant disease), this difference was not statistically significant; however, the differences remained after adjusting for other factors such as access to medical care. The study conducted by Skinner and colleagues (2) compared 99 cancer cases in augmented women to 2,857 cases in non-augmented women. They found that mammography was less sensitive for augmented women (54% compared to 95%) and that augmented women were more likely to be diagnosed with palpable tumors (83%

compared to 59%), invasive carcinoma (82% compared to 72%), and nodal involvement (48% compared to 36%).
Data from the Breast Cancer Surveillance Consortium offer a unique opportunity to more closely examine the effect of breast augmentation on mammographic sensitivity and cancer severity at diagnosis using more recent data from multiple sites throughout the United States. We expect to have more power to detect differences than the previous studies given the large number of cancers in non-augmented women available for comparison (however, we will likely have slightly fewer numbers of cancers in augmented women). In addition, we can adjust for hormone therapy (HT), family history of breast cancer, and time since last mammogram.

Methods:

We will select all women diagnosed with their first invasive cancer or DCIS from January 1994 to present. For these women, we will look at their most recent exam prior to diagnosis (either diagnostic or screening) and their most recent screening exam within two years of diagnosis (which will be the same exam for women with screen-detected cancer). We may need to consider alternative definitions of a screening exam if indication is routinely coded as diagnostic for routine mammograms in asymptomatic women with implants. We will classify augmentation status using self-reported breast augmentation at the screening exam. Among women with only a diagnostic exam, we will use self-reported augmentation at the time of the diagnostic exam. We exclude women with self-report of breast augmentation to only one breast, women with insufficient information about self-report of breast augmentation, women with self-report of mastectomy or breast reconstruction, and women with prior self-report of breast augmentation (if she did not report breast augmentation at either exam).
To determine mode of detection, we will look at all mammograms that occurred within twelve months of diagnosis. Women without a mammogram will be classified as an interval cancer. We will need to agree on the best way to classify women with mammograms as screen or diagnostic detected (for example, how do we classify women with short-interval follow-up?).
We will estimate sensitivity separately for screening and diagnostic exams. We will look at the most recent exams within 24 months of diagnosis.

Variables needed:

Outcome variables
DCIS or invasive
Stage
Tumor size
Nodal involvement
Grade
ER status
Mode of detection (screening vs. diagnostic exam)

Covariates

Age at diagnosis
Site
Time since last screening mammogram (prior to dx)
Result of last screening mammogram (within two years prior to dx)
Indicator of mammogram within two years of the mammogram that lead to diagnosis
Indicator of mammogram within two years of the most recent screening mammogram prior to diagnosis
HT use
Family history of breast cancer
Self-report of symptoms
Race

Study Years:
We will include all women with cancer diagnosed from January 1994 to present.

Inclusion/exclusion criteria:
Women with invasive cancer or DCIS diagnosed 1994 or later. Exclusion criteria include personal history of breast cancer (self-report or found in the registry), self-report of mastectomy or breast reconstruction prior to diagnosis, self-report of breast augmentation to only one breast, or missing or inconsistent self-report of breast augmentation

Power analyses:
Brinton and colleagues (1) found that 35% of women with augmented breasts had stage II or higher disease (regional or distant disease) compared to 17% of women without augmentation. If we have 70 augmented women and 17,000 non-augmented women with cancer, we will have over 80% power to detect this difference.

Analytic plan:
We will use logistic regression (and polytomous or linear regression where noted), adjusting for age, site, HT use, family history, and time since last mammogram (prior to the mammogram from which the cancer was detected) to compare the probability of the following outcomes in augmented women compared to non-augmented women:

1. Invasive disease versus DCIS
2. Mode of detection (screening, diagnostic, interval – polytomous regression)
3. Stage II or higher disease
4. Tumor 20 mm or greater (possible treat as continuous with linear regression)
5. Grade III or higher disease
6. Nodal involvement
7. ER negative status

In addition, to test for an effect of augmentation on mammographic sensitivity, we will fit logistic regression models, adjusting for age, site, HT use, family history, and time since last mammogram (prior to the mammogram from which the cancer was detected), to compare the probability of a positive screening mammogram and the probability of a positive diagnostic mammogram (separate models).

Mock Tables

Table 1. Characteristics of study population.
Table 2. Mode of detection and sensitivity of screening and diagnostic exams by augmentation.
Table 3. Distribution of cancer characteristics by augmentation.
Table 4. Change in odds of outcome for women with augmentation compared to women without augmentation.

Table 1. Characteristics of study population.

	Breast Augmentation		No Augmentation	
	N	(%)	N	(%)
Age (years)				
30-39				
40-49				
50-59				
60-69				
70+				
Education				
High School or Less				
Some College				
College Graduate or beyond				
Missing				
Mammogram within 2 years prior to diagnosis?				
Yes				
No				
HT Status				
HT user				
Non-user				
Family history of BC				
Yes				
No				
Self-report of symptoms				
Lump or nipple discharge				
Other symptoms				
None				
Missing				
Race				
White				
Black				
Asian				
Native American/Alaskan Native				
Other (includes Mixed)				
Missing				

Table 2. Mode of detection and sensitivity of screening and diagnostic exams by augmentation.

	Breast Augmentation		No Augmentation	
	N	(%)	N	(%)
Mode of Detection				
Screening Exam				
Diagnostic Exam				
Interval Cancer				
Result of Prior Screening Exam				
TP				
FN				
Result of Prior Diagnostic Exam				
TP				
FN				
Sensitivity (95% CI)				
Screening exam				
Diagnostic exam				

Table 3. Distribution of tumor characteristics by augmentation.

	Breast Augmentation		No Augmentation	
	N	(%)	N	(%)
Invasive vs. DCIS				
Invasive				
DCIS				
Stage				
Stage 0				
Stage I				
Stage II				
Stage III or IV				
Tumor Size				
<10 mm				
11 - 19 mm				
20 + mm				
Grade				
Grade I				
Grade II				
Grade III				
Grade IV				
ER Status				
Positive				
Negative				
Nodal Involvement				
Yes				
No				

Table 4. Change in odds of outcome for women with augmentation compared to women without augmentation.

	Augmentation vs. No Augmentation	
Outcome	OR	(95% CI)
Positive screening exam		
Mode of detection:		
Diagnostic vs. Screen detected		
Interval vs. Screen detected		
Invasive cancer versus DCIS		
Stage >= 2		
Tumor Size > 20 mm		
Grade III or IV		
ER Negative		
Nodal involvement		

To be completed by the SCC:

What is the assigned Project Number? AB-32DM

Date of Steering Committee Review: April 24, 2001

Steering Committee Action:
☒ Approved ☐ Not Approved ☐ Conditionally Approved (state reason: _____)

Is this proposal a:
- ☐ Grant
- ☒ Manuscript
- ☐ Data Request

Is the lead investigator from:
- ☒ The BCSC
- ☐ External to BCSC
- ☐ Ancillary grant (if checked, please answer the questions below):
  - What is the name of this grant? (e.g., FAVOR, CISNET) _____
  - Is this grant using BCSC data? (YES/NO) _____

What is the current status of the project:
- ☐ In analysis
- ☒ In Queue
- ☐ Completed

SCC analyst needed?
- ☐ YES (who?) _____ Should s/he be added to the author list? _____
- ☒ NO

SCC Programmer needed?
- ☐ YES (who?) _____
- ☒ NO

Type of data requested:
- ☐ N/A – data not requested – SCC will do the analysis
- ☐ Aggregated de-identified data
  - ☐ Does the data contain reader, site, and/or facility IDs?
- ☐ De-identified individual level data (w/o identifiers – e.g., no zip codes, ages >89 or site identifiers)
- ☒ De-identified individual level data with dates, specific age>89, zip codes, or masked BCSC identifiers