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In 1998 approximately 36,000 women less than age 45 will be diagnosed with breast cancer. For these young patients therapeutic options are a major concern. Many have delayed childbearing. Their desire to start a family or have additional children has been found to impact their treatment decisions. Many doctors have been cautious in recommending pregnancy after breast cancer because of the recognized poor outcome of women diagnosed with breast cancer during pregnancy. Current therapeutic modalities are less toxic, of shorter duration and improve prognosis; therefore, many pre-menopausal women remain fertile or regain fertility after primary breast cancer treatment. Recommendations concerning subsequent childbearing may significantly affect the quality of life for these young patients. However, the safety of subsequent pregnancy remains to be confirmed. Several population-based studies which relied on national registries have indicated pregnancy after treatment for breast cancer may enhance survival; however, the authors have suggested that disease free women may be more likely to consider post-treatment childbearing. The current retrospective study conducted through review of Kaiser Permanente medical records will compare survival of women with a positive subsequent pregnancy history with matched cases with a negative post treatment pregnancy history. The ratio of matching is four to one providing adequate power to detect a hazard ratio of two or greater.

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Joanne Petrek MD 10/14/98

PI - Signature Date

DOES SUBSEQUENT PREGNANCY INFLUENCE BREAST CANCER SURVIVAL?

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DOES SUBSEQUENT PREGNANCY INFLUENCE BREAST CANCER SURVIVAL?

INTRODUCTION

Among women less than age 40 invasive breast cancer affects one in 227 American women [1]. Although the incidence rate for this age group has not changed in recent years, the female population under age 40 has increased considerably resulting in an anticipated 36,000 newly diagnosed cases of invasive breast cancer in 1998. National data also indicate that breast cancer is the leading cause of cancer death among women under the age of 55 in contrast to older women for whom lung cancer causes more cancer deaths [1].

Breast cancer was found to be hormone dependent more than one hundred years ago [2]. This led some clinicians to include bilateral oophorectomy in the treatment regimen for young breast cancer patients. The introduction of systemic therapy in the 1970s resulted in successful reduction in the risk of recurrence among young women treated for breast cancer. Since these young patients are assumed to be at greater risk of recurrence, treatment options generally include systemic therapy in order to maximize disease-free and total survival time [3,4]. Recent findings support the expected greater survival among young breast cancer patients primarily associated with administration of systemic therapy [5]. Therapeutic options are a major concern for many young breast cancer patients who have delayed childbearing to complete their educational and professional goals. Their desire to start a family or have additional children after breast cancer treatment has been found to impact their treatment decisions [6].

Some young patients have rejected systemic therapy in order to preserve their fertility and retain the option of pregnancy after breast cancer treatment. Oncologists have frequently been asked by young patients if and when pregnancy is safe. Many doctors have been cautious in recommending pregnancy after breast cancer because of the recognized poor outcome of women diagnosed with breast cancer during pregnancy. Clinicians, committed to eradicating any potential cancer cells that might leave their patients at risk of recurrence, have belittled patients' questions about future fertility [7].

In the past few years adjuvant therapy regimes have been administered for shorter intervals with less toxicity enabling some young patients to retain regular menstrual cycles. Current therapeutic modalities are less toxic, of shorter duration and improve prognosis; therefore, many premenopausal women remain fertile or regain fertility after primary breast cancer treatment. Recommendations concerning subsequent childbearing may significantly affect the quality of life after breast cancer treatment of young women [8].

Physicians tend to be cautious when asked by their patients about their desire to become pregnant because of the concern that the hormonal elevations of pregnancy may stimulate latent foci of carcinoma creating an unnecessary risk of disease recurrence [9]. Therefore, the recommended interval between breast cancer treatment and subsequent pregnancy varies greatly among clinicians ranging from six months to ten years [10,11]. However, the potential hormonal stimulation of pregnancy may not influence the natural history of breast cancer in a homogeneous manner. Stage of disease at diagnosis, type and duration of adjuvant chemotherapy and hormonal therapy, as well as estrogen and progesterone receptor status, are established prognostic factors. In addition, age at diagnosis, prior

pregnancy history, and genetic susceptibility to breast cancer may modify the risk of disease dissemination following subsequent pregnancy. These factors must be assessed before clinical recommendations can be meaningful. More research is needed to define optimal intervals for subsets of patients.

In response to increased requests from breast cancer patients to address their psychological as well as physical well-being [8], several studies have addressed the influence of pregnancy after breast cancer on survival. The few published studies that address these issues have included limited clinical data to adequately answer the specific questions of patients and their doctors. The uncertainty expressed by clinicians reflects the limited data available from recent published reports which have hesitantly implied subsequent pregnancy does not appear to adversely affect survival. Several recent reports using computerized data files in countries with nationalized health records have indicated no adverse effect of subsequent pregnancy [12,13]. However, these prospective analyses could not rule out selection bias; one report noted the 'healthy mother effect' implying that only those young patients free of recurrent disease would be considering pregnancy [14]. The most recent publication by Kroman and colleagues of Denmark compared survival of 84 women with one or more term pregnancies after breast cancer with 77 who chose to have an induced abortion, 12 who miscarried and 5,552 who did not experience a subsequent pregnancy [13]. The authors acknowledged that they were not able to adjust adequately for all factors that may have been associated with improved survival of the 84 women with one or more term pregnancies.

Physicians have been surveyed for their clinical recommendations regarding pregnancy after breast cancer. One study conducted in 1953 reported that most doctors advised their young patients to avoid becoming pregnant [15]. A second survey conducted forty years later in Britain noted physicians remained uncertain about the safety of subsequent pregnancy [16]. The results of this recent survey reflect the limited literature on this topic.

The current clinically based study addresses a major question often asked by young women: will subsequent pregnancy cause a recurrence of breast cancer? To answer this question the complete medical histories of breast cancer patients provided in the Kaiser records are being reviewed and abstracted. The complete records available for a large number of breast cancer patients has enabled this study of breast cancer survival to identify cases with a history of subsequent pregnancy and age and stage match cases without documentation of a post-diagnosis pregnancy.

BODY

Overview of Scope of Work

This retrospective study is a collaborative effort conducted by researchers of the Kaiser Permanente Medical Care Program facilities in Oakland, California with investigators in New York. The databases maintained by the Kaiser Division of Research provide a unique opportunity to identify young breast cancer patients and to follow their course of therapy and outcome through review of their medical records.

Progress during the past 12 months has focused on accomplishing the following:

1. Identification of 87 breast cancer patients age 44 or less at diagnosis with a positive history of one or more subsequent pregnancies. Only pregnancies initiated after diagnosis are being included.

2. Detailed medical record abstracting of each case on standardized form for computerization [sample form included in appendices]

3. Color coded work sheets were developed by the record abstractor to enable careful identification of the timing of pregnancies in relation to breast cancer diagnosis [samples are included in the appendices].

4. Comparison group identification by matching each case with a positive history of subsequent pregnancy to four breast cancer patients without a history of subsequent pregnancy. Matching criteria originally proposed include:
    a) age at diagnosis and year of diagnosis
    b) stage at diagnosis
    c) months of survival from diagnosis to first subsequent pregnancy
    d) disease status during the early trimester of the first subsequent pregnancy

5. Creation of a case comparison log of potential matches for review by the medical record abstractor using color coded worksheets. Comparison cases included in the study will have no medical record indication of any subsequent pregnancy regardless of outcome such as induced or spontaneous abortion.

6. A quality control study was conducted at the time of staff change to assess efficiency and accuracy of medical record abstracting.

Following completion of data collection and computerization, the data files will be sent to the New York team of investigators by the Kaiser research staff. The following will then be conducted:

1. Perform matched statistical analyses to compare the risk of recurrence and death due to breast cancer among women with a positive history of subsequent pregnancy in comparison with their matched cases who did not have a post-treatment pregnancy.

2. If the number of cases with a positive history of post-treatment pregnancy enable case specific analyses, recurrence and death due to breast cancer will be studied in relation to:
    a) the interval between diagnosis and first post-treatment pregnancy
    b) the number of post-treatment pregnancies
    c) pregnancy outcomes: births, spontaneous miscarriages, and/or induced abortions
    d) neonatal outcomes in relation to patient and treatment characteristics

Current Status of Research Project

The research activities at Kaiser began soon after the awarding of support from the U.S. Army Medical Research Acquisition Activity. The first three months were devoted to refining the study protocol and working with Leo Hurley, Data Manager at the Kaiser research center, who conducted the record linkages necessary to identify the cases with a positive pregnancy history for this case-case comparison study. Data files from the Kaiser Permanente Regional Cancer Registry, Kaiser Hospitalization Registry, and the California Automated Mortality Linkage and Information System have been used. The data files also identify the location of the necessary medical records for both inpatient and outpatient care which are permanently maintained and available for research. Since Kaiser members are not restricted to specific outpatient facilities, records related to their medical history before and after breast cancer treatment may be maintained at more than one site. Therefore, the medical record abstracting may require travel to multiple Kaiser locations.

Dr. Jeanne Petrek, principal investigator, and Dr. Ruby T. Senie, co-principal investigator have been kept informed of the study progress at Kaiser by phone, fax, email and in person meetings. Dr. Senie has traveled to Kaiser for several meetings each year. During the initial visit she met with Dr Robert Hiatt, the collaborating epidemiologist, and other key members of the Kaiser Division of Research to launch the project. The study protocol was reviewed with the Project Coordinator, Ms. Barbara Anglin. Before developing a draft of the data collection instrument, several medical records were reviewed to acquaint Ms. Anglin and Dr. Senie with the organization of the medical charts and the location of the essential information in the record including: pathology reports, treatment records and birth notations.

Following extensive record review, the data collection instruments were modified. The most important addition was the recognition that some breast cancer patients may have had pelvic surgery before or during their breast cancer treatment that may have affected their ability to become pregnant. In addition, some women were pregnant at the time of breast surgery but chose to have an induced abortion. This information is not computerized but was identified through medical record review. A copy of the final data collection form is included in the Appendices. The data management division of the Kaiser Division of Research has developed the data entry program for this project and has begun to computerize the data from cases with a positive subsequent pregnancy history.

The medical record analyst, Ms. Judith Tallman, was hired and oriented to the study by Ms Anglin. The essential focus on details required for this study was carefully reviewed with members of the Kaiser staff to insure consistency of data collection and interpretation over time. Reproductive factors preceding breast cancer diagnosis are recorded as well as pregnancy history during and after primary therapy to insure exclusion of cases with co-existing pregnancy and breast cancer. Birth outcomes,

including condition of the newborn, and determination of cause of death is also being recorded. To determine if the cause of death was breast cancer, medical records and death certificates are carefully reviewed to locate evidence of recurrent disease prior to death. Dr. Senie met with Ms Anglin and Ms. Tallman to review completed study data forms, address specific questions pertaining to some breast cancer cases, and interpretation of complexities requiring special attention. To facilitate careful case selection for the study Ms. Tallman developed work sheets with a calendar to enable careful identification of the timing of pregnancies in relation to breast cancer diagnosis. Color codes copies of these are included in the appendices.

The initial computer search identified 89 women diagnosed with breast cancer aged 44 or younger through 1991 who had a link with the hospital admission file indicating one or more subsequent pregnancies. Following careful review of medical records 87 cases with post diagnosis pregnancy meet all study criteria of a total of 149 women younger than 45 years at the time of diagnosed with breast cancer. Those cases excluded were either found to have had benign breast disease or records indicated the woman was pregnant at the time of diagnosis. The number of eligible cases may be increased as the records of comparison cases [4 per positive post diagnosis pregnancy case] are reviewed. Kaiser computer files do not include dates of induced abortion elected by some women who experience an unplanned subsequent pregnancy. During medical record review the date of breast cancer diagnosis has been verified, pathology records reviewed and abstracted to confirm the diagnosis. Dates of diagnosis and pregnancy outcome are compared to eliminate women who were pregnant at the time of diagnosis of breast cancer. Only pregnancies initiated after diagnosis are included. The completed data forms of the 87 cases already identified have been submitted to the data entry department for keypunching.

During the meticulous medical record review, 40 cases were found to have concurrent pregnancy and breast cancer. The dates of these concurrent pregnancy terminations, primarily due to induced or spontaneous abortion, were not included in the computerized Kaiser data files. These cases have been excluded from the current study database; however, the collaborating investigators are considering an additional study to assess the impact on survival of concurrent pregnancy and breast cancer compared to women with breast cancer not complicated by pregnancy.

In May 1998 Ms. Tallman, the medical record abstractor, announced that she would be leaving the position with Kaiser. An experienced Kaiser medical record abstractor, Ms Maureen Duffey, was selected as Ms. Tallman's replacement. Ms. Duffey has been employed by the research division of Kaiser for more than three years. Ms. Duffey was assigned to this study for several weeks overlap before Ms. Tallman's departure from the position. During the overlap Ms. Tallman and Ms. Anglin reviewed all aspects of the carefully developed, detailed data collection protocol with Ms Duffey.

A brief quality control study was incorporated into the training program for Ms. Duffey who was instructed to re-review the medical records of 10 cases previously completed by Ms. Tallman. Green data forms for this quality control/training procedure are included in the appendices. Ms. Anglin reviewed the two sets of abstracted records. In 93% of the cases, the abstracted information was identical. Differences that appeared reflected multiple notes in the medical record for specific items such as method of tumor detection, a frequent source of discordance in medical records. Physicians may note a tumor was detected by mammography; however, the mammography may have recommended by an internist or gynecologist after patient or physician palpation of a lesion. Slight differences in dates of last contact, generally less than 30 days, were noted when several records were

compared. The multiple charts available for review per person require careful check for last contact with the patient as these dates are included in only one record.

The current activities at Kaiser are directed toward identifying the four comparison cases without a subsequent pregnancy for each case with a positive history. This requires careful review of the matching characteristics in each record. To date 174 medical records have been review resulting in identification of 149 meeting matching criteria of the ultimate 348 comparison case records required.

Figure 1 in the appendices presents the current status of the research project and the sequence of tracking events that followed initial case identification. Cases without linkage to pregnancy records will be over-sampled by 25% in order to eliminate any cases found, during medical record abstracting, to have a prior history that would have impacted hormonal status prior to breast cancer such as bilateral oophorectomy or an endocrine condition that may have affected fertility. However, Drs. Petrek and Senie agreed that women with a history of tubal ligation prior to breast cancer diagnosis would be acceptable for inclusion among the comparison cases. During medical record abstracting some comparison cases may be found to have a history of spontaneous miscarriage or induced abortion following diagnosis of breast cancer, information not included in the computerized Kaiser data files. These cases will be added to the subset with a positive history of subsequent pregnancy. For any additional case subjects identified during record review to have a positive post-treatment pregnancy, four control cases will be selected from the cohort with a negative history.

Medical record review of all study subjects will supplement computerized follow-up information. Known or suspected breast cancer prognostic factors are being abstracted. Essential data from medical records includes stage of breast cancer at diagnosis, cancer treatment, and disease status during follow-up. Matched analyses will be conducted to compare survival among cases with and without a history of subsequent pregnancy. Potential prognostic factors, not included as matching variables, such as prior pregnancy history and family history of breast cancer, will be controlled in the analysis. Analyses among cases with a positive history will address prognostic differences by age at diagnosis and age at subsequent pregnancy. If the number of cases with a positive history of subsequent pregnancy permits, the length of the interval between diagnosis and first subsequent pregnancy, pregnancy outcome, and number of post treatment pregnancies will be studied in relation to survival.

Computerized Data

The following figure describes the linking of data files which will produce the composite data set to be transferred to Dr. Senie who is now affiliated with the Columbia University School of Public Health for statistical analyses. No personal identifying data will be included. However, the unique Kaiser medical record number will be scrambled before inclusion in the data file. Members of the Division of Research of Kaiser will retain a file with both the scrambled and actual medical record number in order to identify subjects if questions pertaining to individual cases arise during analysis.

Future Research Activities

After receiving the final data file, the statistical assistant at Columbia will perform univariate and multivariate analyses to provide an overview of the data from the cases abstracted. The first survival analyses will compare risk of recurrence and death due to breast cancer among cases with and without a subsequent pregnancy history. Prognostic factors that influence breast cancer survival will be included in Cox proportional hazards survival models including tumor characteristics, especially estrogen and progesterone receptor levels of the primary tumor, which may influence the impact of pregnancy on the course of breast cancer. Survival time will be measured from the time of first pregnancy until disease recurrence and death due to breast cancer. Cases will be censored at date of death due to causes other than breast cancer or date last known alive. Interaction effects will also be considered. If a second primary breast cancer is diagnosed before a first pregnancy, this event will be included as an independent variable. When a second breast cancer occurs after pregnancy, it will be handled as a time dependent variable.

The second phase will focus on women with a positive history, assessing any survival differences related to months between diagnosis and first post-treatment pregnancy, total number of pregnancies, and pregnancy outcomes (eg. birth, spontaneous miscarriage or induced abortion). Time dependent variables such as number of pregnancies will be assessed using the Cox proportional hazards model.

The third set of analyses will focus on pregnancy related events among cases with a positive history; complications of pregnancy and presence of any fetal abnormalities, detectable at birth, will be studied in relation to characteristics of the cases (eg. breast cancer treatment, prior reproductive history, and age at pregnancy). Complications of pregnancy and the presence of any abnormalities of the neonate noted at birth will be studied in a case-case design in order to identify any factors that differentiate women with and without adverse outcomes during pregnancy, at delivery and in the neonate. Logistic regression will be used to assess risk factors for developing complications of pregnancy. Potential risk factors include age at pregnancy, previous complications of pregnancy and prior pregnancy outcomes. Interaction effects will also be considered.

Power Calculations

Estimates of power were based on an expected number of deaths among the 95 cases preliminarily identified with a positive history of pregnancy after breast cancer and 380 comparison cases without a subsequent pregnancy. Power may be slightly diminished as only 87 cases have met the inclusion criteria at this stage of medical record review. We anticipate the continuing medical record review to locate 4 comparison cases for each case with a subsequent pregnancy will provide at least 3 additional cases meeting study criteria. Therefore our initial power calculations which were performed on an estimated 90 included cases are appropriate. The smallest detectable hazard of death due to breast cancer for power of 0.80 and 0.90 at the 0.05 (2-sided) level of significance is given in Table 1 for a range of deaths that could have occurred in the study population. If by chance, five additional cases are identified, greater power will be provided by the study population of 4 comparison cases for each case with a positive pregnancy history.

The minimal detectable hazard ratio provided in Table 1 was based on two independent samples and range from 1.69 to 2.32 depending on the power and the number of years survived prior to pregnancy. We would anticipate the power to be even greater for the actual matched paired failure time analysis. The influence of pregnancy after breast cancer on risk of disease recurrence will also be studied. The number of women found to have had recurrent disease will be greater than the number of deaths due to breast cancer during follow-up. Consequently, the power will be even greater to detect any differences in risk of recurrence, associated with subsequent pregnancy, than for mortality.

Table 1. Minimal detectable hazard ratio for paired survival times in relation to history of subsequent pregnancy either positive or negative.

# Cases & Pregnancy Hx	Conditioned on Survival to Yr	Expect # Deaths	Power 0.80	Power 0.90
90 Positive	2	108	1.71	1.87
360 Negative	3	90	1.80	1.98
	4	67	1.98	2.21
	5	56	2.11	2.38
95 Positive	2	114	1.69	1.83
360 Negative	3	95	1.78	1.94
	4	71	1.94	2.16
	5	59	2.07	2.32

CONCLUSIONS

The research activities conducted to date support our concern related to the presence of selection bias among breast cancer patients with a history of subsequent pregnancy. Careful medical record review identified 40 cases with pregnancy concurrent with breast cancer among the 323 records reviewed to date. The link between diagnosis and pregnancy for these cases was not detected by computer linkage. Most were terminated by induced abortion and will potentially be the subject of a future study.

Matching a case without a history of subsequent pregnancy on stage of disease at the time of the post diagnosis pregnancy in our case subject is a time consuming but essential task. This step is required in order to avoid the inclusion of breast cancer patients with recurrent disease in the comparison group potentially matching a case who was free of recurrent disease at conception.

The authors of several recent publications addressing the issue of pregnancy after breast cancer continue to be concerned with selection bias [12-14]. Following a presentation by Dr. Jeanne Petrek at a recent meeting of the Metropolitan New York Breast Group, an organization of clinicians and researchers practicing in New York, New Jersey and Connecticut, the discussion revealed a lack of consensus concerning recommendations to young breast cancer patients regarding the safety of subsequent pregnancy. The results of both the retrospective and the prospective studies funded by the Department of Defense are eagerly awaited.

CHANGES IN RESEARCH TEAM

Dr. Jeanne Petrek, Breast Surgeon, Memorial Sloan Kettering Cancer Center, New York, NY

Initially, this project was conceived by Dr. Senie, who was Principal Investigator when the study was submitted by the Department of Defense Breast Cancer Research Program and Drs. Jeanne Petrek and Dr. Ann Zauber of Memorial Sloan Kettering were Co-Investigators. After Dr. Senie accepted a faculty appointment at School of Public Health of Columbia University as Professor of Clinical Public Health, Dr. Petrek assumed the position of Principal Investigator of the study for administrative purposes at Memorial Sloan Kettering.

Dr. Ruby Senie, Professor of Clinical Public Health, Columbia School of Public Health, New York, NY

Dr. Senie has continued to be responsible for working closely with the research team of Kaiser Permanente overseeing the data collection activities, addressing data abstracting questions, etc. Dr. Senie has visited the Kaiser Division of Research four times during the past 12 months to guide the research team in their identification of cases with and without subsequent pregnancy histories for inclusion in the study population. The limited number of very young breast cancer patients required some decisions on matching criteria. Various options for slight relaxation of matching criteria were discussed with a member of the biostatistical staff of Kaiser and agreed upon.

Dr. Catherine Schaefer, Research Investigator, Division of Research, Kaiser Permanente Medical Care Program, Oakland, CA

Early in 1998 Dr. Robert Hiatt, principal investigator of the Kaiser Permanente component of the project, accepted the position of Deputy Director of the Division of Cancer Control and Population Sciences of the National Cancer Institute. Dr. Hiatt selected Dr. Schaefer to assume his role of directing the medical record abstracting and computerization of data at Kaiser. Dr. Schaefer has been a member of the Division of Research at the Kaiser Center for more than nine years. She has many publications addressing women's health issues, many of them with Dr. Hiatt as a co-author. She has expressed great interest and enthusiasm for the study of the safety of pregnancy after breast cancer. Ms. Anglin and Ms. Duffey have commented that Dr. Schaefer is a very supportive project director.

Research Staff of Kaiser Permanente

Ms. Barbara Anglin retains the position of project director and Ms. Maureen Duffey has replaced Ms. Judith Tallman. These long-term Kaiser research staff members are knowledgeable and dedicated to the project. Mr. Leo Hurley has competently handled data management since the study was launched.

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APPENDICES

FLOW CHART – CURRENT STATUS

MEDICAL RECORD ABSTRACT FORM

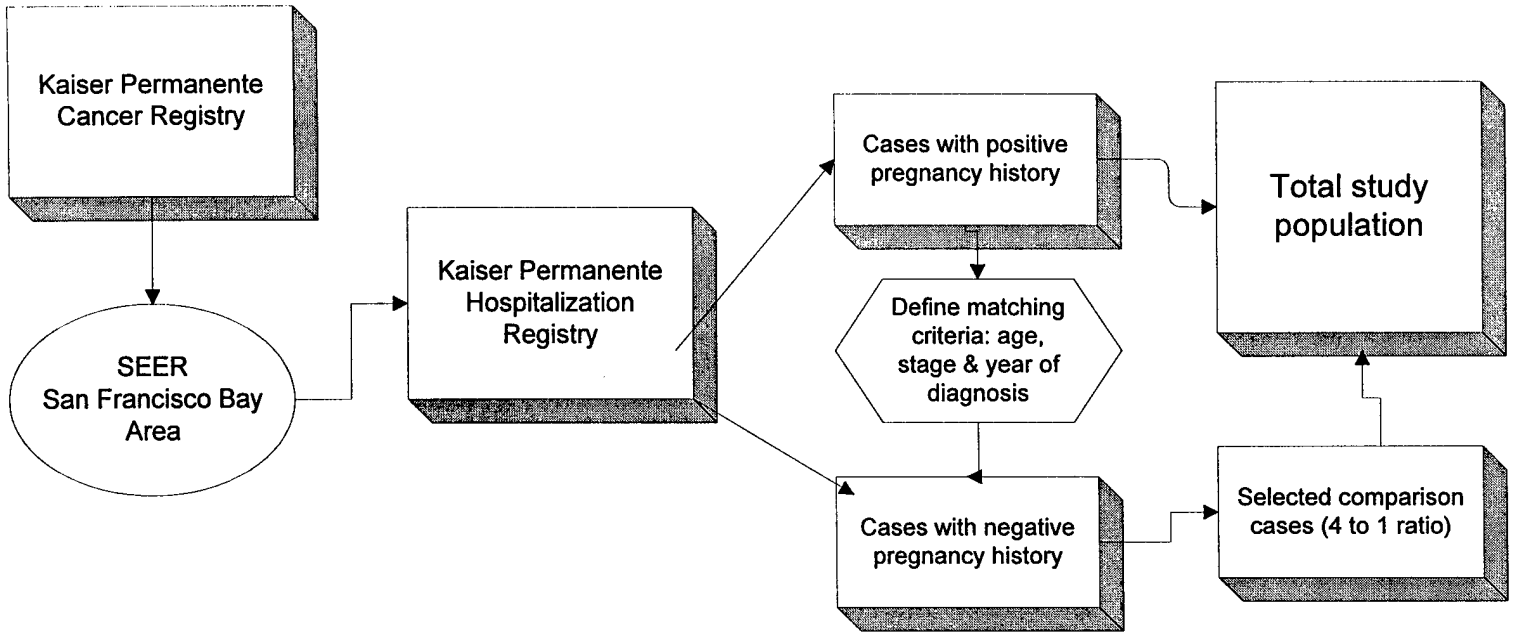
COLOR CODED WORKSHEETS

YELLOW – CASE WITH POSITIVE SUBSEQUENT PREGNANCY HISTORY

BLUE - CASE WITH NEGATIVE SUBSEQUENT PREGNANCY HISTORY

GREEN – QUALITY CONTROL STUDY

Does subsequent pregnancy influence breast cancer survival?



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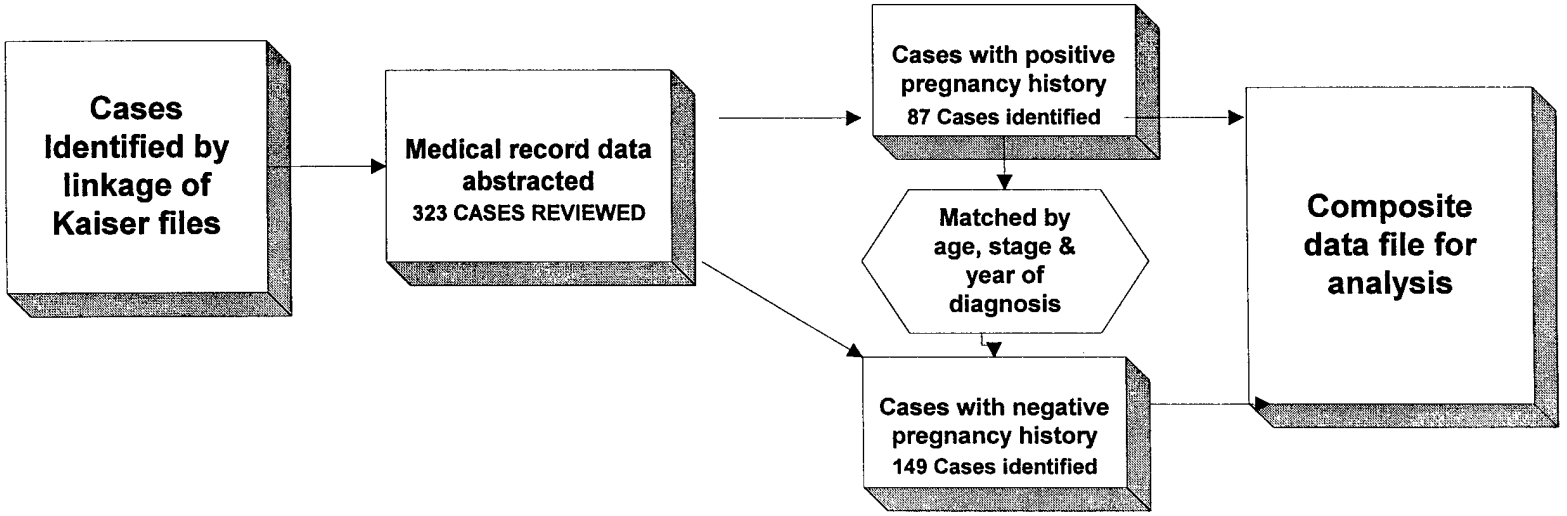

BREAST CANCER STUDY
Medical Record Abstract Form

Date Started __ __ \ __ __ \ __ __ __ __
Date Completed __ __ \ __ __ \ __ __ __ __

1. **Name**_____
   last first
2. **Kaiser Medical Record Number** __ __ __ __ __ __ __ __ __
3. **Date of birth** __ __ \ __ __ \ __ __ __ __
   month day year
4. **Race** 1 = Hispanic 4 = White
   2 = Asian 5 = Other
   3 = Black
5. **Primary Kaiser Facility** __ __ __

Does this woman meet the criteria? (yes = 1, no = 2)

6. **Was diagnosis of breast cancer confirmed?** ____
7. **Age < 45 at time of Dx?** ____
8. **Is this woman able to become pregnant following dx and tx or breast cancer? (Look for history of pelvic surgery before or after breast cancer dx and tx that affects fertility. If her fertility is gone after a subsequent pregnancy, she is still eligible for the study.)** ____

If any of the answers to #6, #7, or #8 are "no", the woman is excluded from the study.

If all the answers to #6, #7, and #8 are "yes", continue the review.

MRN __ __ __ __ __ __ __ __ __

Cancer # 1

1. Date of first diagnosis of breast cancer: __ ____ ____ __ __ __ (month day year) Height ___ft. __ __inches
Weight __ __ __ lbs.

2. Method of first detection:
   1. Self palpation
   2. Clinical exam
   3. Screening mammogram

3. Mammography:
   1. Negative
   2. Suspicious
   3. Not done
   4. Positive

4. *First* Breast Surgery:
   1. Mastectomy
   2. Lumpectomy/Local Excision

5. Axillary Dissection (first surgery):
   1. Yes
   2. No

6. *Second* Breast Surgery : date __ ____ ____ __ __ __ (month day year)
reason: 1. Residual
2. Reccurence

7. *Second* Breast Surgery (type):
   1. Mastectomy
   2. Lumpectomy/Local Excision

8 Axillary Dissection (second surgery):
   1. Yes
   2. No

9. Tumor size at diagnosis - Cancer #1
   Size __ __.__(cm)

10. Tumor type:
   1. In situ
   2. Invasive

11. Lymph nodes:
   Total # removed/examined: __ __
   Total # positive: __ __

12. Tumor ER status - Cancer #1
   0 = Negative
   1 = Positive
   2 = Borderline
   9 = Not Available

MRN _ _ _ _ _ _ _ _ _

13. Tumor PR status - Cancer #1
    0 = Negative
    1 = Positive
    2 = Borderline
    9 = Not Available

14. Adjuvant Treatment of Cancer #1 (1 = Yes 2 = No)

    1. Radiation ____ if yes, Rads _ _ _ _

    2. Chemotherapy ____ if yes , Duration (months) ___ ___

    3. Hormone Therapy ____ if yes, Type _____

Cancer # 2 If no second primary, SKIP to Qx #29

15. Date of second primary diagnosis of breast cancer: __ ____ ____ __ __ __
    month day year

16. Method of first detection:
    1. Self palpation
    2. Clinical exam
    3. Screening mammogram

17. Mammography:
    1. Negative
    2. Suspicious
    3. Not done
    4. Positive

18. First Breast Surgery:
    1. Mastectomy
    2. Lumpectomy/Local Excision

19. Axillary Dissection (first surgery):
    1. Yes
    2. No

20. *Second* Breast Surgery date : __ ____ ____ __ __ __
reason: 1. Residual **month day year**
2. Reccurence

21. *Second* Breast Surgery (type):
1. Mastectomy
2. Lumpectomy\Local Excision

22. Axillary Dissection (second surgery):
1. Yes
2. No

MRN __ __ __ __ __ __ __ __ __

23. Tumor size at diagnosis - Cancer #2
    Size __ __.__(cm)

24. Tumor type:
    1. In situ
    2. Invasive

25. Lymph nodes:
    Total # removed/examined: __ __
    Total # positive: __ __

26. Tumor ER status - Cancer #2
    0 = Negative
    1 = Positive
    2 = Borderline
    9 = Not Available

27. Tumor PR status - Cancer #2
    0 = Negative
    1 = Positive
    2 = Borderline
    9 = Not Available

28. Treatment after Cancer #2 (1 = Yes 2 = No)

    1. Radiation ____ if yes, Rads __ __ __ __

    2. Chemotherapy ____ if yes , Duration (months) ___ ___

    3. Hormone Therapy ____ if yes, Type _____

---

29. If evidence of recurrent breast cancer, date recurrence first detected: __ ____ ____ __ __ __
    month day year

30. Type of Recurrence
    1 = Local (skin, chest wall, remaining breast tissue after lumpectomy)
    2 = Regional (axillary nodes, superclavicular nodes)
    3 = Distant (bone, liver, lungs, etc.)

31. Family history of breast cancer at last Kaiser contact:
    1 = Primary family member with breast cancer (mother, sister, daughter)
    2 = Secondary relative with breast cancer (aunts, grandmother)
    3 = Both primary and secondary relatives with breast cancer
    4 = No family history

MRN _ _ _ _ _ _ _ _ _ _

32. Family history of ovarian cancer at last Kaiser contact:
    1 = Primary family member with ovarian cancer (mother, sister, daughter)
    2 = Secondary relative with ovarian cancer (aunts, grandmother)
    3 = Both primary and secondary relatives with ovarian cancer
    4 = No family history

Pregnancy history **prior** to first breast cancer diagnosis: Including live births, still births, tubal or other ectopic pregnancies, miscarriages and abortions.

33. Fertility tx with hormones?
    1 = Yes
    2 = No

34. Number of pregnancies: _ _
    (Not recorded in chart = 99, Unknown = 88, Never = 00)

If no **prior** pregnancies, SKIP to Subsequent Pregnancies

Outcomes:
1 = Live Birth - Term **2** = Live Birth but pre-term **3** = Still Birth **4** = Abortion
5 = Miscarriage **6** = Ectopic **7** = uncertain **8** = other _____

35. Prior Pregnancy #1 Outcome ___ _ _ \ _ _ _ _
    month year
    Newborn normal?
    1. yes
    2. no if no describe, _____ _ _ _ . _ _

36. Prior Pregnancy #2 Outcome ___ _ _ \ _ _ _ _
    month year
    Newborn normal?
    1. yes
    2. no if no describe, _____ _ _ _ . _ _

37. Prior Pregnancy #3 Outcome ___ _ _ \ _ _ _ _
    month year
    Newborn normal?
    1. yes
    2. no if no describe, _____ _ _ _ . _ _

38. Prior Pregnancy #4 Outcome ___ _ _ \ _ _ _ _
    month year
    Newborn normal?
    1. yes
    2. no if no describe, _____ _ _ _ . _ _

MRN _ _ _ _ _ _ _ _ _ _

39. Prior Pregnancy #5 Outcome ___ __ ____ __ __ __
month year

Newborn normal?
1. yes
2. no if no describe, _____ ___.___

40. Prior Pregnancy #6 Outcome ___ __ ____ __ __ __
month year

Newborn normal?
1. yes
2. no if no describe, _____ ___.___

41. Prior Pregnancy #7 Outcome ___ __ ____ __ __ __
month year

Newborn normal?
1. yes
2. no if no describe, _____ ___.___

42. Prior Pregnancy #8 Outcome ___ __ ____ __ __ __
month year

Newborn normal?
1. yes
2. no if no describe, _____ ___.___

Pregnancy history subsequent to first breast cancer diagnosis: Including live births, still births, tubal or other ectopic pregnancies, miscarriages and abortions.

43. Fertility tx with hormones?
    1 = Yes
    2 = No

44. Number of pregnancies: __ __
    (Not recorded in chart = 99, Unknown = 88, Never = 00)

****If ♀ had a tubal ligation or a hysterectomy after any sugsequent pregnancy, continue and also complete Qx #53.**

If no **subsequent** pregnancies, SKIP to next page

Outcomes:
1 = Live Birth - Term **2** = Live Birth but pre-term **3** = Still Birth **4** = Abortion
5 = Miscarriage **6** = Ectopic **7** = uncertain **8** = other _____

45. Subsequent Pregnancy #1 Outcome ___ __ ____ __ __ __
    month year

    Newborn normal?
    1. yes
    2. no if no describe, _____ __ __ __ . __ __

46. Subsequent Pregnancy #2 Outcome ___ __ ____ __ __ __
    month year

    Newborn normal?
    1. yes
    2. no if no describe, _____ __ __ __ . __ __

47. Subsequent Pregnancy #3 Outcome ___ __ ____ __ __ __
    month year

    Newborn normal?
    1. yes
    2. no if no describe, _____ __ __ __ . __ __

48. Subsequent Pregnancy #4 Outcome ___ __ ____ __ __ __
    month year

    Newborn normal?
    1. yes
    2. no if no describe, _____ __ __ __ . __ __

MRN __ __ __ __ __ __ __ __ __

49. Date of last Kaiser Contact __ ____ ____ __ __ __
month day year

50. Status at last contact
1 = Alive - free of disease
2 = Alive - recurrent disease
3 = Dead from breast cancer
4 = Dead from cause other than breast cancer
5 = Dead, unable to determine cause

51. Date of Death: __ ____ ____ __ __ __
52. Kaiser patient currently? (1 = yes 2 = no)
If no, any forwarding imformation?

_____
_____
_____

53. Date of Tubal Ligation or Hysterectomy: __ ____ ____ __ __ __