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This case-control study examines breast cancer risk in relation to lifetime alcohol consumption. Subjects are 960 pre- and post-menopausal women, age 35-79, from Erie and Niagara counties in New York State, with incident, pathologically confirmed breast cancer. Most controls have been interviewed as part of another study that has just ended. Controls are randomly selected and frequency matched to cases on age, race and county of residence. Subjects receive a computerized interview, which focuses on in-depth lifetime alcohol consumption history. Potential confounding factors are also assessed. A specimen bank is used to store biological samples for future research of serum and urinary markers of hormones, hormone metabolites, vitamins, genetic polymorphisms and blood levels of antioxidants and oxidative stress. This study provides an important opportunity for an efficient examination of alcohol and other risk factors, particularly genetic variability, in relation to breast cancer risk, with potential for clarification of a significant public health problem. Since the inception of the study, 620 breast cancer cases and 2,007 controls have been interviewed and blood samples stored for 520 cases and 1,862 controls. Data collection is still underway, therefore there are **no conclusions to report at this time.**

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FOREWORD

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TABLE OF CONTENTS

FRONT COVER	1
REPORT DOCUMENTATION FORM (SF) 298.....	2
FOREWORD.....	3
TABLE OF CONTENTS	4
INTRODUCTION.....	5
BODY	6

INTRODUCTION

This research is an epidemiologic investigation into the role of lifetime alcohol exposure in breast cancer etiology, research of considerable relevance to the issue of breast cancer prevention, providing insight on the role of a modifiable, and common exposure. The primary purpose of this study is to examine the history of alcohol consumption from adolescence through adulthood as a risk factor for pre- and post-menopausal breast cancer in women. We will also examine the possible role of factors such as genetic factors, estrogen receptor status, histology, and use of estrogen replacement therapy among post-menopausal women in mediating the effect of alcohol on breast cancer risk. In this case-control study, approximately 960 women (215 premenopausal and 745 postmenopausal), age 35-79 from Erie and Niagara counties in western New York with incident, pathologically confirmed cases of breast cancer are being interviewed. Controls are women interviewed as part of the concurrently conducted, previously funded, case-control studies. Controls are randomly selected, those under age 65 from lists provided by the New York State Department of Motor Vehicles, those age 65 and over from enrollment lists of the Health Care Finance Administration. Controls will be frequency matched to cases on age, race, and county. Blood samples are stored in a biological specimen bank for future research. Previous research in this area has relied on relatively crude measures of alcohol consumption, generally not distinguishing infrequent drinkers of larger amounts from individuals who drink smaller quantities more often, and those who drink with meals from those who do not drink with meals. There is some evidence that age when drinking began may also affect risk; studies have not examined in detail characteristics of early drinking. Further, there is some evidence that women may differ in their metabolic response to alcohol depending on genetic polymorphisms for enzymes involved in alcohol metabolism.

In the previous report, the statement of work was amended. Task number 3 was revised to 960 total breast cancer cases (215 premenopausal and 745 postmenopausal women). It was our understanding that because the report was accepted, that the revised statement of work had been accepted too. A memo has now been sent to the Contracting Officer's Representative regarding the revision. We are on track to meet the goal of 960. We will also make every attempt to exceed that goal.

With regard to the previous review of our annual report, there was some misunderstanding of the methods for this study by the reviewer as expressed in the technical issues section. The reviewer was under the impression that controls for this study were chosen from an abuser population. This is not the case. The controls for this study are randomly selected from the population of women aged 35-79, living in Erie and Niagara counties. As noted above, the women under 65 were selected from the list of licensed drivers from the Department of Motor Vehicles. Those age 65 and over were selected from the Health Care Finance Administration list.

We have not included in this report data from the controls. That data is now in the process of being "cleaned." We are identifying outliers, possible data entry errors and inconsistencies in the data set. The final data set of the interviewed cases and controls will be ready for analysis soon and preliminary data on that group will be available.

Body of Report

Task 1: Months 1-3: Obtain Institutional Review Board approval for the study at all area hospitals

This task is completed. We have obtained approval from the Institutional Review Boards of twelve hospitals in the region. One small hospital had approved the protocol but asked that we wait to ascertain cases until a merger with a larger hospital was completed. The merger is completed and we have been identifying cases there for several months. One exception is Sisters' Hospital, a major hospital, that will not allow us to use their patient population in spite of long negotiations and considerable effort on the part of both our group and the hospital Institutional Review Board. However, the practice of breast surgeons who see virtually all of the breast cancer patients at that hospital are cooperating fully with the study and are allowing us to contact patients using their clinic records. Contact with physicians and health care professionals and other breast cancer advocates is ongoing to promote continued cooperation with the study.

Task 2: Months 1-3): Finalization of all arrangements for interviewing: training interviewers, necessary preparations of computer interview, printing of the paper section of the questionnaire, obtaining lists of potential controls from the Department of Motor Vehicles and the Health Care Finance Administration, purchase of all necessary supplies and equipment.

This task is complete. We are proceeding with interviews of breast cancer cases and controls. To date, we have interviewed 620 women with incident, primary, histologically confirmed breast cancer and 2,007 controls. Most of the controls have been interviewed as part of the funding of other case-control studies on the clinical and medical epidemiology of alcohol. Those studies, which have ended, utilized the same protocol and the same interview. An additional 150 controls will be interviewed during the remainder of this grant to ensure that there is no bias related to secular trends.

Training of interviews and supervision of interviewers regarding their administration of the interview is ongoing. We now have a group of interviewers who have been carefully trained and who have been working on this study for up to four years. We meet regularly with them to discuss any concerns and to continue to standardize procedures. We have approval from the Department of Motor Vehicles and from the Health Care Finance Administration to provide us with lists of potential controls and we receive periodic updates from those two sources

Task 3. Months 4-45. During years 3 and 4 we will interview 700 cases, making a total of 960 (approximately 215 premenopausal and 745 postmenopausal women). We will continue interviews of postmenopausal white women in years three and four. In addition, we will interview 150 controls.

As noted above, we have interviewed 620 cases of breast cancer and about 2000 controls. We are on target to interview our goal of 960 cases and the additional necessary controls for comparisons required for analysis of secular trends.

Task 4: Months 3-47: Ongoing data entry of the interview, maintenance of files from computer-assisted interview and entry of data from the sections of the interview completed by the participant.

All necessary arrangements for ongoing data entry of the interview, maintenance of files from the computer-assisted interview, and coding of data from the sections of the interview completed by hand by the participant are progressing in a timely fashion.

Task 5: Months 4-47: Maintenance of the biological specimen bank, processing of samples for immediate determinations and for storage, tracking of all samples, mapping of the freezer.

Procedures for the ongoing maintenance of the biological specimen bank are well underway. Means for tracking of samples and mapping of the freezer have been established and are progressing.

To ensure standardization of specimens collected, all blood is drawn at the same time of the day (7:00AM-9:00AM). For pre-menopausal women, blood drawings are scheduled for the luteal phase of the cycle to reduce, to the extent possible, variation in hormone levels related to the menstrual cycle. The time of the blood draw is recorded for assessment of any variation in blood markers related to the time of the draw. 1,862 control and 520 case blood samples have been processed for immediate determinations and for long term storage.

Tasks 6: Months 25-48: Genetic analyses of samples: DNA extractions and determinations of genetic polymorphisms.

Blood clots for DNA extraction and subsequent genetic analysis have been removed from the freezer and mailed to Dr. Peter Shields at the Laboratory of Human Carcinogenesis at the National Cancer Institute. The data set consists of 870 blood clots: 280 from breast cancer cases, 280 pairs of matched controls, and 30 randomly positioned blind duplicates. These samples represent all the breast cancer cases whom we have interviewed for whom we have a blood sample. We have found that it is also possible to extract DNA from collected urine and saliva samples. At the conclusion of the study, we will also extract DNA samples from urine or saliva from those participants who gave consent but were either unable or unwilling to provide a blood specimen.

Analysis for the genetic polymorphism in alcohol dehydrogenase 3 (ADH3) will be performed at this time for the DNA samples that have been sent to Dr. Shields' lab. Preliminary results from that subset of the total sample will be analyzed to determine the modifying effects of ADH3 on the association between alcohol consumption and breast cancer risk.

Task 7: Months 25-48. Statistical analyses; preparation of variables from the interview and blood determination, all required analyses of the data for reports and presentations.

Statistical analyses will begin when interviewing has been completed. In the next year, preliminary data sets will be assembled and necessary work begun on managing the

data, identifying outliers and implementing procedures for cleaning the data. These procedures are already in place for much of the data set. All necessary data checks on the breast cancer case data will begin this year.

Task 8: Months 25-48. Preparation of publications reports and presentation of the data.

Because data collection is still underway, no presentations have been made yet on these data. Results of the preliminary findings regarding ADH3, alcohol consumption and breast cancer risk will be presented at the next DoD Era of Hope meeting.