Depression, Psychological Distress and Breast and Cervical Cancer Screening:  A Population-Based Study in Ontario Women

by

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A thesis submitted in conformity with the requirements for the degree of Masters of Science
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Abstract

**Purpose:** The objective of this study was to investigate both depression and psychological distress as determinants of breast and cervical cancer screening.

**Methods:** Ontario female respondents to the Canadian Community Health Survey version 1.2 (2002) were assessed for both Major Depressive Disorder (World Mental Health-Composite International Diagnostic Interview for depression) and psychological distress (Kessler 6-item Distress Scale (K6) ≥8). Respondents eligible for screening (N=4042 for cervical cancer; N=1403 for breast cancer) were linked to Ontario administrative health service data to prospectively ascertain screening outcomes.

**Results:** Women with K6 ≥ 8 had reduced breast cancer screening compliance in adjusted analyses (AOR 0.63, 95% CI 0.40-0.97). The association between K6 ≥ 8 and cervical cancer screening approached significance in women over age 40 (AOR=0.65, 95%CI 0.41-1.04).

**Conclusion:** Decreased likelihood of screening in women with clinically significant psychological distress suggests that attention to adequacy of preventive services is a potential target for intervention.
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Chapter 1
Overview, Goals and Study Objectives

The purpose of this chapter is to:

1. Provide an overview of the rationale for this thesis project

2. Introduce the goals of the project and study objectives

1 Overview

Depression affects up to 1 in 5 women over their lifetime and is a leading cause of disability worldwide. There is evidence that women who suffer from depression are at risk, not only of poor mental health outcomes, but physical health outcomes as well. The reasons for this have not been fully elucidated but may be related to risk factors for poor physical health such as smoking, low levels of physical activity and poor self-care as well as under-treatment for chronic medical illness. Preventive health services are an important component of primary care for women that can contribute to optimal physical health outcomes. Yet, although depressed women use primary health care practitioners more often than non-depressed women, likely as a result of the many somatic symptoms that accompany depression, it is not clear that increased primary care health service utilization translates into better preventive health care measures for depressed women. In other words, depressed women may receive a large quantity of health services, but uptake of preventive care services may be poor. Existing literature is conflicting. Studies of women with
mild depressive symptoms or non-specific psychological distress are more likely to reveal associations between depression and screening than studies where more strict definitions of depression are used. The current study was of high priority as it aimed to explore the effect of both major depression and clinically significant psychological distress on secondary prevention for two of the most common cancers in women: cervical and breast cancer.

2 Goals of the current study

Through epidemiological data collected in Ontario we had a unique opportunity to assess this relationship on a population level. The primary objective of the present study was to evaluate depression as a risk factor for reduced preventive care screening for breast and cervical cancers in Ontario women. In this study we used population-based survey data linked to administrative health data. This link provided the advantages of a) standardized measures to distinguish women with Major Depressive Disorder (MDD) from a larger pool of women with clinically significant psychological distress, b) accurate prospective measures for cervical and breast cancer screening and c) adequate information on potential confounding variables such as age, socioeconomic status and primary care service use that are associated with both depression and screening outcomes. In addition, administratively-collected data on primary care health service use allowed for preliminary exploration into how depression affects the known positive relationship between primary care service use and preventive screening outcomes.
2.1 Specific Objectives

1. To compare breast cancer screening rates in women with major depressive disorder (MDD) to women without MDD over two years.

2. To compare breast cancer screening rates in women with clinically significant psychological distress to women without clinically significant psychological distress over two years.

3. To compare cervical cancer screening rates in women with major depressive disorder (MDD) to women without MDD over three years.

4. To compare cervical cancer screening rates in women with clinically significant psychological distress to women without clinically significant psychological distress over three years.

2.2 Specific Hypotheses

The main study hypothesis was that Major Depressive Disorder (MDD) and/or clinically significant psychological distress would be associated with poor breast cancer screening outcomes (and perhaps cervical cancer screening outcomes in older age groups) after adjusting for potential confounding factors. We further hypothesized that these relationships would hold despite greater primary care service utilization by depressed women.
Chapter 2

Background

The purpose of this chapter is to:

1. Review the epidemiology of depressive disorders in women, briefly review current knowledge about the impact of depressive disorders on physical health outcomes in women and introduce the rationale for examining preventive health service use among depressed women

2. Review two female-specific examples of preventive health services: breast and cervical cancer screening and outline existing knowledge about barriers to screening

3. Review existing literature that examines the relationship between depression and preventive screening for breast and cervical cancers and identify the methodological challenges that formed the basis for the present study

3 Depression in Women

3.1 Epidemiology

Major Depressive Disorder (MDD) is approximately twice as common in women as in men and affects up to 1 in 5 women throughout their lifetime (Kessler et al., 2003a). Although depression affects males and females equally in childhood, by early adolescence women are much more commonly affected – a gender difference that persists until well after menopause. Major depressive disorder is defined by the Diagnostic and Statistical Manual of Mental Disorders
(DSM-IV TR) (American Psychiatric Association, 2000) as the presence of one or more major depressive episodes in addition to clinically significant distress or functional impairment (See Appendix A). Symptoms of a major depressive episode can include sadness, loss of interest or pleasure, guilt, fatigue, sleep or appetite disturbance, poor concentration, psychomotor retardation (being physically slowed down) and suicidal ideation. To be diagnosed with a major depressive episode, an individual must experience at least five of the aforementioned symptoms (at least one of which is sadness or loss of interest/pleasure) for most of the day, every day, over the course of a two-week period. The depressive episode cannot be better accounted for by bereavement or bipolar disorder and cannot be substance-induced or a direct result of a general medical condition (e.g. hypothyroidism). Depression is a chronic and recurrent illness with the median length of a depressive episode being 2 months and the average woman with depression experiencing two or more episodes over her lifetime (Patten et al., 2009a; Patten et al., 2010).

Risk factors for depression include biological, psychological and social factors, some of which may help explain the increased prevalence of depression in women. Over the last number of years, ground breaking studies have demonstrated sex differences in brain anatomy, function and neurochemistry, as well as in sex hormones and endocrine stress reactivity (Vigod & Stewart, 2009). There has also been an increased appreciation of psychosocial and socio-cultural risk factors for mental illness that differentially disadvantage girls and women. These risk factors include poverty, poor education, social isolation, discrimination, cultural and societal expectations including role strain and vulnerability to interpersonal violence (World Health Organization, 2000).

Although major depression is described as an episodic disorder, many women experience substantial residual symptoms in between full blown depressive episodes (Patten et al., 2009a).
There are also a substantial number of women who experience psychological distress or depressive symptoms but do not meet DSM-IV-TR criteria for Major Depressive Disorder. This may include individuals with dysthymic disorder, adjustment disorders as well as other mental health problems that include psychotic disorders, anxiety disorders and addictions. In addition, there are women with depressive symptoms who do not meet DSM-IV criteria for specific depressive disorders, yet evidence suggests that these subclinical depressive symptoms may have substantial impact on quality of life (see Section 3.2: Impact). When women with clinically significant depressive symptoms who do not meet criteria for MDD are included in depression prevalence estimates, the lifetime rate approaches 1 in 3 (Ayuso-Mateos et al., 2010).

3.2 Impact

Depression is the leading cause of disability worldwide as measured by years lived with disability (YLDs) and was the fourth leading contributor to the global burden of disease in 2000. According to the World Health Organization, depression will be the second leading contributor to the global burden of disease by the year 2020 (World Health Organization, 2010). Depression is highly associated with other mental disorders such as anxiety in women as well as substance use, suicidality and suicide. Women with depression report reduced quality of life compared to women without depression, not only while experiencing a major depressive episode, but between episodes as well. There is also evidence that the impact on quality of life is not limited to major depressive disorder. Subthreshold depressive disorders have substantial impact on health-related function and quality of life (Ayuso-Mateos et al., 2010).
Research that focuses on the relationship between physical and mental health in women suggests an inter-relationship between physical and psychological well-being. This relationship is likely to be bi-directional in nature. That is, physical health problems may contribute to depression and depression likely contributes to physical health problems. Rates of depression are increased in women with a variety of physical illnesses that disproportionately affect women such as rheumatoid arthritis, multiple sclerosis and urinary incontinence (Vigod & Stewart, 2006; Lok et al., 2010; Paparrigopolous et al., 2010). In addition, interactions between depression and physical health outcomes have been observed in diseases that are common in women such as cardiovascular disease (currently the 2nd leading cause of death in women) (Nicholson et al., 2007).

### 3.3 Rationale for examining preventive health service use in depressed women

There is evidence that depressed women are more frequent users of the health care system than non-depressed women (Vigod & Stewart, 2006). However, it is not clear whether increased health service utilization translates into better health outcomes for depressed women (Mitchell et al., 2009). It may appear logical to assume that if women with depression are in frequent contact with the health care system, they would have increased likelihood of receiving preventive health care. However, there are several reasons to believe that, despite greater health service use in general, depressed women are less likely to receive preventive screening. As described, depressive symptoms include low energy and motivation, poor concentration, poor memory, negativistic thinking and functional impairment. Women with depression may be distressed
enough to seek care for obvious symptoms, but lack motivation to follow through with preventive health care. In addition, socioeconomic disadvantage and limited access to psychosocial resources have been consistently associated with an increased risk of depression (World Health Organization, 2000). These obstacles may make attention to preventive health behaviours beyond the perceived (or actual) capacity of socially disadvantaged women. It is also possible that the effect of having a chronic disease (in this case, depression) creates a competing risk for care whereby care for the most highly visible illness takes precedence. This has held true for women with other chronic diseases. For example, it has been shown that even when women with Diabetes Mellitus make more primary care doctor visits, they are at risk of reduced screening for breast cancer (Lipscombe et al., 2005). This could be even more evident for women with depressive disorders. Depression is associated with amplification of somatic symptoms, creating the potential for competing risk for care from the depression itself as well as its accompanying somatic symptoms. As depression affects so many women, the current study was of high priority as it aimed to explore the effect of depression on secondary prevention for two of the most common cancers in women: cervical and breast cancer.

4 Breast and Cervical Cancer Screening

4.1 Definitions

Over the last 50 years, female mortality from breast and cervical cancers has dropped markedly. Between 1989 and 2005, breast cancer mortality rates in Ontario women aged 50–69 decreased by 35% (Cancer Care Ontario, 2010a). To a large extent this can be attributed to improvements
in technology, but higher screening rates have also led to earlier detection and treatment. Screening women at average risk for breast cancer with mammography has been shown to reduce mortality, although there is some controversy about the magnitude of this effect (Kalager et al., 2010; Welch, 2010). Cervical cancer is preventable as almost all cancers of the cervix can be stopped when early cell changes are found and treated. Annual screening of sexually active women with the Papanicolou (Pap) test has reduced the incidence of invasive cervical cancer by 60% over the last 30 years (Cancer Care Ontario, 2010b).

### 4.1.1 Breast Cancer Screening

Breast screening is the regular examination of a woman's breasts to find breast cancer early. A mammogram is a specialized X-Ray of the breast that is considered the gold standard in breast cancer screening for most women (Cancer Care Ontario, 2010a). In Ontario, women can receive a screening mammogram in one of two ways: through Ontario’s organized provincial screening program the Ontario Breast Cancer Screening Program (OBSP) or through stand-alone clinics funded through the Ontario Health Insurance Plan (OHIP). Women can make an appointment by calling OBSP or can be referred for mammography screening by their health care provider. Current Ontario Clinical Practice Guidelines for breast cancer screening stipulate that 2 years is an appropriate interval for mammography screening in women ages 50-70 with no family history of breast cancer (or known genetic mutation increasing risk of early breast cancer) (Cancer Care Ontario, 2010a).
4.1.2 Cervical Cancer Screening

A Papanicoloou (Pap) test can show unhealthy changes in cervical cells that will sometimes lead to cancer. It most often performed by a physician at a yearly regular health check-up. Almost all cancers of the cervix can be stopped when early cell changes are found and treated. A regular Pap test can show cell changes that can be treated before they become cancer. Annual cervical cancer screening with Pap testing is recommended for sexually active women 18-70 in Ontario. However, a woman in a monogamous relationship who has undergone 3 annual negative screening exams may proceed to screening every 3 years (Cancer Care Ontario, 2010b).

4.2 Known barriers to screening

Unfortunately, not all eligible women are screened. Currently, 66% of women aged 50 to 69 participate in regular mammography screening through OBSP or other screening clinics (Cancer Care Ontario, 2010a). Despite the fact that cervical cancer is preventable with adequate Pap testing, about 500 women are diagnosed with cancer of the cervix, and about 150 women die from this disease yearly in Ontario (Cancer Care Ontario, 2010b). Determinants of screening are similar for both breast and cervical cancer screening and include patient, provider and system-level factors. Patient-level factors associated with reduced screening rates include sociodemographic characteristics (older age, low socioeconomic status, low education level, recent immigrant status and living in a rural area) as well as health-related characteristics such as comorbid medical conditions and physical disability (Kryzanowska et al. 2009; Lipscombe et al., 2005; Drew et al., 2010). Additionally, a robust qualitative literature reveals that women identify
concerns about pain, radiation and embarrassment as key barriers to mammography screening (Hanson et al. 2009) and that concerns about lack of privacy may contribute to sub-optimal pap test screening (Leach & Schoenberg, 2007). At the provider level, not having a primary care physician is an important factor. For example, in Ontario, women without a primary care physician were much less likely to receive guideline-recommended screening mammography than women with a primary care physician (Upshur et al., 2006). In women who do have a primary care physician, it has been reported that having a physician make a recommendation for screening is an influential factor (e.g. Hanson et al., 2009). At the system level, increasing screening rates have been observed with the implementation of public provincial screening programs for both breast and cervical cancer (Kryzanowska et al. 2009). However, as indicated, there remains room for improvement of adherence to screening guidelines.

The relationship between chronic mental illness and screening has been less well studied, and the impact of mental illness may vary by psychiatric diagnosis (Lord et al., 2010). Studies have consistently shown that women with schizophrenia are at risk of suboptimal screening (Chochinov et al., 2009). Women with depression may be at risk of reduced screening for all of the reasons stated above (Section 3.3 Rationale for Examining Preventive Health Service Use in Depressed Women). In addition, they may be prone to feelings of shame that create a barrier because of the uniquely exposing nature of Pap tests and mammography. If depression is a risk factor for reduced breast and/or cervical cancer screening, there are many potential points of intervention. Understanding the particular barriers to screening in depressed women will help with developing education programs and policies to optimize screening on individual, provider, community and health care system levels. Unfortunately, the relationship between depression and breast and cervical cancer screening on a population-level has yet to be adequately clarified.
5 Depression as a Determinant of Breast and Cervical Cancer Screening

5.1 Existing Literature

Data from clinical populations suggest that depression is associated with reduced breast cancer screening (Stecker et al., 2007). However, population-level data offer conflicting results. For example, the US Study of Women’s Health Across the Nation (SWAN) (Pirraglia et al., 2004) found that a high depressive symptom burden was a modest predictor of reduced screening mammography (OR 0.85, 95% CI 0.73 to 0.97) after accounting for age, ethnicity, socioeconomic status, medical history, smoking and obesity. The Women’s Health Initiative Observational Study (WHI) (Aggarwal et al., 2008) found that women with depressive symptoms were 1.5% (95% CI 0.9% to 2.0%) less likely to receive screening mammography than non-depressed counterparts. However, analysis of data from both the Joint Canada/United States Survey of Health (JCUSH, 2002 to 2003) (Blackwell et al., 2008) and the Canadian National Population Health Survey (NPHS, 1994 to 2000) (Patten et al., 2009) revealed no association between depression and mammography screening.

The data examining the association between depression and cervical cancer screening are equally conflicting. A recent Canadian population-based study using data from the Canadian Community Health Survey version 3.1 (CCHS 3.1) (Kaida et al., 2008) investigated depression as a primary predictor of Pap test screening and found that middle-aged depressed women (but not younger women) reported reduced screening over the 3 years preceding the survey (AOR 0.76, 95% CI
0.58 to 0.98 for women aged 40 to 49 years and AOR 0.68, 95% CI 0.50 to 0.93 for women aged 50 to 59 years). However, the aforementioned SWAN study did not find a relationship between depressive symptom burden and Pap testing in women ages 42-52. Neither the previously mentioned JCUSH nor NPHS survey (where age was not considered) reported a relationship between depression and cervical cancer screening.

5.2 Methodological Challenges in Existing Literature

5.2.1 Measurement of Depression

Limitations to existing literature may help explain the conflicting results. A major limitation is the variability with respect to point estimates of depression (ranging from 4% to 15.8% in the aforementioned studies). Studies that used depressive symptom cut-off scores to estimate the probability of depression generated higher prevalence estimates of depression and were more likely to report associations with reduced screening than studies that used diagnostic interviews to detect MDD. For example, the SWAN and WHI used standard cut-off scores for depression on the Centre for Epidemiological Studies of Depression (CES-D) scale whereas both the JCUSH and NPHS used the Composite International Diagnostic Interview – Short Form (CIDI-SF) to identify women with probable Major Depressive Disorder (MDD) within the preceding year. This calls into question whether a woman must be suffering from MDD to be at reduced risk of screening, or perhaps more plausibly, whether the studies detecting positive associations reflect a more general impact of depressive symptoms or psychiatric distress on screening outcomes. Two recent studies support this hypothesis. A recent study involving 905 women
from 65 primary care practices in the US investigated predictors of breast and colorectal cancer screening found that psychological distress (using a composite measure based on depressive symptoms, stress and reduced quality of life) had one of the strongest negative associations with screening practices (O’Donnell et al., 2010). A cross-sectional community survey in Kentucky found that the number of self-reported poor mental health days and depressed days over the preceding year predicted a lack of mammography screening. Adjusting for age, race, marital status, education, income, and health insurance status, women reporting 30 poor mental health days and 30 depressed days were more likely than women reporting zero days to be unscreened within the preceding 2 years (OR 1.68 (95% confidence interval [CI] 1.08-2.63) and 1.49 (0.93-2.40) respectively) (Masterson et al., 2010). In contrast, an analysis of the United States National Health Interview Survey (2000) reported that psychological distress was not associated with having ever had either mammography screening or a Pap test ((Honda et al., 2005). Interestingly, however, in this study “psychological distress” was defined as a cut-off score of ≥12 the Kessler 6-item distress scale (K6), which is highly predictive of severe mental disorder. In keeping with our earlier observation that studies with low prevalence of mental disorders were less likely to generate significant associations between depression and screening, only 2.8% of the women in this sample had a K6 ≥ 12. Furthermore, whether a woman has ever received screening is an outcome of low specificity with respect to adequacy of preventive care.

5.2.2 Measurement of Screening Outcomes
Further limitations to existing literature include reliance on self-reported and retrospective screening outcomes. In all previous population-based studies, mammography and Pap test compliance were measured by retrospective self-report. This creates potential for bias that could compromise the validity of an observed association between depression and screening outcomes. In general, self-report estimates of screening tend to be higher than estimates from health administrative data (Fehringer et al., 2005), perhaps because of a social acceptability bias where people report having been screened because they know that they should have been screened. It is not known how depression might affect this social acceptability bias. In addition, it is not known whether depression has an effect on a woman’s ability to recall whether (or when) she was last screened. It is possible that depressed women may be more somatically preoccupied and therefore more likely to remember exactly when their last screening test took place. Or, conversely, those women who are depressed may have cognitive impairment that compromises their memory.

5.2.3 Measurement of potential confounding factors and effect modifiers

Further limitations to existing literature include failure to consider potential confounding factors. Multiple variables associated with depression are also strong determinants of breast and cervical cancer screening rates, introducing potential for confounding (Gentlemen & Lee, 1997; Fehringer et al., 2005; Upshur et al., 2006). As discussed, epidemiological studies show that depressed women are more likely to be single, and to have lower education and lower income than non-depressed women. These demographic characteristics are also risk factors for poor screening adherence. Without adjusting for these variables, it would be difficult to ascertain
whether any depression-related variation in screening behaviour is actually confounded by sociodemographic variables that are both correlated with depression and associated with the outcome.

Age could also be a confounding factor. Women in younger age groups have higher rates of depression than women in older age group, (Parikh et al., 2001) yet younger women have better screening compliance than older women (Lee et al., 1998; Fehringer et al., 2005). This might bias the study against finding an association - the non-depressed group would have lower screening rates because of their older average age. The age group eligible for screening mammography is from 50-68 therefore the potential magnitude of age as a confounder in this group is small. For cervical cancer screening, age may be an important confounder, as discussed in earlier studies or an effect modifier (i.e. a variable that modifies the effect of depression on screening).

Recent immigration is also a potential confounding variable. Recent immigration might be less prevalent in a group of depressed vs. non-depressed women. Since recent immigrants tend to have lower screening rates (Lee et al., 1998; Fehringer et al., 2005), this could bias results against depression as a barrier to screening.

In addition, few studies have examined the potential influence of co-morbid chronic health conditions on preventive health care in depressed women. Comorbid chronic health conditions are highly prevalent in depressed women and have been identified as barriers to preventive health care (Gentlemen & Lee, 1997; Lee et al., 1998; Fehringer et al., 2005). Therefore, failure to account for comorbid health conditions in analyzing the relationship between depression and preventive care creates potential for confounding.
Related to the potential effect of chronic conditions is the effect of health service utilization (i.e. having a family physician, number of primary care visits). No previous studies have explored how depression might affect the increased likelihood of preventive screening associated with primary health care access typically observed in community-based populations. It is known that screening compliance improves with access to primary care (Upshur et al., 2006). However, it is possible that a chronic condition such as depression may mitigate this effect. Because of this, it is important to examine primary care health service utilization to understand its role in the preventive care of depressed women.

6 Summary

In summary, depression is a chronic and recurrent illness that has substantial impact on the physical health, mental health and quality of life of women around the world. However, existing research into how depression impacts the use of preventive health services yields conflicting results. Specifically, it is unclear whether depression itself is a key determinant of screening or whether psychological distress is the key factor. .
Chapter 3

Methods

The purpose of this chapter is to:

1. Provide an overview of the study design
2. Describe the data sources and study sample
3. Describe the main exposure, outcome and potential confounding variables
4. Describe the approach to statistical analysis

7 Study Design

In this retrospective cohort study design, Ontario respondents to a Canadian population-based mental health survey were linked with administrative health services data. Rates of screening Pap test within the 3 years following the survey (Cohort 1) and screening mammography within the 2 years following the survey (Cohort 2) were compared between depressed and non-depressed women. We also compared screening rates between women with and without evidence of clinically significant psychological distress. The study was conducted at the Institute for Clinical Evaluative Sciences and approved by the Research Ethics Boards of Sunnybrook Health Sciences Centre and the Centre for Addiction and Mental Health. The University of Toronto in Toronto, Ontario conducted an administrative ethics review only because the protocol had already been approved by two affiliated hospital research ethics boards (Appendix B).
8 Data Sources and Study Samples

8.1 Canadian Community Health Survey Cycle 1.2

Both study samples were drawn from the Canadian Community Health Survey Cycle 1.2 (CCHS 1.2, Mental Health and Well-Being Survey) conducted May-December 2002. The CCHS 1.2 was a cross-sectional survey that used computer-assisted interviewing to collect health information for a representative sample of the Canadian population. Responses to CCHS 1.2 were collected from individuals ages 15 and older, living in private occupied dwellings (targeting 98% of the Canadian population). Individuals living on Indian Reserves and on Crown Lands, institutional residents, full-time members of the Canadian Armed Forces, and residents of certain remote regions were excluded from the sampling frame. The CCHS used a multi-stage stratified clustering sample design to select eligible households. To sample in a manner representative of the Canadian population (i.e. ensure representation of various ethnic groups) there was stratification by region and socioeconomic status. The sampling was also designed to ensure adequate sampling of younger persons and seniors. Each respondent is ultimately given a weight to indicate the percentage of the population that he or she represents. These methods are described in detail at www.statscan.com. To reduce the number of non-respondents to the survey, interviewers were extensively trained and refusals were followed up by senior interviewers and in subsequent collection periods. The overall person-level response rate for CCHS 1.2 was 77%.

At the time of administration, greater than 90% of respondents of the CCHS 1.2 consented to linkage of survey responses to health administrative data. This linkage permitted accurate
measurement of screening outcomes using administrative information on health service utilization that is collected for all Ontario residents.

8.2 Description of ICES Administrative Data Sources

The following administrative data sources were accessed through the Institute of Clinical Evaluative Sciences in Toronto, Ontario to define the sample and measure health service utilization: Ontario Cancer Registry (OCR), Canadian Institutes of Health Information discharge and admission database (CIHI-DAD), Ontario cervical cytology database (Cytobase), Ontario Breast Screening Program (OBSP), Ontario Health Insurance Plan (OHIP) and Registered Persons Database (RPDB). The quality of these data sources has been assessed (Williams and Young 1996) and the use of the data sources for the present study are summarized in Table 1. Dataset creation plans detailing the data codes used for cohort determination and variable selection are presented in Appendix C (for the Cervical Cancer Screening Study) and Appendix D (for the Breast Cancer Screening Study).

*Canadian Institutes of Health Information discharge and admission database (CIHI-DAD)*. All hospitals in Ontario are required to submit demographic and clinical information about all hospital admissions and discharges, including transfers and deaths, to CIHI which collate these data. Trained hospital medical records staff transcribe information from each patient’s medical chart using standard diagnosis (ICD-9, the International Classification of Diseases - 9th revision and ICD-10-CA, the enhanced Canadian version of the 10th revision of the International Statistical Classification of Diseases and Related Health Problems) and procedure/intervention
codes (CCP, the Canadian Classification of Procedures and CCI, the Canadian Classification of Health Interventions).

*Ontario Cancer Registry (OCR).* The Ontario Cancer Registry (OCR) is a computerized database of information on all Ontario residents who have been newly diagnosed with cancer ("incidence") or who have died of cancer ("mortality"). All new cases of cancer are registered, except non-melanoma skin cancer.

*Ontario cervical cytology database (Cytobase).* The Cytobase system constitutes a patient oriented computerized medical record of Pap tests performed on patients in the Province of Ontario. Diagnostic data is provided to the CytoBase system by participating laboratories, hospitals, and clinics performing cervical cytology tests. Cytobase was established in 1996 and as of the year 2000, 80% of Pap Tests in Ontario were registered in Cytobase (Cancer Care Ontario, 2000). By 2006, approximately 90% of Pap Tests in Ontario were registered in Cytobase (Cancer Care Ontario, 2010c).

*Ontario Breast Screening Program (OBSP).* Ontario Breast Screening Program (OBSP) is one of Cancer Care Ontario’s cancer prevention programs. OBSP offers important advantages for women and their physicians, including recruitment, recall and follow-up and ongoing quality assurance. All OBSP sites are accredited with the Canadian Association of Radiologists Mammography Accreditation Program. Some OBSP screening sites are affiliated with breast assessment services, allowing timely, coordinated assessment of women with abnormal mammograms. At ICES, this dataset includes a client identification number (to link participants to other ICES databases) and date of screening mammogram. In 2003 and 2004, 47.2% of women receiving screening mammography in Ontario were screened using OBSP (Institute for Clinical Evaluative Sciences Cancer Program, 2010).
Ontario Health Insurance Plan (OHIP). In Ontario, physicians are reimbursed after submitting claims to OHIP for each service provided. These services include: physician consults or assessments in private offices, acute care, and long-term care facilities; technical and professional components of diagnostic and therapeutic procedures; surgical procedures; and laboratory services. These service data are relatively complete because the information submitted is associated with a reimbursement fee and can be linked or combined with other data, such as hospital discharge abstracts. The database also includes some associated diagnostic and demographic information which, unfortunately, is not very reliable at the individual level. These data only capture information for those physicians who work on a fee-for-service basis. Those physicians who are reimbursed by Alternate Funding Plans or salary are not represented.

Registered Persons Database (RPDB). The Registered Persons Database is developed and maintained by the Ministry of Health. It consists of the health card number, date of birth, sex, postal code and death date (where applicable) associated with the carrier of each valid health card. This dataset is enriched with geographic, contact, and death information from other ICES administrative data holdings.

8.3 Inclusion Criteria

Only Ontario residents from CCHS 1.2 were included (N=13,184) because of the requirement to link subjects to Ontario provincial administrative health data. The cervical cancer screening cohort included women aged 18-67. This is based on Canadian screening recommendations of Pap Testing at least every 3 years from ages 18-70 (a woman aged 67 at the time of the CCHS
1.2 survey would be 70 years old by the end of 3 year follow-up) (McLachlin et al., 2005). The breast cancer screening cohort included women aged 50-68. This is based on Canadian screening recommendations for biennial screening of women ages 50-70 for mammography (Cancer Care Ontario 2010a).

8.4 Exclusion Criteria

Subjects were excluded if they were ineligible for screening (e.g. history of prior cancer, mastectomy, hysterectomy based on administrative data) in each sample separately. Linkage of the CCHS 1.2 survey respondents to the Ontario Cancer Registry allowed for exclusion of women with a prior history of cervical, uterine or ovarian cancer in the cervical cancer screening group and breast cancer in the breast cancer screening group (with a look-back period to the beginning of the OCR database in 1979). Linkage to the Canadian Institutes of Health Information discharge and admission database (CIHI-DAD) allowed for exclusion of women with prior hysterectomy in the cervical cancer screening cohort (using OHIP fee codes and weighted-probabilities to estimate likelihood of hysterectomy prior to CIHI data collection that began in 1988) and prophylactic bilateral mastectomy in the breast cancer screening cohort (indicating family history of breast cancer). Women who died during the follow-up period (prior to demonstrating a screening outcome) as identified by a death record in the Registered Persons Database (RPDB) were removed from the cohort prior to the analysis (N=3). It was not expected that there would be a differential emigration from Ontario depending on depression status, therefore this was not accounted for when defining the cohort.
9 Variables

9.1 Depression (Exposure)

9.1.1 Measurement of Major Depressive Disorder

The CCHS 1.2 included the World Mental Health - Composite International Diagnostic Interview (WMH-CIDI). The WMH-CIDI was developed to diagnose major depressive disorder according to Diagnostic and Statistical Manual of Mental Disorders-IV criteria and to be administered by trained lay interviewers. The CIDI is a comprehensive, fully-structured interview that assesses for mental disorders in accordance with both the International Classification of Disease (ICD-10) and Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria. The WMH-CIDI is an instrument that administers screening questions and, if answered positively, administers full diagnostic blocks to respondents. Diagnoses are generated based on responses to diagnostic questions as well as variables related to possible exclusion criteria. For example, if someone responds positively to the depression module but also responds positively to a current or prior manic episode, then that individual would be assigned a diagnosis of bipolar affective disorder rather than major depressive disorder in accordance with the DSM-IV. The WMH-CIDI is different from the CIDI-SF, a depression rating scale that is widely used, but that does not have the capacity to determine whether depressive symptoms are related to MDD vs. other diagnoses (e.g., BAD) and assigns a probability of having depression rather than an actual diagnosis. The WMH-CIDI has high concordance with diagnosis of major depressive
disorder using the Structured Clinical Interview for DSM-IV in community samples (Haro et al., 2006). MDD was defined in this study by a Major Depressive Episode in the 12 months preceding the survey (Yes/No). CCHS interviewers were trained by Statistics Canada prior to data collection through didactic sessions and supervised interviewing. Supervision continued on an ongoing basis during data collection. Interviewers did not know the purpose of the current study, removing potential for differential measurement of depression based on cervical or breast cancer screening status (Statistics Canada, 2002).

9.1.2 Measurement of Psychological Distress

The CCHS 1.2 also contains the Kessler 6-item distress scale (K6) (Appendix B). This instrument takes approximately 5 minutes to complete and does not require extensive training of interviewers. All respondents in the CCHS 1.2 were asked to respond to 6 items (rated 0-4, maximum score 24) that correspond to how the respondent has been feeling over the previous 30 days. Scores ranging from 0-7 have been shown to predict none or mild depressive symptoms, scores 8-12 have been shown to predict moderate but clinically significant symptomatology and scores \( \geq 13 \) are highly predictive of individuals with severe mental disorder (Kessler et al., 2003b, Kessler et al. 2010). In the present investigation, we were unable to stratify participants into these three groups (K6 0-7, 8-12 and \( \geq 12 \)) due to sample size limitations in the highest scoring group (e.g. N=32 for the breast cancer screening sample). Therefore, for the purpose of the present investigation, individuals with K6 \( \geq 8 \) were categorized as having clinically significant psychological distress. This method has been used in a previous study focused on use of routine healthcare among American women (Witt et al. 2009). Note that when compared to a WMH-CIDI diagnosis of MDD in the CCHS 1.2, a cut-off score of \( \geq 8 \) corresponds to a
sensitivity of 0.75, specificity of 0.91, positive predictive value of 0.12 for MDD and negative predictive value of 0.995 for MDD (Cairney et al., 2007).

9.2 Screening (Outcomes)

9.2.1 Measurement of Cervical Cancer Screening (Cohort 1)

The outcome for cervical cancer screening was a dichotomous measure of receiving a screening Pap test (yes/no) within 3 years (36 months) of the CCHS 1.2 survey administration date. This outcome was identified either through Pap test cytology records available through the Ontario Cervical Screening Program database, Cytobase (which covered between 80-90% of Pap test registered in Ontario during the outcome period) or through a procedure code for Pap test in the OHIP Database (G365, E430, G394, L713, L812, L733). Both cytobase and the aforementioned procedure codes will capture Pap tests regardless of which provider performs the test (i.e. primary care provider vs. obstetrician-gynecologist). This outcome measure has been used in previous studies conducted at ICES (Upshur et al 2006) and is the standard method for calculating Pap test participation rates used by Cancer Care Ontario (Cancer Care Ontario, 2010c).

9.2.2 Measurement of Breast Cancer Screening (Cohort 2)

The outcome for breast cancer screening was a dichotomous measure of receiving a screening mammogram within 2 years (24 months) of the CCHS 1.2 survey administration date (yes/no).
Screening was captured via procedure codes for bilateral mammography in the OHIP billing database (X185) and by the screening mammography field in OBSP. When using OHIP billing claims data, a case was defined as screening mammography when there were no OHIP fee codes billed for breast-related investigations or procedures in the preceding 22 months and no fine needle aspiration (FNA) at the time of mammography (Codes: X121 & Z141; J127 & Z141 or Z141 alone). Concurrent FNA and mammography would indicate that the mammogram is being done for diagnostic, not screening, purposes. This outcome measure has been used in previous studies conducted at ICES (Upshur et al., 2006). Some women who are at high risk for breast cancer due to a family history of breast cancer or a known genetic mutation increasing risk for breast cancer are screened using Magnetic Resonance Imaging (MRI) because of its ability to detect some cancers that would not be detected through screening mammography. However, breast MRI can also miss some types of breast cancer that are detected using mammography. Therefore, Cancer Care Ontario recommends that breast MRI be offered in addition to screening mammography in this high risk group of women (Warner et al., 2007). Because women in this group would be expected to have both screening mammography and MRI imaging, breast screening using (MRI) was not included as part of the outcome variable.

### 9.3 Potential Confounding Variables

Age, income level, level of education, immigration (whether or not the participant was born in Canada), geographical variability (urban/rural), Body Mass Index (BMI) and medical and
psychiatric comorbidity were captured in CCHS 1.2 (www.statscan.com). The income level variable classifies the total household income into 4 categories based on total household income and the number of people living in the household. This variable was previously used in the Canadian Community Health Survey version 1.1 as well as 4 previous versions of the Canadian National Population Health Survey (Statistics Canada, 2002). Level of education was also classified into 4 levels as previously done in the CCHS 1.1 (< secondary school, secondary school graduation, some post-secondary education and post-secondary degree/diploma). Classification into urban or rural status was based on geographic identifiers of the sampling frame of the CCHS 1.2 which defines urban areas as “continuously built-up areas having a population concentration of 1,000 or more and a population density of 400 or more per square kilometre based on the previous census” (www.statscan.com).

Both BMI and presence of a comorbid medical condition were captured by participant self-report in the CCHS 1.2 and are therefore subject to potential reporting bias. We used the CCHS 1.2 classification of chronic medical conditions where participants were classified as having a comorbid medical condition if they reported professional diagnosis of one of the following conditions within the 6 months preceding the survey: asthma, fibromyalgia, arthritis, back problems, high blood pressure, migraine headaches, diabetes, epilepsy, heart disease, cancer, stomach or intestinal ulcers, effects of a stroke, bowel disorder, cataracts, glaucoma, thyroid condition, chronic fatigue syndrome, multiple chemical sensitivity, chronic bronchitis, emphysema/chronic pulmonary disease. Not all of the aforementioned conditions are necessarily always chronic (i.e. cataract disease can be treated), nor are all these diagnoses easily ascertainable (e.g. multiple chemical sensitivity). However, all conditions were included to maintain consistency with other analyses generated by the CCHS 1.2. Comorbid psychiatric
disorders were assessed using the derived variables that were generated by the WMH-CIDI for these disorders in the CCHS 1.2.

Primary care health service use was measured using OHIP billing data to calculate both the number of visits to a primary care physician made during the outcome window (for any indication, as any visit theoretically presents an opportunity to arrange for screening) and to determine whether or not women have a usual care provider (defined as >50% of visits to one primary care provider) (Upshur et al., 2006).

10 Statistical Analyses and Power Calculations

Sociodemographic and primary care health service use characteristics in women with and without MDD/clinically significant psychological distress (K6 ≥ 8) were compared using t-tests for continuous variables and chi-square tests for categorical variables. Chi-square tests of association were used to assess bivariate relationships between MDD/clinically significant psychological distress (K6 ≥ 8) and screening for breast and cervical cancers, respectively. Because previous research indicated that there may be an effect of age on the relationship between depression and cervical cancer screening (Kaida et al., 2008), a subgroup analysis was undertaken to explore the relationship between depression and cervical cancer screening in women under and over age 40.

To account for potential confounding variables and evaluate the impact of primary care health service use, logistic regression was used in multivariable analyses where the primary independent variable was either MDD/K6 ≥ 8; other covariates were included in the
multivariable model when their inclusion changed the estimate of the effect of depression on screening outcome by greater than 10% in either direction (Harrell, 2001). All estimates were weighted to represent the population of Ontario using weights generated by Statistics Canada for the CCHS 1.2. As such, results are presented using weighted percentages. Subset sample sizes are presented when the estimates are based on N < 100. A bootstrapping resampling procedure was used to calculate variance estimates to account for the multi-stage sampling design. The analysis was generated using SAS software, version 9.1 of the SAS system for UNIX (2002).

Sample size calculations were performed prior to study initiation. The smaller of the two sample sizes was breast cancer screening because of the tighter age limitations so this was considered in determining adequate power for the analysis. We estimated the sample size of women in Ontario in the CCHS 1.2 sample who were eligible for screening mammograms to be 2,500. According to depression prevalence data from the CCHS 1.2, there was likely to be ~5% prevalence of MDD in the age group of women (50-69) eligible for screening mammograms (N=125). Based on an expected mammography screening rate in non-depressed women of 60%, we would be able to detect a relative risk of 0.79 for women with depression relative to women without depression with probability (power) 0.8 and Type I error probability of 0.05.
<table>
<thead>
<tr>
<th>Data Source</th>
<th>Description</th>
<th>Use(s) in Present Study</th>
<th>Covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Sample</td>
<td>Exposure Variable</td>
</tr>
<tr>
<td>Canadian Community Health Survey version 1.2</td>
<td>Cross-sectional Canadian population-based health survey</td>
<td>Identification of Cohorts</td>
<td>-</td>
</tr>
<tr>
<td>(Mental Health and Well-Being Component)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Ontario Cancer Registry (OCR)</td>
<td>New Cancer Diagnoses in Ontario</td>
<td>Exclude women with history of cervical, uterine or ovarian cancer (Cohort 1) and breast cancer (Cohort 2)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Registered Persons Database (RPDB)</td>
<td>Births, deaths and geographic information</td>
<td>Exclude women who died prior to experiencing an outcome</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Canadian Institute for Health Information –</td>
<td>Inpatient hospitalization and same-day surgery data</td>
<td>Exclude women with prior hysterectomy (Cohort 1) and mastectomy (Cohort 2)</td>
<td>-</td>
</tr>
<tr>
<td>Discharge Abstract Database (CIHI-DAD)</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td></td>
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<tr>
<td>Ontario Health Insurance Plan (OHIP)</td>
<td>Physician Billing Claims</td>
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<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytobase</td>
<td>Ontario cervical cytology database</td>
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<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ontario Breast Screening Program (OBSP)</td>
<td>Information on screening mammograms for women screened through OBSP</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
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</tr>
</tbody>
</table>
Chapter 4

Results

The purpose of this chapter is to:

- Present and compare baseline characteristics for the breast cancer screening and cervical cancer screening cohorts

- Present the bivariable relationships between:
  
  a. Major Depressive Disorder (MDD) and cervical cancer screening (with subgroup analysis by age);

  b. Major Depressive Disorder (MDD) and breast cancer screening;

  c. Clinically significant psychological distress and cervical cancer screening (with subgroup analysis by age); and

  d. Clinically significant psychological distress and breast cancer screening.

- Present adjusted estimates for relationships that were statistically significant in bivariable analysis:

  a. Major Depressive Disorder (MDD) and breast cancer screening;

  b. Clinically significant psychological distress and breast cancer screening; and

  c. Clinically significant psychological distress and cervical cancer screening in women aged 40-70.
11 Baseline Characteristics

The number of women eligible for screening were N=4042 in the cervical cancer screening group (N= 303 with MDD, weighted estimate 6.51%) and N=1403 in the breast cancer screening group (N=67 with MDD, weighted estimate 4.09%). Clinically significant psychological distress as measured by the Kessler 6-item distress scale (K6 ≥8) were present in 10.5% (N=491) of the cervical cancer screening sample and 8.42% (N=134) of the breast cancer screening sample. Sociodemographic and health service use characteristics are presented in Table 2, Table 3 (cervical cancer screening sample) Table 4 and Table 5 (breast cancer screening sample). Overall, two-thirds (66.9%) of eligible women received pap tests and 60.9% of eligible women received screening mammography within the specified outcome windows.

12 Bivariable Relationships

Bivariate relationships between MDD/clinically significant psychological distress and screening are illustrated in Figure 1.

12.1 Major Depressive Disorder (MDD)

There was no difference in the proportion of women with and without MDD who received screening pap tests during the 3 year follow-up period (X²=0.55, p =0.457). Based on previous literature suggesting that the effect of depression on pap testing might be limited to older women, we divided the sample based on the median age (40). Women ages 40-70 were less likely to receive pap tests (53.9% vs. 63.5%), however this difference was not statistically significant (X²=2.02, p = 0.154). For mammography screening, 46.1% of women with MDD were screened
compared to 61.5% of non-depressed women during the 2 year follow-up period ($X^2 = 5.47, p = 0.019$).

### 12.2 Clinically Significant Psychological Distress (K6 ≥ 8)

Only 49.9% of women ($N = 78$) with clinically significant psychological distress had screening mammography in the 2 years subsequent to the CCHS 1.2 survey, compared to 61.9% of women without clinically significant depressive symptoms ($X^2 = 6.61, P = 0.01$). Overall, there was no difference in Pap test screening between women with and without clinically significant psychological distress ($X^2 = 3.63, P = 0.57$). In sub-group analysis by age, women ages 40-70 with clinically significant psychological distress ($N = 185$) were significantly less likely to receive pap tests than those without distress (49.9% vs. 64.1%, $X^2 = 6.47, P = 0.01$) (Figure 2).

### 13 Multivariable Relationships

Multivariable analyses are presented in Table 6. The association between MDD and breast cancer screening was no longer statistically significant after adjusting for potential confounding variables. However, in multivariable modeling, psychological distress continued to predict reduced mammography screening compliance ($OR = 0.63, 95\% CI 0.40$ to $0.97$). The association between psychological distress and cervical cancer screening in women aged 40-70 persisted at the level of a trend in multi-variable analysis ($OR = 0.65, 95\% CI 0.41$ to $1.04$).
### Table 2. Baseline Characteristics: Cervical Cancer Screening – Major Depressive Disorder

<table>
<thead>
<tr>
<th>Demographics</th>
<th>MDD (N=303)</th>
<th>No MDD (N=3739)</th>
<th>Test Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean/ % (95% CI)</td>
<td>Mean/ % (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in years</td>
<td>38.1 (36.4-39.7)</td>
<td>40.9 (40.5-41.3)</td>
<td>t =-3.15</td>
<td>0.10</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>25.9 (25.1-26.7)</td>
<td>25.3 (25.1-25.5)</td>
<td>t =1.26</td>
<td>0.21</td>
</tr>
<tr>
<td>Married/Common-Law</td>
<td>47.4 (39.5-55.2)</td>
<td>68.3 (66.5-70.1)</td>
<td>X^2=24.6</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td>X^2=0.56</td>
<td>0.89</td>
</tr>
<tr>
<td>&lt; Secondary</td>
<td>14.0 (8.58-19.5)</td>
<td>15.7 (14.2-17.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>21.3 (14.6-28.0)</td>
<td>22.3 (20.3-24.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some post-secondary</td>
<td>9.23 (5.27-13.2)</td>
<td>9.69 (8.42-1.10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-secondary</td>
<td>54.6 (45.9-63.2)</td>
<td>51.8 (49.6-54.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Income Quartile</td>
<td></td>
<td></td>
<td>X^2=14.8</td>
<td>0.002*</td>
</tr>
<tr>
<td>Lowest</td>
<td>14.0 (9.82-18.2)</td>
<td>6.98 (5.88-8.07)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-middle</td>
<td>21.1 (14.4-27.7)</td>
<td>16.4 (14.7-18.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper-middle</td>
<td>26.8 (19.9-33.8)</td>
<td>34.2 (32.1-36.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Highest</td>
<td>28.6 (20.5-36.8)</td>
<td>35.6 (33.3-37.9)</td>
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<td>Urban residence</td>
<td>81.9 (74.6-89.2)</td>
<td>83.1 (80.6-85.5)</td>
<td>X^2=0.11</td>
<td>0.74</td>
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<td>Immigrant</td>
<td>24.0 (16.5-31.5)</td>
<td>33.5 (31.3-35.6)</td>
<td>X^2=5.48</td>
<td>0.02*</td>
</tr>
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</table>

### Health Service Use

<table>
<thead>
<tr>
<th></th>
<th>MDD (N=303)</th>
<th>No MDD (N=3739)</th>
<th>Test Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual care provider</td>
<td>53.9 (46.0-61.9)</td>
<td>55.1 (52.8-47.4)</td>
<td>X^2=6.08</td>
<td>0.78</td>
</tr>
<tr>
<td>Primary care visits</td>
<td>26.3 (22.9-29.8)</td>
<td>19.0 (18.3-19.7)</td>
<td>t =4.00</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Chronic medical condition</td>
<td>71.1 (67.4-75.6)</td>
<td>56.8 (54.2-58.9)</td>
<td>X^2=12.4</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>
Abbreviations: CI = Confidence Interval; MDD = Major Depressive Disorder; *p < 0.05

*Percentages are weighted to represent the population of Ontario using Statistics Canada weights generated for Ontario respondents to the Canadian Community Health Survey Version 1.2. Therefore, numerators and denominators are not presented for individual cells. Note that psychiatric comorbidities were not reportable due to small sample sizes (< 5 in some cells) and high coefficients of variation (>15%) that indicate poor reliability and validity of weighted estimates;

b Number of primary care visits (for any indication) over the 3 year follow-up period.

c Chronic health conditions were reported by participants as having been diagnosed by a professional and included: asthma, fibromyalgia, arthritis, back problems, high blood pressure, migraine headaches, diabetes, epilepsy, heart disease, cancer, stomach or intestinal ulcers, effects of a stroke, bowel disorder, cataracts, glaucoma, thyroid condition, chronic fatigue syndrome, multiple chemical sensitivity, chronic bronchitis, emphysema/chronic pulmonary disease.
Table 3. Baseline Characteristics: Cervical Cancer Screening – Psychological distress $^a$

<table>
<thead>
<tr>
<th>Variable</th>
<th>K6 &gt; 8 (N=491)</th>
<th>K6 &lt; 8 (N=3564)</th>
<th>Test Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in years</td>
<td>38.7 (37.2-40.1)</td>
<td>41.0 (40.6-41.4)</td>
<td>$t =-2.81$</td>
<td>0.005*</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>25.7 (25.1-26.7)</td>
<td>25.3 (25.1-25.5)</td>
<td>$t =0.93$</td>
<td>0.35</td>
</tr>
<tr>
<td>Married/Common-Law</td>
<td>55.8 (50.0-61.5)</td>
<td>68.3 (66.3-70.2)</td>
<td>$X^2 =17.1$</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td>$X^2 =12.3$</td>
<td>0.006*</td>
</tr>
<tr>
<td>&lt; secondary</td>
<td>22.4 (17.6-27.3)</td>
<td>14.9 (13.3-16.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>24.3 (18.6-30.0)</td>
<td>22.0 (20.0-24.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some post-secondary</td>
<td>10.5 (7.30-13.8)</td>
<td>9.15 (7.92-10.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-secondary</td>
<td>42.3 (36.0-48.6)</td>
<td>53.0 (50.7-55.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Income Quartile</td>
<td></td>
<td></td>
<td>$X^2 =46.4$</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Lowest</td>
<td>16.2 (12.4-20.1)</td>
<td>6.44 (5.34-7.53)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-middle</td>
<td>23.6 (18.4-28.8)</td>
<td>15.9 (14.2-17.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper-middle</td>
<td>49.4 (36.9-61.9)</td>
<td>34.0 (31.9-36.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Highest</td>
<td>21.2 (16.0-26.4)</td>
<td>36.8 (34.4-39.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban residence</td>
<td>84.5 (79.3-89.7)</td>
<td>82.9 (80.3-85.5)</td>
<td>$X^2 =0.35$</td>
<td>0.56</td>
</tr>
<tr>
<td>Immigrant</td>
<td>31.9 (25.7-38.1)</td>
<td>32.9 (30.6-35.1)</td>
<td>$X^2 =0.09$</td>
<td>0.77</td>
</tr>
<tr>
<td>Health Service Use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usual care provider</td>
<td>49.9 (44.0-55.7)</td>
<td>55.7 (53.4-58.0)</td>
<td>$X^2 =3.57$</td>
<td>0.06</td>
</tr>
<tr>
<td>Primary care visits$^b$</td>
<td>26.9 (24.3-29.4)</td>
<td>18.6 (17.9-19.3)</td>
<td>$t =6.08$</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Chronic medical condition$^c$</td>
<td>75.6 (70.9-80.4)</td>
<td>55.6 (53.3-58.0)</td>
<td>$X^2 =48.3$</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>
**Abbreviations:** CI = Confidence Interval; K6 = Kessler 6-item distress scale; *p < 0.05

*a* Percentages are weighted to represent the population of Ontario using Statistics Canada weights generated for Ontario respondents to the Canadian Community Health Survey Version 1.2. Therefore, numerators and denominators are not presented for individual cells. Note that psychiatric comorbidities were not reportable due to small sample sizes (< 5 in some cells) and high coefficients of variation (>15%) that indicate poor reliability and validity of weighted estimates; 

*b* Number of primary care visits (for any indication) over the 3 year follow-up period.

*c* Chronic health conditions were reported by participants as having been diagnosed by a professional and included: asthma, fibromyalgia, arthritis, back problems, high blood pressure, migraine headaches, diabetes, epilepsy, heart disease, cancer, stomach or intestinal ulcers, effects of a stroke, bowel disorder, cataracts, glaucoma, thyroid condition, chronic fatigue syndrome, multiple chemical sensitivity, chronic bronchitis, emphysema/chronic pulmonary disease.
Table 4. Baseline Characteristics. Breast Cancer Screening\textsuperscript{a}: Major Depressive Disorder

<table>
<thead>
<tr>
<th></th>
<th>MDD (N=67)</th>
<th>No MDD (N=1331)</th>
<th>Test Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean/% (95% CI)</td>
<td>Mean/% (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in years</td>
<td>56.3 (55.1-57.5)</td>
<td>58.0 (57.6-58.4)</td>
<td>(t = 2.31)</td>
<td>0.005*</td>
</tr>
<tr>
<td>Married/Common-Law</td>
<td>47.5 (30.5-64.6)</td>
<td>75.6 (72.5-78.6)</td>
<td>(X^2 = 23.9)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Education</td>
<td>X2=3.62</td>
<td>0.31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; secondary</td>
<td>26.1 (11.9-40.2)</td>
<td>27.7 (24.2-30.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>31.2 (14.0-48.4)</td>
<td>21.6 (18.7-24.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some post-secondary</td>
<td>6.90 (1.70-13.6)</td>
<td>6.46 (4.62-8.29)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-secondary</td>
<td>33.8 (18.4-49.1)</td>
<td>43.7 (40.1-47.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Income Quartile</td>
<td>X2=11.7</td>
<td>0.009*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lowest</td>
<td>10.5 (3.36-17.7)</td>
<td>6.79 (4.82-8.76)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-middle</td>
<td>29.1 (14.3-43.8)</td>
<td>15.8 (13.2-18.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper-middle</td>
<td>21.4 (10.0-32.8)</td>
<td>37.4 (33.7-41.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Highest</td>
<td>25.8 (9.88-41.7)</td>
<td>31.0 (27.1-34.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban residence</td>
<td>85.9 (72.0-99.9)</td>
<td>79.9 (75.8-84.0)</td>
<td>(X^2 = 1.25)</td>
<td>0.26</td>
</tr>
<tr>
<td>Immigrant</td>
<td>29.4 (13.6-45.2)</td>
<td>36.6 (32.7-40.5)</td>
<td>(X^2 = 1.23)</td>
<td>0.27</td>
</tr>
<tr>
<td><strong>Health Service Use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usual care provider</td>
<td>59.5 (44.0-75.1)</td>
<td>65.0 (61.5-68.5)</td>
<td>(X^2 = 0.71)</td>
<td>0.40</td>
</tr>
<tr>
<td>Primary care visits\textsuperscript{b}</td>
<td>23.0 (17.9-28.0)</td>
<td>14.9 (14.0-15.8)</td>
<td>(t = -4.30)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Chronic medical condition\textsuperscript{c}</td>
<td>91.2 (80.6-100)</td>
<td>78.0 (74.5-81.4)</td>
<td>(X^2 = 5.71)</td>
<td>0.02*</td>
</tr>
</tbody>
</table>
Abbreviations: CI = Confidence Interval; MDD = Major Depressive Disorder; *p < 0.05

aPercentages are weighted to represent the population of Ontario using Statistics Canada weights generated for Ontario respondents to the Canadian Community Health Survey Version 1.2. Therefore, numerators and denominators are not presented for individual cells. Note that psychiatric comorbidities were not reportable due to small sample sizes (< 5 in some cells) that indicate poor reliability and validity of weighted estimates and high coefficients of variation (>15%); bNumber of primary care visits (for any indication) over the 2 year follow-up period.

Chronic health conditions were reported by participants as having been diagnosed by a physician and included: asthma, fibromyalgia, arthritis, back problems, high blood pressure, migraine headaches, diabetes, epilepsy, heart disease, cancer, stomach or intestinal ulcers, effects of a stroke, bowel disorder, cataracts, glaucoma, thyroid condition, chronic fatigue syndrome, multiple chemical sensitivity, chronic bronchitis, emphysema/chronic pulmonary disease. Note that Body Mass Index was not contrasted in this group as it is not known to be a predictor of mammography screening compliance and therefore was unlikely to be an important confounding variable.
Table 5. Baseline Characteristics. Breast Cancer Screening\textsuperscript{a}: Psychological distress

<table>
<thead>
<tr>
<th></th>
<th>K6 ( \geq 8 ) (N=134)</th>
<th>K6 (&lt; 8) (N=1269)</th>
<th>Test Statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean/ % (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in years</td>
<td>58.0 (56.8-51.2)</td>
<td>57.9 (57.6-58.3)</td>
<td>t= 0.12</td>
<td>0.91</td>
</tr>
<tr>
<td>Married/Common-Law</td>
<td>68.5 (58.5-78.5)</td>
<td>75.0 (71.9-78.2)</td>
<td>( X^2=2.01 )</td>
<td>0.16</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td>( X^2=9.76 )</td>
<td>0.02*</td>
</tr>
<tr>
<td>(&lt;) secondary education</td>
<td>40.8 (29.1-52.6)</td>
<td>26.3 (23.1-29.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td>24.3 (13.8-34.9)</td>
<td>21.8 (18.8-24.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some post-secondary</td>
<td>9.71 (2.54-16.9)</td>
<td>5.89 (4.17-7.61)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-secondary</td>
<td>24.8 (15.4-34.1)</td>
<td>45.0 (41.4-48.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Income Quartile</td>
<td></td>
<td></td>
<td>( X^2=21.5 )</td>
<td>(&lt;0.001^*)</td>
</tr>
<tr>
<td>Lowest</td>
<td>18.1 (9.44-26.7)</td>
<td>5.92 (4.09-7.74)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-middle</td>
<td>32.6 (21.6-43.7)</td>
<td>14.9 (12.4-17.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper-middle</td>
<td>42.5 (21.9-63.1)</td>
<td>38.3 (34.5-42.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Highest</td>
<td>16.3 (7.33-25.3)</td>
<td>32.0 (28.0-36.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban residence</td>
<td>82.7 (72.0-93.3)</td>
<td>80.0 (75.8-84.2)</td>
<td>( X^2=0.22 )</td>
<td>0.64</td>
</tr>
<tr>
<td>Immigrant</td>
<td>42.4 (30.0-55.7)</td>
<td>35.7 (31.7-39.6)</td>
<td>( X^2=0.98 )</td>
<td>0.32</td>
</tr>
<tr>
<td><strong>Health Service Use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usual care provider</td>
<td>64.3 (55.3-75.3)</td>
<td>64.8 (61.2-68.4)</td>
<td>( X^2=0.09 )</td>
<td>0.93</td>
</tr>
<tr>
<td>Primary care visits\textsuperscript{b}</td>
<td>22.1 (18.2-26.0)</td>
<td>14.6 (13.7-15.5)</td>
<td>( t=-3.69 )</td>
<td>0.002*</td>
</tr>
<tr>
<td>Chronic medical condition\textsuperscript{c}</td>
<td>90.0 (82.9-97.1)</td>
<td>77.4 (73.8-80.1)</td>
<td>( X^2=8.68 )</td>
<td>0.003 *</td>
</tr>
</tbody>
</table>
**Abbreviations:** CI = Confidence Interval; K6 = 6-item Kessler Distress Scale; *p < 0.05

*Percentages are weighted to represent the population of Ontario using Statistics Canada weights generated for Ontario respondents to the Canadian Community Health Survey Version 1.2. Therefore, numerators and denominators are not presented for individual cells. Note that psychiatric comorbidities were not reportable due to small sample sizes (< 5 in some cells) and high coefficients of variation (>15%) that indicate poor reliability and validity of weighted estimates; bNumber of primary care visits (for any indication) over the 2 year follow-up period.

Chronic health conditions were reported by participants as having been diagnosed by a physician and included: asthma, fibromyalgia, arthritis, back problems, high blood pressure, migraine headaches, diabetes, epilepsy, heart disease, cancer, stomach or intestinal ulcers, effects of a stroke, bowel disorder, cataracts, glaucoma, thyroid condition, chronic fatigue syndrome, multiple chemical sensitivity, chronic bronchitis, emphysema/chronic pulmonary disease. Note that Body Mass Index was not contrasted in this group as it is not known to be a predictor of mammography screening compliance and therefore was unlikely to be an important confounding variable.
Figure 1. Screening outcomes

*<p < 0.05; Percentages are weighted according to Statistics Canada weights for Ontario participants of the CCHS 1.2.
Figure 2. Cervical cancer screening outcome by age-group in women with and without clinically significant psychological distress (K6 > or = 8)

*\(p < 0.05\); This finding approached statistical significance in adjusted analyses. Percentages are weighted according to Statistics Canada weights for Ontario participants of the CCHS 1.2.
### Table 6. Multivariable Models

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% Confidence Interval)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pap Tests (Ages 40-70)</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Clinically Significant Psychological Distress (K6 ≥ 8)</td>
<td>0.65 (0.41-1.04)</td>
</tr>
<tr>
<td>Age</td>
<td>0.98 (0.95-0.98)</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Marital Status&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.64 (0.48-0.85)</td>
<td>0.002*</td>
</tr>
<tr>
<td>Income (quartile) – lowest as referent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-middle</td>
<td>1.05 (0.58-1.92)</td>
<td>0.87</td>
</tr>
<tr>
<td>Upper-middle</td>
<td>1.03 (0.59-1.79)</td>
<td>0.93</td>
</tr>
<tr>
<td>Highest</td>
<td>1.55 (0.88-2.75)</td>
<td>0.13</td>
</tr>
<tr>
<td>Education - &lt; Secondary as referent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary Graduate</td>
<td>1.71 (1.13-2.57)</td>
<td>0.01*</td>
</tr>
<tr>
<td>Some post-secondary</td>
<td>1.50 (0.88-2.56)</td>
<td>0.14</td>
</tr>
<tr>
<td>Post-secondary graduate</td>
<td>1.59 (1.11-2.28)</td>
<td>0.01*</td>
</tr>
</tbody>
</table>

| Mammography c | Major Depressive Disorder | 0.68 (0.29-1.59) | 0.38 |
| Age | 1.00 (0.97-1.04) | 0.76 |
| Marital Status<sup>b</sup> | 0.58 (0.42-0.80) | <0.001* |
| Income (quartile) – lowest as referent | | | |
| Low-middle | 1.23 (0.68-2.25) | 0.50 |
| Upper-middle | 1.71 (0.94-3.11) | 0.08** |
| Highest | 2.49 (1.33-4.67) | 0.005* |
| Chronic Medical Condition | 1.05 (0.69-1.61) | 0.81 |
| Number of primary care visits | 1.02 (1.00-1.03) | 0.01* |

| Mammography d | Clinically Significant Depressive Symptoms (K6 ≥ 8) | 0.63 (0.41-0.97) | 0.04* |
| Marital Status<sup>b</sup> | 0.55 (0.34-0.76) | <0.001* |
| Income (quartile) – lowest as referent | | | |
| Low-middle | 1.21 (0.65-2.23) | 0.55 |
| Upper-middle | 1.56 (0.84-2.89) | 0.16 |
| Highest | 2.10 (1.09-4.07) | 0.03* |
| Education - < Secondary as referent | | | |
| Secondary Graduate | 1.32 (0.87-2.01) | 0.20 |
| Some post-secondary | 1.52 (0.78-2.97) | 0.22 |
| Post-secondary graduate | 1.31 (0.88-1.96) | 0.18 |
| Number of primary care visits | 1.02 (1.00-1.03) | 0.01* |

<sup>a</sup>Using a process of normalized weights (because the bootstrapping procedure does not allow for model fit testing) there was good model fit (Hosmer and Lemeshow test: $X^2=15.4$, p=0.05) and no significant multi-collinearity (Tolerance all >0.80);<sup>b</sup> divorced/separated/widowed vs. married/common-law;<sup>c</sup> There was good model fit (Hosmer and Lemeshow test: $X^2=13.4$, p=0.100) and no significant multi-collinearity (Tolerance all > 0.85);<sup>d</sup> There was good model fit (Hosmer and Lemeshow test: $X^2=16.3$, p=0.06) and no multi-collinearity (Tolerance all > 0.85).
Chapter 5
Discussion

The purpose of this chapter is to:

1. Review the main findings of the study.
2. Outline the strengths of the study.
3. Outline and address the potential limitations of the study.
4. Outline potential explanations for the study results.
5. Describe the clinical and public health practice implications of the study results.
6. Describe future plans to extend the findings of this thesis.

14 Main Findings

Women with major depressive disorder (MDD) were less likely to receive screening mammography than women without MDD, although this association did not persist after controlling for potential confounding factors. However, having clinically significant psychological distress (K6 ≥ 8) reduced the odds that a woman in Ontario would receive screening mammography within the subsequent 2 years by 37% (i.e. OR = 0.63), even after adjusting for known sociodemographic predictors of mammography compliance such as age, marital status, socioeconomic status and primary care service use. Neither women with MDD nor clinically significant psychological distress were less likely to receive cervical cancer screening
than their non-depressed or distressed counterparts across the full age range. However, women aged 40-70 with clinically significant psychological distress were less likely to receive cervical cancer screening than their non-distressed counterparts. This association approached conventional levels of statistical significance in multivariable analysis. All of these findings occurred in the context of increased use of primary care services by depressed and distressed women (whereas one might expect that depressed women should be more likely to be screened on the basis of their increased primary health care utilization).

The results of this study are in keeping with existing literature that suggests as many as half of eligible women do not receive screening at recommended intervals for breast and cervical cancers (Gentlemen & Lee, 1997; Ringash et al., 2001; Fehringer et al., 2005; Upshur et al., 2006). Our results lend further support to the assertion that clinically significant psychological distress is independently associated with screening mammography compliance and potentially Pap test compliance in middle-aged and older women. With respect to mammography compliance, this is the first Canadian population-level data to support a relationship and with respect to cervical cancer compliance, the findings complement previous findings using self-reported cervical cancer screening as an outcome (Kaida et al., 2008). The results of this study strengthen the results in the existing literature where studies measuring depressive symptoms or psychological distress were more likely to reveal an association between depression and screening outcomes than studies using strict diagnostic criteria for major depression. Additionally, in the present study, this phenomenon was observed in the same sample of women.

15 Strengths of the study
There are several elements of this study that strengthen its contribution to existing literature. In this study we used population-based survey data linked to administrative health data. This provided the advantages of standardized measures of major depression and psychological distress, accurate measures for cervical and breast cancer screening and adequate information on potential confounding variables. The high response rate of the community-based CCHS 1.2 survey and the high number of participants who agreed to data linkage argues that the results can be generalized to the population of Ontario, Canada and perhaps other developed countries with similar screening guidelines, processes and funding.

16 Potential Limitations

1. It is not known whether MDD was a factor in non-response to the CCHS 1.2 survey. Previous research has shown that telephone respondents tend to report very sensitive information and that telephone surveys are an optimal method for reaching the most respondents (Siemiatycki and Campbell, 1984). However, the concern is that severity of depression might result in a sampling bias. This might limit the ability to generalize results to the most severely depressed women in Ontario. In addition, it is possible that the most severely depressed women are less likely to participate in a community survey and also less likely to get cervical and breast cancer screening. This would bias the present study against finding an association. However, an association was found between having clinically significant psychological distress and mammography screening (even though more severely depressed women may not have been part of the sample).
2. A second potential limitation of the present investigation is that the mental status of the participating women is not known over the course of the follow-up period. It is not known whether women with MDD or those with clinically significant psychological distress received treatment targeting their symptoms over the study period (or whether they achieved a spontaneous remission of symptoms). Neither is it known whether women originally classified as non-depressed or non-distressed became so over the follow-up period. However, in both of these situations, one would expect bias to be in direction against finding an association (i.e. resolution of symptoms improving screening outcomes or emergence of symptoms worsening screening outcomes). The fact that a cross-sectional measure of depressive symptoms/distress predicts reduced mammography screening over the subsequent 2 years (despite the fact that some women may have received treatment), strengthens the validity of the observed association. Future research into whether treatment of psychological distress improves screening outcomes is warranted as a next investigative step.

3. A further limitation of the study is that it was not designed to determine the detailed mechanisms for reduced screening. However, our findings that women with clinically significant psychological distress have lower screening rates despite extensive primary care health service use suggest that primary care physicians may be in an optimal position to intervene to improve screening outcomes, regardless of the mechanism(s) behind the findings. Although Pap testing is an office-based procedure, most women in Ontario receive screening mammography through the Ontario Breast Screening Program (OBSP). Therefore, there is not necessarily a direct referral route from primary care practitioner to screening. To obtain screening through OBSP, women may be required to make or return multiple telephone calls and then attend an appointment in an unfamiliar place for a fairly uncomfortable procedure (that requires them to expose private body parts). It is plausible
that symptoms of psychological distress and depression such as lack of motivation, poor self-care, and feelings of guilt/shame, distraction by other somatic symptoms or distraction by life crisis situations could compromise the sustained effort required for women to receive a screening mammogram through OBSP. Further investigation (using primary data collection) will be needed to clarify where along the pathway from referral (or screening recommendation) women with depressive symptoms may be stalled.

17 Explanations for Study Findings

The reason why the symptom-based measure of psychological distress was more strongly associated with screening outcomes than the diagnostic measure of depression in predicting screening participation in this study warrants consideration. It is possible in the present study that the larger number of women with symptoms of psychological distress than with MDD (N=185 vs. N=132 for women ages 40-70 for cervical cancer screening; N=134 vs. N=67 for breast cancer screening) increased the power to detect significant effects. It is notable that the point estimates of mammography screening for the two variables (0.68 in women with MDD versus 0.63 for women with clinically significant psychological distress) are virtually identical while the confidence intervals differed. This suggests that the difference between the two findings is due to inadequate sample size in the MDD group. However, given the consistency of this finding with those in the existing literature, it is important to consider other explanations. As discussed, the K6 is intended to be a non-specific psychiatric distress scale (Kessler et al., 2003b). Many individuals with positive scores have sub-threshold depressive symptoms, while still others have anxiety disorders, adjustment disorders or are experiencing psychological stress. The sample
sizes in this study were not large enough to generate meaningful subgroup analysis by psychiatric diagnosis. However, the key point is that patients with clinically significant symptoms of psychological distress (some of whom may have MDD, some of whom may have other mental illness or adjustment disorders) are at risk of reduced mammography screening. Perhaps psychological distress is actually the key determinant, with major depression being only one source of distress. Consistent with other emerging evidence regarding the impact of subthreshold depressive disorders on health-related function and quality of life (Ayuso-Mateos et al., 2010), these results suggest a broadening of the conceptualization of the relationship between depression and screening compliance to consider clinically significant depressive symptoms or psychiatric distress as a determinant of preventive screening.

The mechanisms explaining the observed associations between psychological distress and reduced screening are likely to be complex and involve patient, provider and systemic factors. The results of our study introduced a new finding that clinically significant symptoms of psychological distress were associated with reduced mammography screening and reduced pap test screening (in older women), despite significantly more visits to primary care practitioners. This type of association has been shown in other diseases: for example, Lipscombe et al., (2005) found that even when women with diabetes made more doctor visits, they had reduced mammography screening. It was outside the scope of the present study to investigate the mechanism behind this finding in more detail. However, it is plausible that clinically significant symptoms (irrespective of psychiatric diagnosis) may somehow interfere with screening processes, resulting in reduced attention to preventive health in the women who suffer such symptoms. Depressive symptoms such as psychological distress, lack of motivation, poor self-care, guilt/shame, anxiety, feeling overwhelmed or even distraction by other somatic symptoms could compromise standard processes for screening and/or create a competing risk for care in the
primary care setting that results in reduced attention to secondary prevention services. This may be particularly important in older depressed or distressed women, supported by the fact that the women in the breast cancer screening cohort were all over age 50 and only women over age 40 with a high depressive symptom burden had reduced pap test screening in our study.

18 Implications

In this study, women with clinically significant psychological distress had 37% reduced odds of receiving screening mammography compared to non-distressed women. In Ontario, on a population level, this translates into almost 6000 “missed” opportunities for screening mammography in a 2 year time-frame. This represents a significant number of women. In addition, the findings that women aged 40-70 with clinically significant psychological distress appear to be at risk for reduced cervical cancer screening may have particularly importance. The development of cervical cancer is slow and most incident cases present in women over the age of 35, arguing the need for increased vigilance in that age group (Hemminki et al., 2001). As this study demonstrated that women with clinically significant mental health symptoms do present to their primary care providers, this may be an important point of intervention to optimize screening compliance. In addition, mental health providers treating women with clinically significant psychological distress should be alert to the possibility that this may be a barrier to good preventive health care. It may be important for providers to extend their scope of practice to inquiring about compliance with preventive screening and collaborating with primary care practitioners to optimize screening compliance. Intervention at both the psychiatric specialist and
primary care levels might include raising the topic of the need for screening, exploring barriers to screening, helping women arrange for screening and ensuring systematic follow-up.

19 Further Investigation

Further investigation in this area will focus on the mechanisms that underlie the relationship between psychological distress and screening outcomes; clarify whether these findings can be generalized to other health care indicators; and continue to explore how depression and/or distress might modify the known positive relationship between primary care service use and screening behaviours. Investigation into whether treatment of depressive symptoms might improve screening outcomes is also warranted. This will include collection of quantitative and qualitative primary data from patients and care providers.

20 Conclusions

This rigorous population-based study adds to converging evidence that depressive symptomatology is a risk factor for reduced screening mammography and likely pap testing in older women. The results suggest a broadening of the conceptualization of the relationship between depression and screening compliance to consider clinically significant distress as a determinant of health service use. Clinicians should be alert to the possibility of missed screening in patients with psychological distress. Attention should be focused on systemic factors that can increase uptake of screening services in distressed and depressed women.
References


Appendices

Appendix A. Major Depressive Episode and Major Depressive Disorder – DSM IV-TR Diagnostic Criteria

Major Depressive Episode

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

(1) depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). Note: In children and adolescents, can be irritable mood.

(2) markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)

(3) significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. Note: In children, consider failure to make expected weight gains.

(4) insomnia or hypersomnia nearly every day

(5) psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)

(6) fatigue or loss of energy nearly every day

(7) feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)

(8) diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)

(9) recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

B. The symptoms do not meet criteria for a Mixed Episode.

C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

E. The symptoms are not better accounted for by Bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.
Major Depressive Disorder

Single Episode

A. Presence of a single Major Depressive Episode

B. The Major Depressive Episode is not better accounted for by Schizoaffective Disorder and is not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.

C. There has never been a Manic Episode, a Mixed Episode, or a Hypomanic Episode. Note: This exclusion does not apply if all the manic-like, mixed-like, or hypomanic-like episodes are substance or treatment induced or are due to the direct physiological effects of a general medical condition.

Recurrent

A. Presence of two or more Major Depressive Episodes.

   Note: To be considered separate episodes, there must be an interval of at least 2 consecutive months in which criteria are not met for a Major Depressive Episode.

B. The Major Depressive Episodes are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.

C. There has never been a Manic Episode, a Mixed Episode, or a Hypomanic Episode. Note: This exclusion does not apply if all the manic-like, mixed-like, or hypomanic-like episodes are substance or treatment induced or are due to the direct physiological effects of a general medical condition.

Specify (for current or most recent episode):

   Severity/Psychotic/Remission Specifiers
   Chronic
   With Catatonic Features
   With Atypical Features
   With Postpartum Onset

Specify

Longitudinal Course Specifiers (With and Without Interepisode Recovery)
   With Seasonal Pattern
## Appendix B. Kessler 6-item Distress Scale

**During the past 30 days, about how often did you feel ...**

<table>
<thead>
<tr>
<th></th>
<th>All of the time</th>
<th>Most of the time</th>
<th>Some of the time</th>
<th>A little of the time</th>
<th>None of the time</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td>…nervous?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>b.</td>
<td>…hopeless?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>c.</td>
<td>…restless or fidgety?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>d.</td>
<td>…so depressed that nothing could cheer you up?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>e.</td>
<td>…that everything was an effort?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>f.</td>
<td>…worthless?</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>
Appendix C. Research Ethics Board Approvals

- University of Toronto
- Centre for Addiction and Mental Health
- Sunnybrook Health Sciences Centre
University of Toronto
Office of the Vice-President, Research
Office of Research Ethics

PROTOCOL REFERENCE #23561

November 24, 2008

Dr. Paula Goering
Department of Psychiatry
Health Systems Research and Consulting Unit
Centre for Addiction and Mental Health
33 Russell Street, 3rd Floor Tower
Toronto, ON M5S 2S1

Dr. Simone Vigod
Health Policy, Management and Evaluation
T315A, 33 Russell Street
Toronto, ON M5S 2S1

Dear Dr. Goering and Dr. Vigod:

Re: Administrative Approval of your research protocol entitled, "Relationship between Major Depression and Breast and Cervical Cancer Screening Compliance in Ontario Women"

We are writing to advise you that the Office of Research Ethics has granted administrative approval to the above-named research study. The level of approval is based on the following role(s) of the University, as you have identified with your submission:

- Graduate Student research – hospital-based only
- Storage or analysis of De-identified Personal Information (data)

This approval does not substitute for ethics approval, which has been obtained from your hospital Research Ethics Board. Please note that you do not need to submit Annual Renewals, Study Completion Reports or Amendments to the ORE unless the involvement of the University changes so that ethics review is required. Please contact the ORE to determine whether a particular change to the University’s involvement requires ethics review.

Best wishes for the successful completion of your project.

Yours sincerely,

Daniel Gyewu
Research Ethics Coordinator
PROTOCOL REFERENCE #284/2008

November 6, 2008

Paula Goering, RN, PhD
Health Systems Research and Consulting Unit
Centre for Addiction and Mental Health
33 Russell Street, 3rd Floor Tower
Toronto, ON M5S 2S1

Dear Dr. Goering:

Re: Research protocol #284/2008 entitled, "Relationship Between Major Depression and Breast and Cervical Cancer Screening Compliance in Ontario Women" by Goering P, Vigod S,

We are writing to advise you that the Centre for Addiction and Mental Health Research Ethics Board (CAMH REB) has granted expedited approval to the above-named research study for a period of one year from the date of this letter1. IF THE STUDY IS EXPECTED TO CONTINUE BEYOND THE EXPIRY DATE, YOU ARE RESPONSIBLE FOR ENSURING THE STUDY RECEIVES RE-APPROVAL BY SUBMITTING THE CAMH REB "ANNUAL RENEWAL OF ETHICS APPROVAL" FORM ON OR BEFORE October 1, 2009. Should the study be completed prior to the annual renewal date, please submit a final report. The level of continuing review for this study is Level I.2

During the course of the research, any significant deviations from the approved protocol (that is, any deviation which would lead to an increase in risk or a decrease in benefit to human subjects) and/or any unanticipated developments within the research should be brought to the attention of the Research Ethics Office.

Best wishes for the successful completion of your project.

Yours sincerely,

Susan Pilon, MHSc
Manager, Research Ethics Office, CAMH

SP/md
Cc: Dr. Simone Vigod

---

1 CAMH Investigators are reminded that should they leave CAMH, they are required to inform the Research Ethics Board of the status of any on-going research. If a study is to be closed or transferred to another facility, the REB must be informed and any advertisements must be discontinued.

2 Level 1: Review of routine annual reports, changes and amendments to the approved protocol, adverse events, filing of a final report.

Transforming Lives - Transformer des vies
MEMORANDUM

To: Dr. D. Henry
President and CEO
ICES Room G106

From: Philip Hébert MD

Date: October 16, 2008

Subject: ICES Administrative Database Research

The Research Ethics Board is in receipt of your memo dated September 30, 2008 regarding research performed at ICES using administrative data in the last six months for the period April 1, 2008 – September 30, 2008 as well as the update on recent activities.

The Board has reviewed and approved the listed studies and notes that there have been no public breaches of confidentiality or privacy.

The Board has also reviewed and placed on file the Privacy Impact Assessment Form dated September 2008, which will be used in the next reporting period.

Please provide copies of the following files, which the Board would like to review:

- Child Maltreatment and the Risks of Deliberate Self-Harm
- The Young Adult Survivors of Cancer Study
- Mortality and Antipsychotic Use in Parkinsonism

This work may continue at Sunnybrook Health Sciences Centre.

Thank you for keeping the Board informed.

Philip C. Hébert MD PhD FCFPC
Chair, Research Ethics Board
## Appendix D. Dataset Creation Plan – Cervical Cancer Screening

<table>
<thead>
<tr>
<th>Name and Number of Study</th>
<th>Impact of major depression on compliance with Pap smear and mammography screening in Ontario women</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI and P&amp;B Contacts</td>
<td>Dr. Simone Vigod (MSc student) Dr. William Gnam (ICES supervisor)</td>
</tr>
<tr>
<td>PIA Approved?</td>
<td>Yes</td>
</tr>
</tbody>
</table>
| Date Last Modified and by Whom |          | October 10, 2008 by Simone Vigod/Pam Slaughter  
Feb 19, 2009 by Minh Duong-Hua  
- updated DCP as per conference call  
Feb 27, 2009 by Minh Duong-Hua and Simone Vigod  
- move exclusive of death without outcome in the follow-up period to FLAG them in the covariates session  
Mar 3, 2009 by Minh Duong-Hua  
- add details changes in this modified session |
| Short Description of Research Question | Is major depressive an independent risk factor for reduced compliance with pap test screening in Ontario women? |
| List of Datasets Used | CCHS 1.2 linked; CIHI-DAD, OCR, OHIP, Cytobase, RPD |

### Defining the Cohort

<table>
<thead>
<tr>
<th>Index Event</th>
<th>Major Depressive Episode</th>
</tr>
</thead>
</table>
| Exclusions (In order) | From CCHS 1.2  
1. non- “linked” data (SAMBDLNK ^= ’1’)  
2. Non-Ontario respondents (ADM_Q03B)  
3. ”male” sex (SEX_Q01: DHHB_SEX=1)  
4. Age <18 (DHHB_AGE)  
5. From CIHI-DAD: Hysterectomy from beginning of CIHI-DAD data to Interview event:  
- CCP Codes: 80.2, 80.3, 80.4, 80.5, 80.6, 80.7, 86.42  
- CCI Codes: 1RM89, 1RM91  
6. From OCR: History of cervical (DXCODE= 180), uterine (DXCODE= 182) |

The next step is to link the CCHS to administrative data to exclude ineligible women (ie with hysterectomy, history of cervical, uterine or ovarian cancer, death)
or ovarian (DXCODE= 183) cancer prior to interview date

7. From RPDB: Died before interview date (Data error – this usually none, but might happen)

Size of Cohort  CCHS 1.2 Ontario female residents > age 18 eligible for screening pap tests

Time Frame Definitions

Accrual Start/End Dates  Time frame of CCHS 1.2 (May-December 2002) – Index event is inclusion in CCHS 1.2 – please keep variable: “date of survey administration”

Max Follow-up Date  December 31, 2005

When does observation window terminate?  3 years post index event: December 31, 2005 (for cervical cancer screening)

Lookback Window(s)  1. Will need to look back to beginning of collection of CIHI-DAD data to find cases of hysterectomy.
   2. Look-back for mammography should be 3 years prior to index date (May 1, 1999)

Variable Definitions

Main Exposure or Risk Factor  Major Depressive Episode in 12 months preceding CCHS 1.2 survey date (defined by a combination of depression variables in CCHS 1.2)

1. Keep all Depression (includes lifetime, whether in past 12 months, suicidal and help-seeking behavior): Please keep ALL individual and derived variables (let me know if I should list them!!)
   2. Keep mania questions to rule out bipolar depressions: derived variable MIABDEPS

Baseline  Age, income, education, marital status, urban/rural, employment status, immigration, Body
**Characteristics**  Mass Index (BMI) --- all found in CCHS 1.2

For socio-demographic variables and other predictors:

1. Keep derived variable GEOBDUR2 (urban=1, rural=2)
2. Keep derived variable EDUBDR04 (4 levels of education status)
3. Keep marital status block (MSNC_Q01: DHHB_MS)
4. Keep height/weight derived variables: BMI (HWYBDBMI) and Canadian standards (HWTBDSW)
5. Keep labor force derived variables: LBFBDJST (job status over past year), LBFBDSSTU (students)
6. Keep income derived variables: INCBDIA4 (4 categories), INCBDIA2 (2 categories) and INCBDHH (total household income)
7. Keep socio-demographic characteristics derived variables: SDCBFIMM (immigration flag), SDCBGCB (country of birth grouped), SDCBDAIM (age at time of immigration), SDCBDRES (length of time in Canada since immigration)

**Other Variables**  Chronic conditions, having a family physician, number of primary care visits in preceding year, mental health and substance abuse correlates, severity of depression

**Mental Health Predictor variables from CCHS 1.2:**

1. Chronic conditions: keep all individual variables and derived variable CCCBF1
2. Keep Screening Questions (SCRB_) derived variables: Depression (SCRBFDEP); Mania (SCRFBFMA); Panic (SCRFPPAD); Generalized anxiety disorder (SCRFAGD); Social phobia (SCRFSSOP); Agoraphobia (SCRFAGP)
3. Keep all derived variables for panic, social phobia and agoraphobia to understand contribution of co-morbid psychiatric illness in the final model: PADBATT, PADBBPDS, PADBBATY, PADBBDDY, SOPBDSOP, SOPBDY, AGPBAD, AGPBDPY, AGPBBDPY
4. Keep distress scales K6 and K10 for validation: DISBDFK6, DISBDDSX
5. Keep chronic of distress and impairment: DISBDFCHR
6. Keep derived mental health service variables for severity indices:
   a. Overnight hospitalization: derived variable SERBFLHO
   b. More than one hospitalization: derived variable SERBT7DY
   c. 12-month hospitalization: derived variable SERBHYR

8. CIHI – DAD: Hysterectomy within 3 years after interview date
   - CCP Codes: 80.2, 80.3, 80.4, 80.5, 80.6, 80.7, 86.42
   - CCI Codes: 1RM89, 1RM91

9. OCR: Cervical Diagnosis (DXCODE= 180) within 3 years after interview date

10. OHIP, Number of GP visits within 3 years after interview date

11. Main Physician (GP/FP). Using OHIP - extract all OHIP visits within 3 years after
interview date, the family doctor will be defined if the percentage of visits to the physician is greater than 51% (note: only use people with at least 3 visits in the time window to define the physician)

12. From RPDB: We would like to FLAG all people who died during the time from interview event to follow-up. If the individual had the outcome of interest prior to dying, she could still be included. **However, if she died without the outcome of interest, she will not be included in the analysis** (but we will want to report how many people died within the window to eventually do a sensitivity analysis to make sure this does not alter the results).

13. Keep all bootstrapping weights from CCHS 1.2 weight file.

**NOTE: For # 10, and 11, use OHIP location to define OFFICE visits to the GP**

<table>
<thead>
<tr>
<th>Outcome Definitions</th>
<th>Screening Pap test (Y/N) within 3 years before and after interview date found either in cytobase or OHIP (for each of the database, flag the latest date to interview date if it happened before interview date, and the earliest date to interview date if it happened after interview date)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. Add dates of pap smears in cytobase</td>
</tr>
<tr>
<td></td>
<td>2. Add dates of pap smears in OHIP</td>
</tr>
<tr>
<td></td>
<td>a. Use OHIP fee codes: G365, E430, G394, L713, L812, L733</td>
</tr>
</tbody>
</table>

**Outline of Analysis Plan**

1. Cervical Cancer screening and Breast cancer screening outcomes will be analyzed separately
2. Use dates of procedures and cancer diagnoses to appropriately exclude individuals not eligible for screening
3. Descriptive statistics on key predictor variable (12-month depression)
4. Descriptive statistics on other potential predictor variables (see above)
5. Bivariate analyses to examine relationships between predictors
6. Logistic regression model with dichotomous outcome for screening
   a. Keep all sampling and bootstrapping weights from CCHS 1.2
7. May look at stratification by age and depression severity as indicated
8. May look at time to screening outcomes using survival analysis technique
Appendix E. Dataset Creation Plan - Breast Cancer Screening

<table>
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<tr>
<th>Name and Number of Study</th>
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- move exclusive of death without outcome in the follow-up period to FLAG them in the covariates session  
Mar 3, 2009 by Minh Duong-Hua  
- add details changes in this modified session |
| Short Description of Research Question | Is major depressive an independent risk factor for reduced compliance with mammography in Ontario women? |
| List of Datasets Used    | CCHS 1.2 linked; CIHI-DAD, OCR, OHIP, OBSP, RPB |

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</thead>
<tbody>
<tr>
<td>Exclusions</td>
<td>From CCHS 1.2</td>
</tr>
</tbody>
</table>
| (In order)  | 8. non- "linked" data (SAMBDLNK ^= ‘1’)  
9. Non-Ontario respondents (ADM_Q03B)  
10. "male" sex (SEX_Q01: DHHBSEX=1)  
11. Age <50 (DHHBAGE) |

The next step is to link the CCHS to administrative data to exclude ineligible women (ie
12. From CIHI-DAD: Mastectomy from beginning of CIHI-DAD data to Interview event:

- **CCP**
  
  97.12  (UNILATERAL) COMPLETE MASTECTOMY
  97.13  BILATERAL COMPLETE MASTECTOMY
  97.14  (UNILATERAL) EXTENDED SIMPLE MASTECTOMY
  97.15  BILATERAL EXTENDED SIMPLE MASTECTOMY
  97.16  (UNILATERAL) RADICAL MASTECTOMY
  97.17  BILATERAL RADICAL MASTECTOMY
  97.18  (UNILATERAL) EXTENDED RADICAL MASTECTOMY
  97.19  BILATERAL EXTENDED RADICAL MASTECTOMY
  97.21  (UNILATERAL) SUBCUTANEOUS MASTECTOMY W/ prosthesis
  97.22  OTHER (UNILATERAL) SUBCUTANEOUS MASTECTOMY
  97.23  BILATERAL SUBCUTANEOUS MASTECTOMY w/ prosthesis
  97.24  OTHER BILATERAL SUBCUTANEOUS MASTECTOMY

- **CCI**

  1YM89LA, 1YM89LAXXA, 1YM90LAPM, 1YM90LAPME, 1YM90LAPME
  1YM90LAPMG, 1YM90LAQF, 1YM90LAQFE, 1YM90LAQFF, 1YM90LAQFG
  1YM90LATP, 1YM90LATPF, 1YM90LATPG, 1YM90LAXXE, 1YM90LAXXF
  1YM90LAXXG, 1YM91LA, 1YM91LATP, 1YM91LAXXA, 1YM91LAXXE, 1YM91TR
  1YM91TRXXA, 1YM91TRXXE, 1YM91WP, 1YM91WPXXA, 1YM91WPXXE
  1YM92LAPME, 1YM92LAPMF, 1YM92LAPMG
  1YM92LAQFE, 1YM92LAQFF, 1YM92LAQFG,
  1YM92LATPE, 1YM92LATPF, 1YM92LATPG,
  1YM92LAXXE, 1YM92LAXXF, 1YM92LAXXG,
  1YM92TRPME, 1YM92TRPMF, 1YM92TRPMG,
  1YM92TRQFE, 1YM92TRQFF, 1YM92TRQFG,
  1YM92TRTPE, 1YM92TRTPF, 1YM92TRTPG,
  1YM92TRXXE, 1YM92TRXXF, 1YM92TRXXG,
  1YM92WPPME, 1YM92WPPMF, 1YM92WPPMG,
  1YM92WPQFE, 1YM92WPQFF, 1YM92WPQFG,
  1YM92WPTPTE, 1YM92WPTPF, 1YM92WPTPG,
  1YM92WPXXE, 1YM92WPXXF, 1YM92WPXXG
13. From OCR: history of breast cancer (DXCODE= 174) prior to interview date

14. From RPDB: Died before interview date (Data error – this usually none, but might happen)

Size of Cohort: CCHS 1.2 Ontario female residents > age 50 eligible for screening mammography

**Time Frame Definitions**

![Diagram of time frame definitions]

**Accrual Start/End Dates**: Time frame of CCHS 1.2 (May-December 2002) – Index event is inclusion in CCHS 1.2 – please keep variable: “date of survey administration”

Max Follow-up Date: December 31, 2004

When does observation window terminate?: 2 years past index event: December 31, 2004

**Lookback Window(s)**

3. Will need to look back to beginning of collection of CIHI-DAD data to find cases of bilateral mastectomy.

4. Look-back for mammography should be 2 years prior to index date (May 1, 2000)

**Variable Definitions**

**Main Exposure or Risk Factor**: Major Depressive Episode in 12 months preceding CCHS 1.2 survey date (defined by a combination of depression variables in CCHS 1.2)
3. Keep all Depression (includes lifetime, whether in past 12 months, suicidal and help-seeking behaviors): Please keep ALL individual and derived variables (let me know if I should list them!!)

4. Keep mania questions to rule out bipolar depressions: derived variable MIABDEPS

Baseline Characteristics
Age, income, education, marital status, urban/rural, employment status, immigration, Body Mass Index (BMI) --- all found in CCHS 1.2

For socio-demographic variables and other predictors:

8. Keep derived variable GEOBDUR2 (urban=1, rural=2)
9. Keep derived variable EDUBDR04 (4 levels of education status)
10. Keep marital status block (MSNC_Q01: DHHB_MS)
11. Keep height/weight derived variables: BMI (HWYBDBMI) and Canadian standards (HWTBDSW)
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Mental Health Predictor variables from CCHS 1.2:

14. Chronic conditions: keep all individual variables and derived variable CCCBF1
15. Keep Screening Questions (SCRB_) derived variables: Depression (SCRBFDEP); Mania (SCRBFMIA); Panic (SCRBFPAD); Generalized anxiety disorder (SCRBFGAD); Social phobia (SCRFSSOP); Agoraphobia (SCRFAGP)
16. Keep all derived variables for panic, social phobia and agoraphobia to understand contribution of co-morbid psychiatric illness in the final model: PADBATT, PADBDDS, PADBDATY, PADBDYY, SOPBDSP, SOPBDPY, AGPBDDAP, AGPBAPP, AGPBDDPY, AGPBDDPPY
17. Keep distress scales K6 and K10 for validation: DISBDK6, DISBDDSX
18. Keep chronic of distress and impairment: DISBDCHR
19. Keep derived mental health service variables for severity indices:
   a. Overnight hospitalization: derived variable SERBFLHO
   b. More than one hospitalization: derived variable SERBT7DY
   c. 12-month hospitalization: derived variable SERBFHYR


21. CIHI – DAD: Mastectomy within 2 years after interview date: (codes as in Exclusive criteria)

22. OCR: breast cancer diagnosis (DXCODE= 174) within 2 years from interview date

23. OHIP, Number of GP visits within 2 years after interview date

24. Main Physician (GP/FP), Using OHIP - extract all OHIP visits within 2 years after interview date, the family doctor will be defined if the percentage of visits to the physician is greater than 51% (note: only use people with at least 3 visits in the time window to define the physician)

25. From RPDB: We would like to FLAG all people who died during the time from interview event to follow-up. If the individual had the outcome of interest prior to dying, she could still be included. However, if she died without the outcome of interest, she will not be included in the analysis (but we will want to report how many people died within the window to eventually do a sensitivity analysis to make sure this does not alter the results).

26. Keep all bootstrapping weights from CCHS 1.2 weight file.

NOTE: For # 10, and 11, use OHIP location to define OFFICE visits to the GP.

### Outcome Definitions

Mammography (Y/N) within 2 years before and after interview date found in OBSP or OHIP database (for each of the database, flag the latest date to interview date if it happened before interview date, and the earliest date to interview date if it happened after interview date)

1. Add dates of screening mammograms in OBSP (only include if MAMDONE= ‘Y’)
2. Add dates of bilateral mammography in OHIP (fee code X185)
3. Flag if there is fine needle aspiration, core breast biopsy and breast ultrasound done within 22 months prior to the EARLIEST date of OBSP (in 1) or OHIP (in 2) where these happened AFTER the interview date

- Use OHIP FEECODE Z141

**Outline of Analysis Plan**

1. Use dates of procedures and cancer diagnoses to appropriately exclude individuals not eligible for screening
2. Descriptive statistics on key predictor variable (12-month depression)
3. Descriptive statistics on other potential predictor variables (see above)
4. Bivariate analyses to examine relationships between predictors
5. Logistic regression model with dichotomous outcome for screening
   a. Keep all sampling and bootstrapping weights from CCHS 1.2
6. May look at stratification by age and depression severity as indicated
7. May look at time to screening outcomes using survival analysis technique