Breast Cancer Incidence and Stage at Diagnosis in Ontarians with and without Intellectual Disabilities

by:

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Abstract

This thesis examines breast cancer incidence and stage at diagnosis in Ontarians with and without intellectual disabilities. The objectives were 1) To describe and compare the incidence of breast cancer in women with and without intellectual disabilities from 2000 to 2014; 2) To describe and compare breast cancer stage at diagnosis in women with and without intellectual disabilities from 2010-2014.

Manuscript 1 (Incidence): Through a retrospective cohort methodology, breast cancer incidence in women with intellectual disabilities was found to be not significantly different from women without intellectual disabilities.

Manuscript 2 (Stage): A cross sectional study demonstrated women with intellectual disabilities were significantly more likely to be diagnosed at a later stage (II-IV) (odds ratio 1.6; 95%CI=1.03-2.48) when compared to women without intellectual disabilities.

Conclusion: The results of this study suggest women with intellectual disabilities have a comparable incidence of breast cancer to women without intellectual disabilities, but they may have an increased risk of being diagnosed at a later stage.

Keywords: intellectual disability, breast cancer, incidence, stage at diagnosis

Statement of Originality

I, Natasha Batchelor, hereby declare that this thesis is, to the best of my knowledge, original, except as acknowledge in the text. I further declare that the material contained in this thesis has not been previously submitted, either whole or in part, for a degree at this or any other university.

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Parts of this material are based on data and/or information compiled and provided by CIHI. However, the analyses, conclusions, opinions and statements expressed in the material are those of the author(s), and not necessarily those of CIHI.

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List of Abbreviations

ACD	Australian Cancer Database
ACG	Adjusted clinical groups case-mix system
AIHW	Australian Institute of Health and Welfare
ASIR	Age standardized incidence rate
CCO	Cancer Care Ontario
CI	Confidence interval
CCR	Canadian Cancer Registry
CHS	California Health Interview Survey
CIHI-DAD	Canadian Institute for Health Information Hospital Discharge Abstract Database
CVS: D	Canadian Vital Statistics – Death Database
DSM	Diagnostic and Statistical Manual of Mental Disorders
ID	Intellectual disability
IQ	Intelligent quotient
FN	First Nations
FNAB	Fine needle aspiration biopsy
FSA	Forward sortation area
H-CARDD	Health Care Access Research and Developmental Disability
HES	Hospital Episode Statistics Database
HRT	Hormone replacement therapy
ICD	International Classification of Diseases
ICES	Institute of Clinical Evaluative Science

IKN	ICES key number
MHDD	Model of Healthcare Disparities and Disability
MRI	Magnetic resonance imaging
NACRS	National Ambulatory Care Reporting System
NCIRS	National Cancer Incidence Reporting System
NCRS	National Cancer Registration Service
OBSP	Ontario Breast Screening Program
OCR	Ontario Cancer Registry
ODD	Ontario Diabetes Database
OHIP	Ontario Health Insurance Plan
OMHRS	Ontario Mental Health Reporting System
RPDB	Registered Persons Database
RUB	Resource utilization band
SEER	Surveillance, Epidemiology and End Results program
SIR	Standardized incidence rate
TNM	Tumour, lymph nodes, metastasis
WHO-ICF	World Health Organization International Classification of Functioning

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1 INTRODUCTION

1.1 Introduction to Thesis

1.1.1 Introduction

The introduction to the thesis provides important and relevant definitions and brief descriptions of relevant background and epidemiological information. It also describes the theoretical framework and how it was applied in the present study and ends with a description of how the thesis was organized.

1.1.2 Intellectual disabilities

The Diagnostic and Statistical Manual of Mental Disorders (DSM) -5 defines intellectual disabilities (ID) as impairments in both general mental abilities and adaptive functioning (American Psychiatric Association, 2013). Adaptive functioning is measured using standardized testing and clinical assessments in three main domains: conceptual, social and practical. Conceptual functioning refers to skills in language, reading, writing, and math. The social domain includes areas such as empathy, interpersonal communication and the ability to make and retain friends. Lastly the practical domain refers to areas that center on self-management. Symptoms must begin in the developmental period of life. The severity of an intellectual disability can be categorized into four groups: mild, moderate, severe and profound. Most people with intellectual disabilities are diagnosed in the mild category (Maulik, Mascarenhas, Mathers, Dua & Saxena, 2011).

In order to gauge an individual's general mental abilities, intelligence quotient (IQ) tests can be administered to assess intellectual functioning. A score of 70 or less indicates a limitation in intellectual functioning (American Psychiatric Association, 2013). ID can be caused by genetic, congenital or acquired factors (Brown & Percy,

2007; Tasman, Kay, Lieberman, First & Riba, 2015). Some examples of conditions that are associated with ID are Down syndrome, fragile X syndrome and fetal alcohol syndrome (Tasman et al., 2015).

1.1.3 Health disparities in people with ID

Currently in Canada, people with ID make up approximately 0.78% of the total population (Lunsky, Klein-Geltink & Yates, 2013). They represent a small subset of the general population that experiences a variety of disadvantages and higher levels of morbidity.

Their life expectancy is shorter than people without ID, although it is increasing in a parallel fashion to those without ID (Bittles et al., 2002; Emerson & Baines, 2011; Kapell, et al., 1998; Perkins & Moran, 2010). The study by Janicki, Dalton, Henderson & Davidson (1999) found that the average age of death in people with ID was 66. Whilst the study by Patja, Iivanainen, Vesala, Oksanen & Ruoppila, 2000 found the median age at death in their study to be 62. Although people with ID do die younger, people with ID, specifically those with mild ID are beginning to live as long as people without ID (Janicki et al., 1999; Patja et al., 2000). As their life expectancy increases they are more likely to experience age-related health concerns or diseases, consistent with those found in people without ID including: cardiovascular pathology, respiratory illnesses, gastrointestinal conditions and cancers (Emerson & Baines, 2011; Perkins & Moran, 2010).

Research has shown that people with ID are more likely to experience health problems than those without ID (Lunsky et al., 2013). In a study conducted by van Shrojenstein Lantman-De Valk, Metsemakers, Haveman and Crebolder (2000), adults

with ID in the Netherlands were 2.5 times more likely to be diagnosed with various health conditions than patients without ID. Health conditions found in high rates include epilepsy, behavioural/mental health problems, fractures, skin conditions, poor oral health and respiratory disorders (Krahn, 2006). They are also more likely than people without ID to be diagnosed with chronic conditions such as congestive heart failure, obstructive pulmonary disease, diabetes or asthma (Lunsky et al., 2013). Overall, people with ID are more likely to have higher levels of morbidity when compared to people without ID (Lunsky et al., 2013). The high morbidity levels and disadvantages faced by this sub population make them a priority group for further research aimed at addressing the disparities they experience.

Multiple studies have been conducted that report on the increased health problems and high morbidity experienced by people with ID (Lunsky et al., 2013; van Shrojenstein Lantman De Valk et al., 2000; Emerson & Baines, 2011). Less research has been performed looking at specific health conditions such as cancer. The cancer research in people with ID that does exist has used clinically based samples (e.g. hospitals) and very few are population based.

1.1.4 Cancer in Canada

It is estimated that nearly half of all Canadians will be diagnosed with cancer in their lifetime (Canadian Cancer Statistics, 2016). Overall, the incidence of cancer has been increasing in Canada while cancer mortality has been decreasing. Canada is currently faced with an aging population, and as a result, the number of people diagnosed with age-related diseases such as cancer is expected to increase (Canadian Cancer Statistics, 2016). It is estimated that 89% of cancers will be diagnosed in those over the

age of 50 and 44% diagnosed at 70 years of age and older in Canada in 2016 (Canadian Cancer Statistics, 2016). Overall more males than females are diagnosed with cancer and it is the leading cause of death in Canada (Canadian Cancer Statistics, 2016). Measuring the cancer burden in Canada is essential for health policy and plays a pivotal role in guiding how decision-makers allocate health resources.

1.1.5 Breast cancer incidence in Canada

Breast cancer is a malignant disease that proliferates in breast tissue and can metastasize to other parts of the body. Breast cancer can be broadly classified as either in situ or invasive (Bouhassira, 2015).

Breast cancer incidence is determined by the number of new cases of disease diagnosed in a population over a specified period of time (Gordis, 2014). Incidence data provides a measure of cancer burden in a population. One in nine Canadian females are expected to be diagnosed with breast cancer in their lifetime and it is the leading cancer in women (Canadian Cancer Statistics, 2016). Women between the ages of 50 -74 represent the majority of people diagnosed with breast cancer (Cancer Care Ontario, 2015a). Along with other age-related diseases the number of people diagnosed with breast cancer is expected to increase.

Women who participate in primary, secondary or tertiary preventive measures can reduce their risk of being diagnosed with breast cancer or improve their chance of receiving a diagnosis at a stage where they have an increased chance of survival. Primary prevention in breast cancer involves health promotion and risk reduction including lifestyle, diet modification and cessation of smoking (Al-Amri, 2005). Breast cancer screening is a secondary preventative measure as it involves the early detection of

disease when treatment is more effective (Youlden et al., 2012). Tertiary prevention aims to improve breast cancer prognosis and quality of life through providing the best treatment methodologies after a diagnosis is made.

1.1.6 Breast cancer risk factors

Various factors contribute to an increased risk of being diagnosed with breast cancer. Some risk factors of breast cancer include: age, age at menarche and menopause, age at first pregnancy, family history, previous benign disease, body weight, hormone replacement therapy, the use of certain contraceptives and alcohol consumption (McPherson, Steel & Dixon, 2000). Developing breast cancer is a result of multiple personal, familial, reproductive and lifestyle factors. As women age, breast cancer risk increases, thus women in their 40s have a lower incidence of breast cancer in comparison to women over 50 (Elmore, Armstrong, Lehman & Fletcher, 2005; Humphrey, Helfand, Chan & Woolf, 2002; McPherson et al., 2000). The start and ending of menarche plays a role as women who start menstruating early or have late menopause are at an increased risk of developing breast cancer (McPherson et al., 2000). Women who do not have children or have their first child after 30 are at a greater risk of being diagnosed with breast cancer. Family history also plays an important role, as having a first-degree relative diagnosed with breast cancer before the age of 50 increases an individual's risk. In postmenopausal women, obesity is associated with increased breast cancer risk (Basen-Enquist & Chang, 2011). Hormone replacement therapy increases the risk of breast cancer while also increasing breast density resulting in a reduction in the sensitivity and specificity of breast cancer screening (Kerlikowske et al., 2010).

Little research has been performed on women's health issues in people with ID. Thus, it is unknown if having an ID is an independent contributor to the risk of being diagnosed with breast cancer. Women with ID experience a variety of risk factors that may make them more susceptible to breast cancer. People with ID tend to lead sedentary lives and obesity is a common occurrence; prevalence estimates are approximately twice as high as those without an ID (Beiser & Stewart, 2005). Women with ID experience menopause three to five years earlier than women without ID, which may play a protective role (Ouellette-Kuntz et al., 2005). It is currently unknown why women with ID experience earlier menopause. They are also more likely to be nulliparous, which is a risk factor for breast cancer (Emerson & Baines, 2011).

1.1.7 Breast cancer screening

Breast cancer screening is a secondary prevention tool that aims to diagnose breast cancer in the early stages of disease progression. Mammography is considered the gold standard screening tool to detect breast cancer (Miller, 2001; Ontario Breast Screening Program, 2008). It uses x-rays to detect and evaluate changes in the breasts and can help find small breast cancers while they are asymptomatic. It is the most frequently used method to screen for breast cancer in women 50 -74 years of age and aims to reduce the incidence of advanced breast cancer (Cancer Care Ontario, 2015a). Other common modalities that can be used to screen for breast cancer include magnetic resonance imaging (MRI) and sonography. MRI produces images through the combination of a strong magnetic field, radio waves and computer processing, while sonography uses sound waves to produce an image (Medical Imaging & Technology

Alliance, n.d.). Early detection is linked with an improved prognosis and a reduction in breast cancer mortality (Cancer Care Ontario, 2015a).

While technological advancements have improved the sensitivity of mammography, controversies remain surrounding both its benefits and harms. The potential benefit is avoiding advanced cancer. The risks associated with mammography screening include false positive/negative results, over diagnosis and radiation-induced cancer. Over diagnosis is defined as, "the detection of tumours at screening that might never have progressed to become symptomatic or life-threatening in the absence of screening" (Loberg, Lousdal & Kalager, 2015, p.2). Currently all breast tumours are treated since non- and life-threatening tumours are indistinguishable (Loberg et al., 2015). A false positive mammogram occurs when a radiologist sees something abnormal that turns out to be benign upon further investigation. False positive test results can cause women to have anxiety, worry about being diagnosed with breast cancer, and increase their perception of their breast cancer risk (DeFrank & Brewer, 2010). These thoughts may in turn make some women hyper vigilant to continue with routine screening. Other women experiencing a false positive may have a more negative experience and believe the tests are not very accurate, deterring them from future screening (DeFrank & Brewer, 2010). A false negative test occurs when breast cancer is present but was not detected in the mammogram. False negative mammogram results may lead to delays in treatment and advanced clinical stage when diagnosed. The risk of radiation-induced breast cancer is small in comparison to the expected mortality reduction associated with breast cancer screening (Yaffe & Mainprize, 2011).

1.1.8 Breast cancer diagnosis

A biopsy is performed when a suspicious area has been found either through a breast imaging modality or a physical exam. A biopsy is the only definitive method to diagnose breast cancer. Biopsies retrieve the suspicious sample from the breast, which is then microscopically analyzed (Compton et al., 2012). Three types of biopsies can be performed to diagnose breast cancer: fine needle aspiration biopsy (FNAB), core biopsy and surgical biopsy (Canadian Cancer Society, 2016).

1.1.9 Breast cancer staging

Cancer is staged through the tumour, lymph nodes and metastasis (TNM) classification system. It is a classification system that encompasses the characteristics of a tumour that define its behaviour and indicates the extent of disease (Compton et al, 2012). TNM breast cancer staging describes the size of the tumour, whether the cancer has spread to the lymph nodes and whether it has metastasized to other organs (Compton et al, 2012). The stage of breast cancer can be categorized into five stages (See Appendix A, Table 1).

1.2 Theoretical Framework

1.2.1 Model of Healthcare Disparities and Disability

The model of healthcare disparities and disability (MHDD) is an integrated model that takes into consideration the interactions between personal and environmental factors experienced by people with disabilities and the role they play in regards to health and health disparities (Meade, Mahmoudi & Lee, 2015). This integrated model amalgamated various factors from the Aday and Andersen framework (Aday & Anderson, 1974), the Institute of Medicine (IOM) Model of Access to Healthcare Services (Institute of Medicine, 1993) and conceptualizations within the World Health Organization International Classification of Functioning (WHO-ICF) (World Health Organization, n.d.). Its purpose was to enhance the understanding of disability and disparity in health and healthcare (Meade, Mahmoudi & Lee, 2015).

The components of the MHDD retained from the WHO-ICF are body functions and structures, activities, participation, and environmental factors.

When discussing disability in the context of health and healthcare disparities this model considers the role of individual factors, environmental factors, interactions (between individual and environmental factors) and health outcomes. The relationship between characteristics in the environment and personal factors are hypothesized to be related to healthcare disparities for various populations (Meade, Mahmoudi & Lee, 2015). Personal factors relate to how race/ethnicity, gender, income, health literacy and disability influence health care. Environmental factors include health systems, health policies, and social support (Meade, Mahmoudi & Lee, 2015). The interaction of these factors plays an important role in healthcare disparities. Only when both personal and

environmental factors are linked and optimized can improvements be made to improve healthcare outcomes (Meade, Mahmoudi & Lee, 2015).

1.2.2 Application of the Model of Healthcare Disparities and Disability

Disparities associated with breast cancer in women with ID have received very little attention. Breast cancer policies and other related environmental factors designed for people without ID might not meet the needs of the population of people with ID. The MHDD is a useful framework providing guidance for this thesis that aims to assess whether disparities related to breast cancer exist between women with and without ID while also incorporating personal and environmental factors. This model recognizes the wealth of factors that affect healthcare quality and outcomes for people with ID (Meade, Mahmoudi & Lee, 2015).

The framework was helpful when selecting relevant variables especially as applied in manuscript 2. The components of the MHDD that are the most relevant to my research are: health status, body functions, activity, access to healthcare, environmental factors and personal factors (see Figure 1).

Figure 1.
The model of healthcare disparities and disability showing the interaction between various factors and how they affect healthcare disparities

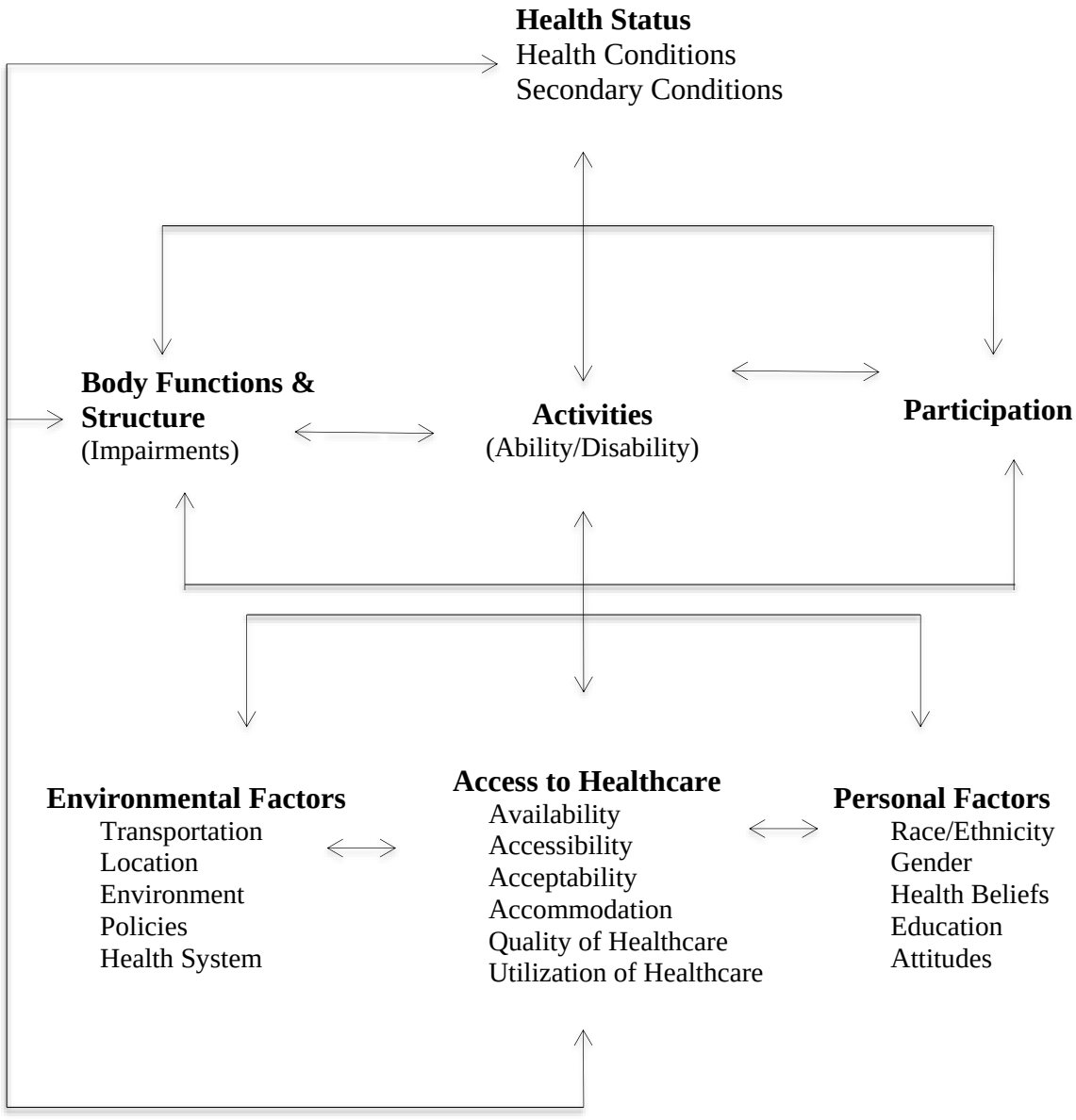


Figure 1. Model of healthcare disparities and disability. Reprinted from " The intersection of disability and healthcare disparities: a conceptual framework," by M.A.Meade, E. Mahmoudi and S.Y. Lee, 2014, *Disability and Rehabilitation, 37*(7), p. 639.

Health status

Health status refers to the health conditions experienced by the study participants and breast cancer is the focus of this thesis. Secondary conditions that affected the health status of study participants were addressed in the breast cancer stage manuscript (manuscript 2) of this thesis. The health status of women with ID in manuscript 2 was also evaluated using a measure of morbidity and by determining the presence of diabetes.

Body function/structure

According to the WHO-ICF intellectual functions are a component of 'body functions' and are defined as "general mental functions, required to understand and constructively integrate the various mental functions, including all cognitive functions and their development over the life span" (WHO, 2001; WHO, n.d.). This conceptualization is consistent with the definition of ID provided earlier by the American Psychiatric Association (see section 1.1.1)

Activity

The WHO-ICF describes activities as the, "functioning at the level of the individual and the activity limitations they experience" (WHO, n.d.).

In the context of breast cancer and ID, activity can refer to a variety of things. Adaptive behaviour, which is also part of the American Psychiatric Association's definition of ID, can be considered an element of activity. An example of an activity could be a person's ability to communicate with health care providers the signs and symptoms of breast cancer that they may be experiencing. People with ID frequently need extra support and health education, as they may not independently raise subtle health issues with their healthcare provider.

Environmental factors

According to the WHO-ICF environmental factors pertain to, " the physical, social and attitudinal environment in which people live and conduct their lives" (WHO, n.d.). Specifically, environmental factors may include services, systems and policies that may contribute to health disparities and poorer health outcomes in people with ID. Social and attitudinal factors may contribute to delay in diagnosis if people with ID are not educated by healthcare professionals about the importance of breast screening. This includes people at all levels in the healthcare systems that are not adequately trained or skilled to work with people with ID.

Access to Healthcare

In the MHDD access to healthcare has five main components, affordability, availability, accessibility, accommodation and acceptability. These factors may, "influence the extent to which an individual is able to maintain their health as well as future utilization of services" (Meade, Mahmoudi & Lee, 2015, p. 637). Access to healthcare in the current study refers to the utilization of breast screening services (see manuscript 2). Some factors that can affect breast screening utilization are the availability of locations offering breast screening services, accommodating equipment and the accessibility of locations. A lack of participation may also be a result of a lack of education about the importance and benefits of breast screening.

Personal Factors

This research addresses the role of personal factors and breast cancer. Specifically a measure of income is included in the analysis of manuscript 2.

Summary

The MHDD is a multi-faceted tool that embodies multiple frameworks of disability to create an all-encompassing framework that recognizes the importance of environmental and personal factors and how their roles and interactions can affect the health status of people with ID. This framework will help guide the research about women with ID diagnosed with breast cancer highlighting any disparities in comparison to women without ID.

Using the MHDD has some disadvantages. For instance, the model makes it difficult to distinguish between activity and participation because these concepts are not clearly defined. Previous research has defined and used activity/participation concepts in different ways when applying it to people with ID (Arvidsson, Granlund & Thyberg, 2015).

1.3 Thesis organization

A manuscript format in compliance with the requirements of the Graduate Department of Health Sciences and the School of Graduate Studies at the University Of Ontario Institute Of Technology was used in this thesis. The objectives of this thesis are addressed in manuscripts 1 and 2 and stand alone as manuscripts that will be submitted for journal publication. For this reason the organization of this thesis will result in instances of repetition.

Manuscript 1: The first manuscript addresses the first objective to describe and compare breast cancer incidence in women with and without intellectual disabilities.

Manuscript 2: The second manuscript addresses the second objective using a subset of the cohort created in manuscript 1. This manuscript describes and compares breast cancer stage at diagnosis in women with and without intellectual disabilities.

1.4 Objectives, Rationale & Thesis Methodology

1.4.1 Objectives

Manuscript 1

1. The objectives for manuscript 1 are:
    a. Describe the incidence of breast cancer in women with and without intellectual disabilities
    b. Compare the incidence of breast cancer between women with and without intellectual disabilities

Manuscript 2

2. The objectives for manuscript 2 are:
    a. Describe the stage at breast cancer diagnosis in women with and without intellectual disabilities
    b. Compare the stage at breast cancer diagnosis between women with and without intellectual disabilities

1.4.2 Rationale

As the life expectancy of people with ID continues to increase, they become more likely to develop age-related diseases such as cancer. As they age, it is important to establish whether women with ID are at the same risk for developing breast cancer as women without ID.

In addition to data on the incidence of breast cancer in women with ID, this research will provide data on their stage at breast cancer diagnosis.

The small proportion of women with ID that I see in my professional practice as a mammographer motivated me to perform this study. In my personal experience

performing mammograms on women with ID does present some challenges. They are often very anxious, likely do to the lack of understanding of the procedure. To reduce their anxiety and increase compliance, I spend a lot of time explaining the procedure and the importance of obtaining diagnostic quality images for the radiologist. By using simple terms I aim to increase their understanding of the necessity of this procedure. The methods I use to approach performing mammograms on women with ID have resulted in diagnostic quality exams. Women with ID have often come with family members. Although the family is not allowed to stay in the room while the images are taken, they are usually very helpful when trying to explain the procedure to the women with ID. Although in my personal experience I have never had a women with ID refuse a mammogram either verbally or behaviourally, other mammographers have. I hypothesize that this may occur if not enough time is spent communicating to the patient the steps in the procedure and the importance of the exam. These experiences and observations have led me to think that it is possible that women with ID are not receiving timely access to breast cancer screening services and diagnostic procedures thus delaying diagnosis and treatment. These clinical observations led me to see if any research had been performed on breast cancer screening, incidence and stage at diagnosis in this population. My early literature search revealed that there was very little research on these topics. In addition, upon discussions with my supervisor and other researchers in the area, it became clear that gaps exist in the literature that need to be addressed.

The aim of this study was to gain a better understanding of the impact of breast cancer in this population and to identify disparities in breast cancer incidence and stage at diagnosis between women with and without ID. This research expects to find that people

with ID are at the same risk for being diagnosed with breast cancer, but are diagnosed at a later stage. These findings are expected, as women with ID are less likely to participate in breast screening programs.

Currently there is very limited information on breast cancer at the population level for people with ID in Canada. There is a need for population-based research to understand the impact of breast cancer on women in with ID in Ontario in comparison to the women without ID. This information is essential for government, policy makers and health professionals to make decisions based on Canadian evidence. The results of this study will provide important information about the impact of breast cancer in women with ID.

1.4.3 Thesis Methodology

Epidemiological approaches were employed to identify breast cancer incidence and stage at diagnosis in women with and without ID.

For manuscript 1, a retrospective cohort study was used to identify the incidence of breast cancer in Ontario. A cohort design was selected and administrative health databases were used to compare the incidence of breast cancer in two cohorts. The first cohort consisted of women with ID and the second consisted of women without ID. Identifying the number of women with ID diagnosed with breast cancer conceptualized the burden breast cancer has on this population and whether it is different from that of women without ID. An advantage of applying a retrospective cohort design was that it allowed the researcher to look back in time and report on cancer trends over a long period. In addition, a retrospective cohort study was beneficial in studying women with ID as they represent such a small proportion of the population and administrative databases allowed for a relatively large sample to be identified. As well a retrospective cohort study is both less expensive and time consuming as the databases used in the present study were already well established.

To report the breast cancer stage at diagnosis in manuscript 2, a retrospective cross-sectional study design was used. This method was used to investigate whether there is a difference in breast cancer stage at diagnosis between women with and without ID. The study consisted of two groups of women: one group consisted of women with ID diagnosed with breast cancer and the other consisted of women without ID diagnosed with breast cancer. Once both groups were identified they were further classified into early (stage I) and late stage (stage II-IV) breast cancer. Administrative health databases

were used to identify women with breast cancer and their stage at diagnosis. Health databases are both a cost effective and useful source of health information.

A disadvantage of both the cohort and cross-sectional study is the potential for misclassification bias. There is a possibility in both studies that some women with ID were not identified and were misclassified as not having ID.

2 LITERATURE REVIEW

2.1 Literature Review

A narrative literature review was performed providing a synthesis of relevant reports and published studies. The topics included in this literature review include: breast cancer incidence and stage at diagnosis in the general population, subpopulations and in people with ID.

The primary objective of this literature review was to identify studies with methodologies applicable to the approaches used in both manuscripts. The study descriptions in this review include a summary of the methods, results, strengths and limitations followed by a comment on why the study was useful. In addition, Appendix C, Table 1 provides a brief summary of the studies included in the literature review.

2.1.1 Incidence of breast cancer in the general population

Breast cancer incidence provides information about the risk of developing the disease. Updated information about breast cancer incidence is necessary for health policy implementation and decision-making. Policy makers and public health workers use the data to assess population level needs for cancer management and prioritizing prevention strategies. The following section reports on relevant population level research from developed countries using administrate databases.

Canadian Cancer Statistics is a publication produced annually since 1987. The aim of the publication is to provide information about the incidence, mortality and other measures of cancer burden. The main data sources for the publication include the Canadian Cancer Registry (CCR), National Cancer Incidence Reporting System (NCIRS), Canadian Vital Statistics – Death Database (CVS: D), population life tables, censuses and forecasts. The CCR retrieves data from provincial and territorial cancer

registries, which collect clinical and demographic data on newly diagnosed cancer cases in their respective provinces. From 2004 -2010, the incidence of breast cancer in Canada has stabilized following fluctuations since 1988 (Canadian Cancer Statistics, 2016). The fluctuations noted prior to 2004 were in part attributed to a lead time bias related to increased mammographic screening and reductions in the use of hormone replacement therapy (HRT) (Canadian Cancer Statistics, 2016).

A study by Kachuri, De, Ellison & Semenciw (2013) examined cancer incidence, mortality and survival trends in Canada from 1970 – 2007. Incidence data was compiled from the CCR. The study reported that the incidence of breast cancer in Canada rose at a rate of at 0.9% yearly between 1970 and 1998. After that period the incidence began to decline at a rate of 0.7% yearly (Kachuri et al., 2013). A limitation within this study is the completeness and accuracy of the data source, used to estimate incidence. Registry data can vary across Canada resulting in an under or overestimation of disease rates. This source is useful as it analyzed long-term trends using Canadian national databases to monitor cancer trends through a retrospective cohort. This population-based approach can be applied to my research as it demonstrates how incidence can be calculated using data acquired from population-based databases in a Canadian setting.

The Australian Institute of Health and Welfare (AIHW) uses administrative databases to provide an overview of the epidemiology of cancer in Australia. The article by the Australian Institute of Health and Welfare (2013) focuses on the incidence of cancer, mortality and the burden of disease from 1991 to 2009. Cancer data was acquired from the Australian Cancer Database (ACD), which holds information about cancer diagnoses since 1982. Population level incidence was derived using the ACD and the

resident population data was based on the 2006 Census. From 1991-1995 the incidence rate of breast cancer increased. After this period the incidence rates stabilized.

Molinié et al. (2014) performed a retrospective cohort that detailed the incidence of breast cancer from 1990-2008 in France. Nine population based French registries were used to report on breast cancer incidence in the population. The incidence of breast cancer increased from 1990 – 2003. Incidence began to stabilize after 2006. The strength of the study is the registry data because the procedure for collecting data is standardized. A limitation is that the regions and registries selected may not be representative of the entire French population.

The study conducted by Kohler et al. (2015) was a population-based study that reported on cancer trends in the United States. Population based incidence data was obtained from the North American Association of Central Cancer Registries and the National Program of Cancer Registries. The study reported that breast cancer incidence remained relatively stable from 2002 -2011 (Kohler et al., 2015). Breast cancers were generally diagnosed at a local stage and less likely to be diagnosed at a distant stage in all racial/ethnic groups. Breast cancer at a local stage is solely confined to the breast as opposed to a distant stage where the cancer has metastasized to other parts of the body. A limitation of this study is that long-term trends (1992-2011) were reported based on only 13 state registries, which only represent 14% of the US population. This study informs my methodological approach through its use of cohort methodology spanning multiple years reporting on incidence.

After increasing for many decades due to a combination factors such as early detection through breast screening and HRT, studies addressing breast cancer in the

general population in developed countries have found that, the incidence of breast cancer has stabilized in recent years (Canadian Cancer Statistics, 2016; Kohler et al., 2015; Molinié et al., 2014). Multiple factors may have contributed to this stabilization such as the reduced use of HRT and screening saturation whereby all prevalent cases have been discovered (Ferlay, Héry, Autier & Sankarananarayanan, 2010). There is no questioning the usefulness of breast cancer incidence statistics for the general population. However, data on subpopulations is also relevant as it can be used to identify possible disparities that may exist between certain subpopulations. Interventions targeting the specific needs of the population at higher risk for breast cancer can then be developed to help decrease the level of disparity.

2.1.2 Incidence of breast cancer in subpopulations

The following describes studies that report on breast cancer in various populations to identify if any disparities exist.

The study by Marrett & Chaudry (2003) reported the incidence of breast cancer in Ontario First Nations (FN) people in comparison with the Ontario population. This retrospective cohort was comprised of 141 290 FN people from 1968 – 1991. They were identified through files maintained by the federal government Department of Indian and Northern Affairs Canada that identifies those registered under the Indian Act. This file was linked with the Ontario Cancer Registry (OCR) and vital statistics files to identify deaths and cancer diagnoses. The incidence of breast cancer in Status Indian women was between 40 and 50% lower than the incidence in the general population (Marrett & Chaudry, 2003). Marrett & Chaurdry (2003) hypothesized that since FN women generally have their first child at a younger age and have more children, these factors

may be protective resulting in a reduced incidence of breast cancer. This study's use of the OCR was a strength, as the OCR includes all residents of Ontario with cancer and is recognized for its high completeness of registration. A limitation of this study is that to be included in the FN cohort you had to be registered as a status Indian under the Indian Act. A proportion of FN people who were not status Indians were therefore not captured in the study.

The impact of breast cancer may propagate differently across various populations. The study by Ali, Barnes, Kan & Beral (2010) compared incidence between British Indians and British whites in Leicester. Leicester was chosen for analysis because it has a large population of British Indians. Cancer data was acquired from the Trent Cancer Registry from January 2001 – December 2006 for residents of Leicester. The Hospital Episode Statistics (HES) database records self-assigned ethnicity: this database was linked with the cancer registry to identify the study cohort. Cases of breast cancer (n=6615) were diagnosed during the study period and ethnicity data were available for 98% of those cases. Incidence rate ratios for breast cancer in British Indians were significantly less when compared to British Whites (Ali et al, 2010). The strength of this study is the accuracy of the HES database that provided ethnic status for 98% of cancers. The cohort was however only from a particular region of the country, thereby possibly limiting the generalizability of the findings to the rest of England or the UK.

Sexual minorities exhibit known risk factors attributed to lung, colorectal and female breast cancer. Sexual minorities included people that identify as lesbian, gay or bisexual. The associated risk factors include smoking, alcohol use, obesity and nulliparity. Boehmer, Miao, Maxwell & Ozonoff (2014) reported on the relationship

between colorectal, lung and breast cancer incidence and sexual minority identity in California. Data for this research was acquired from the California Health Interview Survey (CHIS), which includes data on sexual orientation. To increase the sample of people identified as a sexual minority, 4 years of survey data were combined (2001, 2003, 2005 and 2007). Data on the incidence of cancer from 2001 - 2008 was taken from the California Cancer Registry. The results reported two associations: being a lesbian was associated with a higher incidence of breast cancer and being a bisexual woman was associated with a lower incidence of breast cancer (Boehmer et al., 2014). A strength of this study is that the survey is considered an accurate representation of California's population; the results may however not be generalizable to the entire U.S. population.

Breast cancer incidence in some subpopulations in North America and Britain have been studied to better understand the burden of breast cancer. The population-based approach in these studies demonstrated how data from administrative databases can be used to identify subpopulations and then linked to cancer registries making it possible to calculate incidence in these groups. A limitation of reporting on subpopulations with administrative data is the potential for misclassification error, where all of those within a subpopulation are not properly identified and included within the study. This thesis used a similar approach to study breast cancer in people with ID.

2.1.3 Incidence of breast cancer in people with intellectual disabilities

Very few studies have been conducted that report on the incidence of cancer in people with ID. In order to identify people with ID the reviewed studies used various methods.

In Finland, Patja, Eero & Iivanainen (2001) obtained participants though the use of a large countrywide survey. The survey was able to capture people within the general population that had ID. People suspected or known to have ID were further identified by examinations through the National Board of Health to assess if they met the criteria for ID. Once identified the cohort was linked to the Finnish Cancer Registry to identify cancer diagnoses. This study was a nationally representative cohort that had an average of 29-year follow-up with a total of 2173 individuals with ID. The study expected 25.8 cases of breast cancer and observed 23. The incidence of breast cancer in both people with and without ID was comparable even though there was a low prevalence of smoking and lower participation in breast screening in people with ID (Patja et al., 2001). This study's strengths reside from a nationally representative cohort and a lengthy follow up period. Biases were reduced because the cancer registration system in Finland is essentially complete. A limitation of the study is the relatively small sample size, which limits the power of the study to make statistically significant observations. Nonetheless, the study was useful because of the cohort methodology employed and the usage of administrative databases to identify cancer diagnoses. The data compiled from the study was of importance as it demonstrated that breast cancer is comparable in the general population and the population with ID.

The study by Sullivan et al., 2003 looked at breast cancer in people with ID coupled with breast screening practices. Participants were identified through the Disability Services Commission of Western Australia. Participants diagnosed with breast cancer were identified through the Western Australia Cancer Registry. The study period was from 1982 – 2001 and included women with ID over the age of 25. "The incidence

of breast cancer among women with intellectual disability was 64.0 per 100 000 person-years, in comparison with 146.7 per 100 000 person-years in the general population" (Sullivan et al., 2003, p.507). Of the 2 370 women with ID included in the study sample, 20 were diagnosed with breast cancer and 11 were <50 years of age at diagnosis. The mean age at diagnosis was 49 years old. A limitation of the study is the small proportion of people with ID that received a breast cancer diagnosis; this was in party due to 795 cases being excluded due to incomplete information.

A study by Janicki et al. (1999) looked at mortality in people with intellectual disabilities in New York State. The population was identified through the state agency responsible for reviewing deaths involving children and adults with disabilities. The deaths within this database included ICD codes, which were used to identify deceased people with ID. The most prevalent causes of death in the study were cardiovascular disease, respiratory diseases and cancers. Although, the older generations of people with ID still generally die at an earlier age, many are living as long as people without ID (Janicki et al., 1999). This study is very important because its results suggest a trend that people with ID are living longer. As their life expectancy increases their chances of living into the highest risk age groups for breast or other cancers also increases. A limitation of the study is that only deaths in people associated with New York state's ID agency were included. Therefore, the study may not be representative of everyone with an ID. As well, the study did not differentiate the types of cancer that were diagnosed in people with ID.

As the focus on the health needs of people with ID is increasing, more research needs to be conducted to promote longevity and healthy ageing in people with ID. As

their life expectancy increases, they are surviving into the age groups that are more often diagnosed with breast and other cancers. The study conducted by Patja et al. (2001) concluded that the incidence of breast cancer in people with ID is comparable to that of the general population; this is inconsistent with findings from the study by Sullivan et al. (2003) that found breast cancer incidence in people with ID was lower than the general population. Rigorous population level research is needed to accurately determine the incidence of breast cancer and identify its impact in people with ID. More studies on this topic will make breast cancer incidence results more conclusive.

2.1.4 Breast cancer stage at diagnosis in the general population

Breast cancer stage is based on three characteristics: tumour size and degree of spread, lymph node involvement, and degree of metastasis (Canadian Cancer Society, n.d.). Staging is considered an important determinant of cancer outcome. Information about breast cancer staging provides important information for clinical decision making but can also be used to determine the severity or impact of cancer in a population.

Anderson, Reiner, Matsuno & Pfeiffer (2007) conducted a study that reported on shifting breast cancer trends in the United States. To provide a broader context for breast cancer incidence, rates and age distributions were examined during five decades. Incidence data was obtained from the National Cancer Institute's Connecticut Historical Database (CHD) from 1950-1972 and from the Surveillance, Epidemiology and End Results (SEER) program from 1973-2003. The overall median age at diagnosis was 61. The mean age at diagnosis for women diagnosed at an early stage was 44, while the mean age for women diagnosed at a late stage was 73. Incidence rates for early-stage tumours increased 110% from 1973 to 2003 (Anderson et al., 2007). Incidence rates for late stage

tumours decreased 2.9% (Anderson et al., 2007). The strength of this study was in its large-scale population based design. The SEER registry used to report incidence covers 14% of the US population which, although is a small proportion of the total population, has meticulous and consistent data collection standards. This study is useful because it provides valuable population based data about mean ages at diagnosis especially for those diagnosed at earlier ages. This provides perspective on the age groups that should be included within my thesis.

Henley, King, German, Richardson & Plescia (2010) performed a study to report on incidence rates for late-stage cancers of the colon, breast and cervix. Data was retrieved from the Centre for Disease Control's National Program of Cancer Registries and the SEER database. In breast cancer patients Henley et al. (2010) reported that incidence rates for late stage breast cancer cases were lowest among women aged 50 – 59, highest among women aged 60 – 69 and 70-79 years of age and highest among black women. "During 2004-2006, approximately one third of breast cancers in the United States were diagnosed at a regional or distant stage, when treatment is not effective and survival is worse compared with cancers diagnosed at a localized stage" (Henley et al., 2010, p. 6). A regional stage refers to when the cancer has spread past the primary site to nearby lymph nodes or tissues and organs. When cancer is limited to the organ of origin it is at a local stage. Since this study specifically looked at late-stage cancer cases, it measured the proportion of cancers not detected at an earlier more treatable stage of disease. A higher proportion of cancers diagnosed at later stages may be indicative of contributing factors such as low screening rates. Although this study included 96% of the U.S. population, high quality incidence data was not available from Arizona or

Wisconsin. This study was a very useful resource because it described the ages in which late stage breast cancer was the most prevalent. This provides pertinent information about the age-range that should be included in my thesis. This study also informs my research because of the retrospective cohort methodology that used linkages within administrative databases to highlight individuals diagnosed with cancer.

A retrospective cohort conducted by McPhail, Johnson, Greenberg, Peake & Rous (2015) reported on the stage at diagnosis of breast, colorectal, lung, prostate and ovarian cancer and early mortality in England. Data was retrieved from the National Cancer Registration Service's (NCRS). The Office of National Statistics provided information on deaths in England. The study consisted of 152 821 people newly diagnosed with cancer, of which 42 071 were breast cancer. The median age at diagnosis for breast cancer was 63. McPhail et al. (2015) reported that greater than two-thirds of breast cancer subjects presented at either stage I or II. The highest proportion of stage I breast cancers was diagnosed between the ages of 60 and 69. A strength of this study was the completeness of the administrative databases, which cover between 80-90%, of the entire population of England. A limitation of this study is that the data is limited to only 2012 and therefore cannot demonstrate any trends.

These studies provided important information on the most common ages that breast cancer is being diagnosed in the general population. The studies by McPhail et al. (2015) and Anderson et al. (2007) reported comparable median ages at diagnosis of 63 and 61 respectively. The study by Henley et al. (2010) reported that the highest incidence of late stage breast cancer was in the 60 – 69 age group. These studies have

informed my research as they have demonstrated the importance of including people between the ages of 60 – 69 in my study population.

2.1.5 Breast cancer stage at diagnosis in subpopulations

It is useful to understand the descriptive epidemiology of breast cancer in various subpopulations. As certain populations may be diagnosed at younger ages and at later stages in disease progression.

The study conducted by Newman & Alfonso (1997) compared the age related differences in breast cancer stage at diagnosis between black and white patients in an urban community hospital. The study reported on women diagnosed with breast cancer that were treated at the Long Island College Hospital between January 1990 and September 1994. A retrospective review of hospital and physician records coupled with pathology reports and tumour registry data were used to determine the age, ethnic background and staging information of each study participant. Newman & Alfonso (1997) found a significant shift towards a younger age at diagnosis among black females. The mean age for black patients was 56 in comparison to 63 for white patients. Black patients were diagnosed at a younger age and at a more advanced stage at diagnosis. Newman & Alfonso (1997) proposed several explanations for the higher mortality and later stage at diagnosis among black breast cancer patients. They hypothesized socioeconomic factors may result in poor access to medical care, a delay in seeking treatment and higher rates of obesity may contribute to breast cancer stage at diagnosis and mortality. The biggest limitation of this study is the small sample size, making it difficult to establish statistical significance. Another limitation is that, since the study was conducted in one institution, it may not representative of the American population.

This study informed my research project because it demonstrated that vulnerable populations may be diagnosed at different stages of disease progression.

Deshpande, Jeffe, Gnerlich, Iqbal, Thummalakunta & Margenthaler (2009) conducted a retrospective population based cohort study that reported on the survival of Black and White women diagnosed with breast cancer. The study period was from January, 1988 – December, 2003. The database used to identify the study cohort was retrieved from nine registries in the SEER. The final sample consisted of 224 930 Black and White women diagnosed with breast cancer. Black women were more likely to be diagnosed with breast cancer in the <40 grouping as well as the 40-49 age groups while white women were more likely to be diagnosed in the >65 age group (Deshpande et al., 2009). Within each age grouping, black women were more likely to be diagnosed at a more advanced stage, have larger higher-grade tumours and lymph node involvement. A greater proportion of black women died due to breast cancer when compared to White women. The authors hypothesized that underutilization of mammographic screening may be responsible for the lower survival rates and later stages at diagnosis.

Detroit has a large population of Arab-American women. This large community provided authors Hensley, Alford, Soliman, Johnson, Gruber & Merajver (2009) with the opportunity to use administrative data to report on breast cancer in Arab women versus other ethnic groups. Cancer information was provided by Detroit's national tumour registry. Women of Arab descent were identified in the registry through a validated name algorithm. Breast cancer in Arab women was compared to white, non-Hispanic and African-American women. Data were used from the inception of the Detroit SEER registry. The cohort consisted of 80 316 women diagnosed with breast cancer between

1973 and 2003. The mean age at diagnosis was 60. The majority of breast cancer cases were at a local stage. Arab-American and African-American women were more likely to be diagnosed with regional disease (Hensley Alford et al., 2009). In comparison with both European and African-Americans, Arab-American women were diagnosed at a younger age and regional stages of cancer (Hensley Alford et al., 2009).

The aim of the study by Ginsburg et al., 2015 was to compare breast cancer stage at diagnosis in Chinese and South Asian women with the general population. Women diagnosed with breast cancer between 2005 – 2010 were identified through Ontario population-based administrative databases. The databases used in this study included the Ontario Cancer Registry (OCR), the Ontario Health Insurance Plan (OHIP), the Canadian Institute for Health Information Hospital Discharge Abstract Database (CIHI-DAD), and the National Ambulatory Care Reporting System (NACRS). The databases were linked through encoded identifiers. The study design was a retrospective population-level cross sectional study of women that compared stage at diagnosis in three mutually exclusive groups: Chinese women, South Asian women and the general population. To determine ethnicity two validated surname lists were used. The cohort consisted of 45 075 women, 1543 of which were Chinese and 798 that were South Asian. Chinese and South Asian women were more likely to be diagnosed before the age of 50 (Ginsburg et al., 2015). The results demonstrated South Asian women were more likely to be diagnosed at a later stage while Chinese women were less likely to be diagnosed at a later stage (Ginsburg et al., 2015). Ginsburg et al. (2015) hypothesized South Asian women may not be exposed to breast education and prevention. As well cultural values and stigma associated with breast cancer may pose a barrier to seeking care for a breast problem or participation in

screening programs. In some Chinese communities in Ontario, community agencies have collaborated with cancer agencies on health promotion initiatives that encourage healthy lifestyles and cancer screening. A limitation of this study is the surname algorithm used to identify Chinese and South Asian last names, which likely excluded many women particularly of South Asian descent.

Lipscombe et al. (2015) examined the stage at cancer diagnosis in women with diabetes. New research is suggesting that female patients with diabetes may be at a higher risk of developing breast cancer. They may also be at a higher risk of more advanced breast cancers at diagnosis. The study objective was to compare women with and without diabetes according to their stage at diagnosis. This Ontario population based study used the OCR, Cancer Care Ontario (CCO) stage data, the Ontario Diabetes Database (ODD), the CCO Ontario Breast Screening Program (OBSP), OHIP, CIHI-DAD and the Registered Persons database (RPDB). Information from these databases was linked using encoded identifiers. This study employed a cross-sectional study design to compare the stages at diagnosis between women with and without diabetes. The study population consisted of Ontario women between the ages of 20 – 105, that were newly diagnosed with breast cancer between January 1, 2007 and December 31, 2012. Cancer stages were categorized I – IV. The results demonstrated that the majority of women presented with stage I or II breast cancer. Women diagnosed with diabetes were significantly more likely to be diagnosed at a more advanced stage of breast cancer than those without. Women with diabetes were more likely to have larger tumours and lymph node metastases at diagnosis. Diabetes may be a risk factor that predisposes women to more aggressive breast cancers. The risk demonstrated to be the greatest among younger

women with a longer duration of diabetes. The strength of this study is the population-based data that used validated methods to identify both diabetes and breast cancer..

The studies by Newman & Alfonso (1997), Deshpande et al. (2009) and Hensley Alford et al. (2009) demonstrated that being in a visible minority was correlated with being diagnosed at a younger age and a later stage. Some hypothesized factors for this observation are attributed to socioeconomic factors.

Both studies by Ginsburg et al. (2015) and Lipscombe et al. (2015) implemented cross-sectional methodologies to report the stage of breast cancer in Ontario's population. I intend to implement a similar study design in a defined population to report on the stage of breast cancer. These studies demonstrated how Ontario's administrative databases can be used to identify both the study population and breast cancer diagnoses.

2.1.6 Cancer stage at diagnosis in people with intellectual disabilities

Tuffrey-Wijne, Bernal, Hubert, Butler & Hollins (2009) performed an ethnographic study that aimed to provide insight into the experiences of people with ID with cancer. Of the 13 participants, 10 were diagnosed at advanced stages in disease progression. The mean age at diagnosis for the study participants was 53. Cancer diagnoses were often dependent on someone other than the patient either noticing something was wrong or interpreting complaints or behavioural changes. Four patients complained of symptoms but their concerns were either ignored or disbelieved. Misdiagnosis from a physician was a contributing factor to delays in the appropriate diagnoses. This study provides rich insights into the lives and experiences of people with ID that have been diagnosed with cancer.

A study performed by Satgé et al. (2014) reported on the age and stage at diagnosis of 11 women with ID diagnosed with breasts cancer. The study sample was retrospectively selected from a single hospital amongst all women treated for invasive breast cancer from 1989 - 2006. The study reported on the tumour grade, age, tumour size and disease stage at diagnosis in 11 patients with ID compared to patients without ID. The mean age at diagnosis for women with ID was 55.64 in comparison with 62.35 in those treated without ID. Women with ID were at a higher risk of having greater tumour size, metastases to lymph nodes and higher tumour grades. Unadjusted OR's showed women with ID were 3.2 times more likely to be diagnosed at stage II and 10.2 times more likely to be diagnosed at stage III when compared to women without ID. Although women with ID were more likely to be diagnosed at a later stage, significant differences were not observed in the histological types of breast cancer in both groups of women. Due to this finding Satgé et al. (2014) hypothesized breast cancers in women with ID were not more aggressive, but rather delays in diagnosis were responsible for the later stage at diagnosis. Limitations of this this study are that it was not population based and few patients were studied. Nonetheless, this was the first study of breast cancer characteristics at diagnoses in women with ID.

2.1.7 Health disparities experienced by people with intellectual disabilities

It has been well established that social and environmental factors play an important role in determining the health of the general population (Beiser & Stewart, 2005). More recently, the disparities in the health status of people with ID have been attributed to social and environmental factors (Hatton & Emerson, 2015). Researchers have found that people with ID are more likely to live in socioeconomically deprived

environments, yet little is known about how their socioeconomic position affects their overall health (Graham, 2005).

The social and environmental factors experienced by people with ID places them at a higher risk of experiencing poor health. People with ID are often unemployed, have lower levels of literacy and live in unsafe, lower income neighbourhoods, which are all associated with poor health (Ouellette-Kuntz et al., 2005).

This population also experiences the negative effects of stigma. The extent to which negative societal values are embedded in social institutions perpetuates and restricts access for people with ID to opportunities that improve health (Llewellyn, Vaughan & Emerson, 2015). The stigma experienced by people with ID creates additional distress and erects barriers that can lead to inadequate health care. People in society, including healthcare providers, who hold negative views of people with ID are more likely to bully, avoid, ridicule, infantilize or harass them (Llewellyn et al., 2015). The cultural, societal and environmental barriers coupled with the discrimination experienced by people with ID act as barriers to positive health and life experiences (Emerson & Baines, 2010).

Some researchers have suggested that people with ID experience a double disadvantage: they not only have to cope with their disability itself but also with the added burden of compromised health and inadequate health services (Ali et al., 2013; Beiser & Stewart, 2005). For example difficulties in communication experienced between people with ID and their health care providers can create a major challenge in addressing their complex health needs (Ouellette-Kuntz, 2005). Communication challenges coupled with poor bodily awareness and a decreased ability to recognize

health problems, makes people with ID more likely to receive suboptimal medical care (Ali et al., 2013; Emerson & Baines, 2011; Hollins, Attard, von Fraunhofer, McGuigan & Sedgwick, 1998; Ouellette-Kuntz, 2005; Perkins & Moran, 2010).

The current structure of the healthcare environment does not effectively support people with ID. Currently chronic disease management frameworks rely heavily on self-management. While these self-management methods have proven to be successful in improving health status and reducing hospitalizations in people without ID (Coleman, Austin, Brach & Wagner, 2009; Lawn & Schoo, 2009), people with ID may not be capable of self-management. It is important that healthcare providers alter disease management models to fit the needs of people with ID to optimize their health. People with ID need to be actively engaged and involved with their health at their level of understanding through tailored health awareness, self-advocacy, health literacy, health promotion and caregiver education (Ervin, Hennen, Merrick & Morad, 2014).

Evidence has demonstrated that people with ID are more likely to experience a variety of health disparities when compared to people without ID. In this research, disparities refer to "differences in health without inference to the cause of these differences" (Krahn, Hammond & Turner, 2006). The differences in health that were addressed are differences in the incidence of breast cancer and stage at breast cancer diagnosis using population level data.

2.1.8 Summary

There is little research in the areas of incidence and stage at diagnosis for people with ID diagnosed with breast cancer. This information is pertinent to assess the impact breast cancer has on people with ID in Canada. As well this data may provide pertinent

information on stage at diagnosis that may highlight disparities within the healthcare system.

3 MANUSCRIPT 1

Incidence of Breast Cancer in Women with and without Intellectual Disabilities

3.1 Abstract

Background: People with intellectual disabilities represent approximately 1% of Ontario's population and they experience a variety of disadvantages. As the life expectancy of people with intellectual disabilities increases they are more likely to experience the same age-related health concerns as people without intellectual disabilities, such as cancers. Very little cancer research has been performed in this population, and even less breast cancer specific research.

Objective: The objective is to describe and compare breast cancer incidence in women with and without intellectual disabilities living in Ontario.

Methods: Ontario based population-level administrative databases were used to identify women with and without ID between the ages of 30 to 105 diagnosed with breast cancer. To determine the yearly cumulative breast cancer incidence from 2000-2014, the total number of women (n=119,516) were linked to the Ontario Cancer Registry identifying new breast cancer diagnoses.

Results: We identified 330 women with intellectual disabilities and 119 186 women without intellectual disabilities diagnosed with breast cancer throughout the study period. Baseline characteristics of women with intellectual disabilities identified there were more likely to reside in the lowest income quintiles. The age composition of women with intellectual disabilities was younger than women without. Their mean age at diagnosis was 57 in contrast with 62 in women without intellectual disabilities. The incidence of breast cancer in women with intellectual disabilities was not significantly different from the incidence in women without intellectual disabilities.

Conclusions: The yearly breast cancer incidence was comparable between both cohorts of women, suggesting women with intellectual disabilities are at no greater or lesser risk of being diagnosed with breast cancer.

3.2 Introduction

3.2.1 Intellectual disability

Currently in Canada, people with intellectual disabilities (ID) make up approximately 0.78% of the total population (Lunsky et al., 2013). ID is defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 as impairments in adaptive functioning and general mental abilities (American Psychiatric Association, 2013). Adaptive functioning is evaluated in three domains: conceptual, social, and practical (American Psychiatric Association, 2013). Conceptual functioning refers to skills in language, literacy, and math. The social domain refers to an individual's social skills such as empathy, interpersonal communication, and social problem solving. Lastly, the practical domain refers to areas based on the activities of daily life. Intelligence quotient (IQ) tests are used to assess intellectual functioning gauging an individual's general mental abilities. An IQ of 70 or less is indicative of a limitation in intellectual functioning (American Psychiatric Association, 2013). Symptoms of ID must begin in the developmental period of life, and ID can be caused by genetic, congenital or acquired factors. Some examples of conditions that are commonly associated with ID are Down syndrome, fragile X syndrome, and fetal alcohol syndrome (Tasman et al., 2015).

As the life expectancy of people with ID increases, they become more likely to experience age-related health concerns or diseases consistent with those found in people without ID (Bittles et al., 2002; Kapell et al., 1998; Perkins & Moran, 2010). Some of the age-related health concerns or diseases include cardiovascular pathology, respiratory illnesses, gastrointestinal conditions, and cancers.

Cancer, and breast cancer in particular, is a significant contributor to the morbidity and mortality of women in the general population. Nonetheless, breast cancer has not been well studied in people with ID to assess its impact in this vulnerable population. For instance, very little research has been conducted that compares breast cancer incidence in women with and without ID. The lack of research in this field may be attributed to the fact that historically people with ID had a significantly lower life expectancy (Sullivan et al., 2003).

3.2.2 Breast cancer incidence

Breast cancer is a malignant disease that develops in breast tissue. One in nine Canadian females are expected to be diagnosed with breast cancer in their lifetime (Canadian Cancer Statistics, 2016). The majority of women diagnosed with breast cancer are between the ages of 50 and 74 (Cancer Care Ontario, 2015a). As the Canadian population ages, the number of people diagnosed with age related diseases such as breast cancer is also expected to increase.

Few studies have been conducted on the incidence of cancers in people with ID and even fewer have been conducted looking specifically at breast cancer using administrative health data. A study by Sullivan et al. (2003) examined breast cancer in people with ID coupled with breast screening practices. Participants were identified through the Disability Services Commission of Western Australia. Those with breast cancer were identified through the Western Australia Cancer Registry. This study used administrative databases to identify the study participants. Once the participants were identified, the study population was linked to the cancer registry to identify breast cancer diagnoses. The study period was from 1982 – 2001 and included women with ID over

the age of 25. 2 370 women with ID were included in the study, 20 of those women were diagnosed with breast cancer with a mean age at diagnosis of 49 years of age. "The standardized breast cancer incidence rates (SIR) for women with ID across all age groups was lower than what would be expected in women without ID" (Sullivan et al, 2003, p.509). The data demonstrated that the SIRs were significantly lower from 1982-1995, but were not significantly lower from 1995 – 2000 (Sullivan et al., 2003). The reduced rate of overall breast cancer specifically before 1995 may be partially due to the lower life expectancy of people with ID (Sullivan et al., 2003). As the life expectancy of people with ID continues to increase, current research on breast cancer incidence in people with ID may yield different results. A limitation of this study, however, is the small proportion of people with ID that received a breast cancer diagnosis. This study needs to be developed further to address these limitations and provide updated results on breast cancer in people with ID. This study is particularly important, as it is was the only study that used administrative databases to report population level data specifically on breast cancer incidence.

3.2.3 Significance and objectives

Currently no studies have been performed in Canada that report on the incidence of breast cancer in people with ID. Previous research outside of Canada has focused broadly on cancer in general, but little breast cancer specific research has been conducted (Patja et al., 2001; Sullivan et al., 2003).

Although still shorter than people without ID, the life expectancy of people with ID is increasing in a parallel fashion to people without ID (Ouellette-Kuntz et al., 2005). Therefore, it would be useful to conduct research to identify any disparities between

women with and without ID. It is often wrongly assumed by health care practitioners that women with ID are not at the same risk for developing breast cancer as women without ID (Ouellette-Kuntz et al., 2005).

Although there are some population-based studies that reported on the incidence of breast cancer in people with ID none have been conducted since 2003 and none have been done in Canada. This research aims to provide current population level data to demonstrate breast cancer incidence in both women with and without ID. Although this research is not able to identify causation, it can identify whether a disparity exists between both groups of women.

The objectives of this research are to: 1) Describe the incidence of breast cancer between women with and without intellectual disabilities and 2) Compare the incidence of breast cancer between women with and without intellectual disabilities.

3.3 Methods

3.3.1 Study design

This research used retrospective population cohorts to report on yearly breast cancer incidence from 2000 – 2014 in women with and without ID. This study design allowed the researcher to go back in time to identify women with and without ID and follow them throughout the study period to identify whether they were diagnosed with breast cancer. Women with and without ID retrieved from administrative databases were included in this study. This study was approved by the institutional review board at Sunnybrook Health Sciences Centre, Toronto, Canada and the University of Ontario Institute of Technology.

3.3.2 Data sources and linkages

Administrative health databases collect, store and de-identify health data that is compiled through health care programs (Manitoba Centre for Health Policy, 2013). The data is initially collected for administrative or billing purposes but can be a rich source of information to answer health and health services related research questions. Administrative health databases provide researchers with historical data allowing them to study changes over time.

The Institute of Clinical Evaluative Science (ICES) has access to a vast range of secure administrative health data in Ontario and is known internationally as a credible source of high quality health research (ICES, 2016). Data collected by ICES has personal identifiers removed, which are replaced with a unique confidential ICES key number (IKN). Every Ontario resident that has been eligible for the Ontario Health Insurance

Plan (OHIP) has an associated IKN consistent through all health service databases within ICES's inventory of administrative databases (ICES, 2016). These datasets were linked using unique encoded identifiers and analyzed at ICES. The IKN is an essential component to the research conducted at ICES since it is used to successfully link individuals across databases.

3.3.3 Databases

Data for this study was acquired from ICES. Eight administrative databases were used including six health databases, one registry and census data. The health databases were the Ontario Mental Health Reporting System (OMHRS), the Canadian Institute of Health Information Discharge Abstract Database (CIHI-DAD), the National Ambulatory Care Reporting System (NACRS), Same Day Surgery (SDS), the Ontario Health Insurance Plan (OHIP), and the Ontario Cancer Registry (OCR). The administrative health databases include clinical information about Ontario residents. Some of the information included in the databases are: mental health problems, inpatient hospital discharges, emergency department visits, same day surgeries, physician claims and cancer diagnoses (See Appendix B, Table 1).

The registry accessed for this study was the Registered Persons database (RPDB), which includes demographic information on all Ontario residents eligible for OHIP. The Canadian census was accessed for postal codes and information on neighbourhood income (See Appendix B, Table 1).

3.3.4 Study populations

Two cohorts of Ontario women 30 to 105 years of age were created from the databases. One consisted of women with ID, and the other a comparison cohort of women without ID.

Diagnostic codes from five administrative health databases held at ICES (See Appendix B, Table 2) were used to identify people with ID (See Appendix B, Table 3).

A coding algorithm to identify people with ID developed by the Health Care Access Research and Developmental Disabilities research program (H-CARDD) was used in this project (Lunsky et al., 2013). ID is often only recorded in health records when an individual is first assessed during childhood. To ensure people with ID were not excluded from the sample, they were identified from the inception of the five administrative health databases (Lin et al., 2013). Using the widest time frame possible is a strategy that has been evaluated by Lin et al. (2013) to maximize the detection of ID cases and aids in identifying people with ID across all ages.

The Ontario female population without ID was identified using the RPDB to serve as a comparator.

Women with and without ID diagnosed with breast cancer were identified in the OCR and linked using the IKN. The OCR includes information about all newly diagnosed cases of breast cancer in Ontario.

Exclusion criteria

Individuals under the age of 30 and over the age of 105 in both the comparison cohort and the cohort of people with ID were excluded from this study. People under 30 are unlikely to be diagnosed with breast cancer. Men were excluded as well as women

that were not eligible for OHIP coverage at any point in the yearly observation window. Prevalent cases of breast cancer were excluded.

3.3.5 Other variables and measures

Baseline demographic characteristics such as age and income quintile were reported. Age was determined using the RPDB. Retrieved from the RPDB, forward sortation area (FSA) data based on the first three characters of the postal code (Statistic Canada, 2008) were used to determine the neighbourhood income level for individuals from the Canadian census. Income quintiles highlight information about a person's socioeconomic status. The covariates (age and income quintile) were used to describe both cohorts of women.

3.3.6 Data analysis

3.3.6.1 Breast cancer incidence

Cumulative incidence was calculated yearly from 2000 - 2014 in both cohorts. The formula used to calculate breast cancer incidence in women with ID is shown below:

$$\text{Women with ID yearly breast cancer incidence} = \frac{\text{Number of women between 30 and 105 with a new diagnosis of breast cancer in Ontario with ID in (year)}}{\text{Number of women between 30 and 105 no history of breast cancer in Ontario with ID in (year)}}$$

The denominator was the number of women in a given year in Ontario between 30 and 105 with ID that were eligible for OHIP, with no prior breast cancer diagnosis.

The yearly incidence formula for women without ID was:

$$\text{Women without ID yearly breast cancer incidence} = \frac{\text{Number of women between 30 and 105 without an ID with a new diagnosis of breast cancer in Ontario (year)}}{\text{Number of women between 30 and 105 without ID with no history of breast cancer in Ontario in (year)}}$$

The denominator was the number of women in a given year in Ontario between 30 and 105 without ID that were eligible for OHIP, with no prior breast cancer diagnosis.

3.3.6.2 Incidence rate ratio

To address objective 2, yearly incidence rate ratios were calculated to compare breast cancer incidence between women with and without ID. The incidence in women with ID was divided by the incidence in women without ID. The formula used to calculate incidence rate ratios is shown below:

$$\text{Yearly Breast Cancer Incidence Rate Ratio} = \frac{\text{Breast cancer incidence in women with ID in Ontario (year)}}{\text{Breast cancer incidence in women without ID in Ontario (year)}}$$

3.3.6.3 Age-Specific Incidence

Cumulative age-specific incidence was calculated from 2010 – 2014 to compare breast cancer incidence by age between both cohorts of women.

$$\text{Age-Specific Incidence in women with ID (2010 – 2014)} = \frac{\text{Number of women with ID and a new diagnosis of breast cancer in Ontario (in the specified age range)}}{\text{Number of women with ID with no history of breast cancer in Ontario (in the specified age range)}}$$

3.3.6.4 Standardized incidence and incidence rate ratio

Age standardized incidence rates (ASIR) and standardized rate ratios for breast cancer were calculated using the 2006 Canadian population as a standard to account for different age distributions. Age adjustments make both cohorts more comparable by adjusting for differences in population structures.

3.3.6.5 Significance Testing

P-values were used to report on the statistical significance of baseline demographic variables between women with and without ID. Two-tailed Z-tests for sample proportions were used to determine p-values, where $p < 0.05$ was considered statistically significant. Z-test for comparing mean age were used to determine a statistical significance at $p < 0.05$.

Confidence intervals of 95% were used to describe the incidence and incidence rate ratios in women with and without ID. They were used to provide a measure of the precision of the incidence point estimate where there was a 95% probability that the true value is within the interval (Baptist du Prel, Hommel, Rohrig & Blettner, 2009). The size of the sample and variability of the data directly affect the size of the confidence interval (Baptist du Prel et al., 2009). Larger sample sizes lead to narrower confidence intervals. A wide confidence interval is indicative of a small sample. When there is high dispersion in the sample, the conclusions are less certain resulting in a wider confidence interval. Regardless of the size of the confidence interval, the point estimate based on the data in the sample provides the best approximation of the true value (Baptist du Prel et al., 2009).

Confidence intervals were included to provide an approximation of statistical significance or insignificance. If the confidence intervals for women ID include the point

estimate of women without ID the results between both cohorts are not considered significantly different.

3.4 Results

3.4.1 Baseline characteristics of women with and without ID in 2000 and 2014

Tables 1 and 2 show the baseline characteristics of Ontario females, by ID. These characteristics include age and income quintile at the beginning (2000) and final year of the study period (2014). Both years showed that the majority of women with and without ID were between the ages of 30-59. Women with ID in both 2000 and 2014 were more likely to reside in the lowest income quintiles (quintile 1=27.9% (2000), 27.5% (2014), quintile 2= 21.8%(2000), 20.5% (2014)). In contrast, women without ID were roughly evenly distributed throughout all income quintiles.

Table 1.
Baseline characteristics of women with and without intellectual disability by age group and income quintile (Ontario, 2000)

2000	ID Cohort N= 10,231	Comparison Cohort N= 4,490,946	Total N = 4,501,177
Age on Dec 31 (n, col %)			
30-39 years	3,214 (31.4%)*	1,327,974 (29.6%)	1,331,188 (30.0%)
40-49 years	3,006 (29.4%)*	1,142,803 (25.4%)	1,145,809 (25.5%)
50-59 years	1,850 (18.1%)	806,704 (18.0%)	808,554 (18.0%)
60-69 years	996 (9.7%)*	536,707 (12.0%)	537,703 (11.9%)
70-79 years	664 (6.5%)*	429,156 (9.6%)	429,820 (9.5%)
80+	501 (4.9%)*	247,602 (5.5%)	248,103 (5.5%)
Income quintile (n, col %)			
Quintile 1 – Low	2,858 (27.9%)*	870,708 (19.4%)	873,566 (19.4%)
Quintile 2	2,234 (21.8%)*	882,329 (19.6%)	884,563 (19.7%)
Quintile 3	1,823 (17.8%)*	859,480 (19.1%)	861,303 (19.1%)
Quintile 4	1,681 (16.4%)*	829,233 (18.5%)	830,914 (18.5%)
Quintile 5 – High	1,388 (13.6%)*	854,271 (19.0%)	855,659 (19.0%)
Missing	247 (2.4%)	194,925 (4.3%)	195,172 (4.3%)

***** Compared with the comparison cohort of women without ID, statistically significant at $p < 0.01$, according to z test for comparing proportions

Table 2.
Baseline characteristics of women with and without intellectual disability by age group and income quintile (Ontario, 2014)

2014	**ID Cohort N= 17, 472**	**No ID Cohort N= 5,548,903**	**Total N= 5,566,375**
Age on Dec 31 (n, col %)			
30-39 years	4,238 (24.3%)*	1,164,744 (21.0%)	1,168,982 (21.0%)
40-49 years	4,233 (24.2%)*	1,259,480 (22.7%)	1,263,713 (22.7%)
50-59 years	4,409 (25.2%)*	1,256,815 (22.6%)	1,261,224 (22.7%)
60-69 years	2,662 (15.2%)*	902,262 (16.3%)	904,924 (16.3%)
70-79 years	1,167 (6.7%)*	532,514 (9.6%)	533,681 (9.6%)
80+	763 (4.4%)*	433,088 (7.8%)	433,851 (7.8%)
Income quintile (n, col %)			
Quintile 1 – Low	4,807 (27.5%)*	1,001,124 (18.0%)	1,005,931 (18.1%)
Quintile 2	3,587 (20.5%)*	1,024,639 (18.5%)	1,028,226 (18.4%)
Quintile 3	3,095 (17.7%)*	1,026,928 (18.5%)	1,030,023 (18.5%)
Quintile 4	2,976 (17.0%)*	1,085,922 (19.6%)	1,088,898 (19.6%)
Quintile 5 – High	2,687 (15.4%)*	1,066,927 (19.2%)	1,069,614 (19.2%)
Missing	320 (1.8%)	343,363 (6.2%)	343,683 (6.1%)

***** Compared with the comparison cohort of women without ID, statistically significant at $p < 0.01$, according to z test for comparing proportions

3.4.2 Incidence of breast cancer in women with and without ID

From 2000 – 2014

There were 119, 516 incident breast cancers identified between January 1, 2000 and December 31, 2014. Of these women, 330 had ID. Table 3 shows the background characteristics of breast cancer patients including age and income quintile by ID status. A greater proportion of women with ID (29.3%) were diagnosed at a younger age (<50) in comparison with 21.3% of women without ID ($p<0.01$). The mean ages at diagnosis for women with and without ID was 57 and 62 respectively and the difference was statistically significant ($p<0.05$). For women without ID in all age groups, the proportion of women diagnosed with breast cancer was greatest in the highest income quintiles. The reverse was true in women with ID; where the highest proportion of women diagnosed with breast cancer resided in the lowest income quintile.

Table 4 shows the crude and age-standardized breast cancer incidence with 95% confidence intervals (CI) as well as the crude and age-standardized incidence rate ratios with 95% CI's. For each year observed, the 95% CI's for breast cancer incidence in women with ID were wide, and included the point estimate for women without ID (Figure 1), indicative of non-significant differences. Figure 2 shows breast cancer incidence in both groups of women with trendlines for women with and without ID. When compared, the trendlines were not significantly different ($p=0.5$).

Over the 15-year period, the standardized rate ratios comparing women with and without ID ranged between 0.59-1.38. None of the years showed statistically significant rate ratios. Thus, the incidence for breast cancer in both women with and without ID was comparable for each year over the 15-year period.

Table 3.
Characteristics of women with breast cancer (N=119,516), by intellectual disability status (Ontario, 5-year periods)

	Year 2000 - 2004		Year 2005 - 2009		Year 2010 - 2014		Total	
	ID	No ID	ID	No ID	ID	No ID	ID	No ID
	N=84	N=35740	N=100	N=39234	N=146	N=44212	N= 330	N = 119 186
Average age at breast cancer diagnosis								
Mean	57.7	61.5	56.0	61.6	58.5	62.2	57.4[a]	61.7
Age groups (n, col %)								
30-39 years	6 (7.1%)	1756 (4.9%)	8 (8.0%)	1711 (4.4%)	8 (5.5%)	1732 (3.9%)	22 (6.7%)*	5199 (4.4%)
40-49 years	20 (23.8%)	6276 (17.6%)	23 (23.0%)	6931 (17.7%)	32 (21.9%)*	6922 (15.7%)	75 (22.7%)*	20129 (16.9%)
50-59 years	19 (22.6%)	8814 (24.7%)	35 (35.0%)*	9669 (24.6%)	43 (29.5%)	10750 (24.3%)	97 (29.4%)*	29233 (24.5%)
60-69 years	24 (28.6%)	7886 (22.1%)	18 (18.0%)	9161 (23.4%)	33 (22.6%)	11477 (26.0%)	75 (22.7%)	28524 (23.9%)
70+ years	15 (17.9%)*	11008 (30.8%)	16 (16.0%)*	11762(30.0%)	30 (20.6%)*	13331 (30.2%)	61 (18.5%)*	36101 (30.3%)

Income quintile (n, col %)								
Quintile 1 – Low	26 (31.0%)*	6432 (18.0%)	23 (23.0%)	6965 (17.8%)	38 (26.0%)*	7644 (17.3%)	87 (26.4%)*	21041 (17.7%)
Quintile 2	19 (22.6%)	7069 (19.8%)	19 (19.0%)	7560 (19.3%)	30 (20.6%)	8527 (19.3%)	68 (20.6%)	23156 (19.4%)
Quintile 3	14 (16.7%)	7086 (19.83%)	21 (21.0%)	7720 (19.7%)	33 (22.6%)	8664 (19.6%)	68 (20.6%)	23470 (19.7%)
Quintile 4	15 (17.9%)	7111 (19.9%)	22 (22.0%)	8262 (21.1%)	20 (13.7%)*	9341 (21.1%)	57 (17.3%)	24714 (20.7%)
Quintile 5 - High	8 (9.5%)*	7951 (22.3%)	14 (14.0%)	8610 (22.0%)	25 (17.1%)	9863 (22.3%)	47 (14.2%)*	26424 (22.2%)

***** Compared with women without ID, statistically significant at $p < 0.05$, according to the two tailed Z test for comparing proportions

[a] Statistically significant at $p < 0.05$, according to the Z test for comparing independent sample means

Table 4.
Crude and age-standardized breast cancer incidence (per 1000) among Ontario females with ID and without ID and breast cancer rate ratios (Ontario, from 2000-2014)

Year	Population	Incidence	Crude incidence per 1000 persons		Standardized incidence rate per 1000 persons		Crude incidence rate ratio		Standardized incidence rate ratio	
			Rate per 1000 persons	95% CI[a]	Rate per 1000 persons	95% CI[a]	Rate	95% CI[a]	Rate	95% CI[a]
2000	ID	17/9240	1.84	1.07-2.95	2.22	1.26-3.63	0.97	0.60-1.56	1.09	0.68-1.75
	No ID	6846/3623352	1.89	1.84-1.93	2.04	2.00-2.09				
2001	ID	12/9662	1.24	0.64-2.17	1.46	0.73-2.60	0.65	0.37-1.15	0.72	0.41-1.27
	No ID	7031/3707948	1.90	1.85-1.94	2.04	1.99-2.09				
2002	ID	15/10121	1.48	0.83-2.44	1.99	1.09-3.33	0.77	0.46-1.28	0.96	0.58-1.59
	No ID	7332/3794095	1.93	1.89-1.98	2.08	2.03-2.12				
2003	ID	17/10552	1.61	0.94-2.58	1.65	0.95-2.67	0.88	0.55-1.41	0.84	0.52-1.35
	No ID	7119/3872047	1.84	1.80-1.88	1.96	1.91-2.00				
2004	ID	23/10955	2.10	1.33-3.15	2.73	1.70-4.17	1.12	0.74-1.67	1.38	0.92-2.08
	No ID	7412/3943686	1.88	1.84-1.92	1.98	1.94-2.03				
2005	ID	15/11330	1.32	0.74-2.18	1.76	0.94-2.98	0.70	0.42-1.16	0.89	0.54-1.48
	No ID	7590/4010489	1.89	1.85-1.94	1.98	1.93-2.02				
2006	ID	13/11664	1.11	0.59-1.91	1.17	0.61-2.05	0.58	0.34-1.00	0.59	0.34-1.02
	No ID	7676/4008820	1.91	1.87-1.96	1.98	1.93-2.02				
2007	ID	29/12235	2.37	1.59-3.40	2.55	1.67-3.74	1.20		1.26	0.88-1.88

	No ID	7922/4014271	1.97	1.93-2.02	2.02	1.98-2.07		0.83 – 1.72		
2008	ID	25/12771	1.96	1.27-2.89	2.16	1.37-3.25	1.02	0.69-1.5	1.10	0.74-1.62
	No ID	7857/4081289	1.93	1.88-1.97	1.96	1.91-2.00				
2009	ID	18/13263	1.36	0.80-2.14	1.37	0.80-2.20	0.69	0.43-1.10	0.69	0.43-1.1
	No ID	8189/4152503	1.97	1.93-2.02	1.99	1.94-2.03				
2010	ID	31/13759	2.25	1.53-3.20	2.74	1.83-3.96	1.10	0.77-1.57	1.34	0.94-1.91
	No ID	8634/4221050	2.05	2.00-2.09	2.05	2.00-2.09				
2011	ID	21/14196	1.48	0.92-2.26	1.64	0.99-2.57	0.73	0.59-1.12	0.81	0.53-1.24
	No ID	8782/4296895	2.04	2.00-2.09	2.03	1.99-2.07				
2012	ID	33/14608	2.26	1.56-3.17	2.39	1.62-3.41	0.84	0.60-1.18	1.21	0.86-1.70
	No ID	8738/4366498	2.00	1.96-2.04	1.98	1.94-2.02				
2013	ID	36/15085	2.39	1.67-3.30	2.34	1.62-3.27	1.20	0.87-1.66	1.20	0.87-1.66
	No ID	8807/4428435	1.99	1.95-2.03	1.95	1.91-1.99				
2014	ID	25/15586	1.60	1.04-2.37	1.85	1.17-2.79	0.77	0.52-1.14	0.92	0.62-1.36
	No ID	9251/4478662	2.07	2.02-2.11	2.01	1.97-2.05				

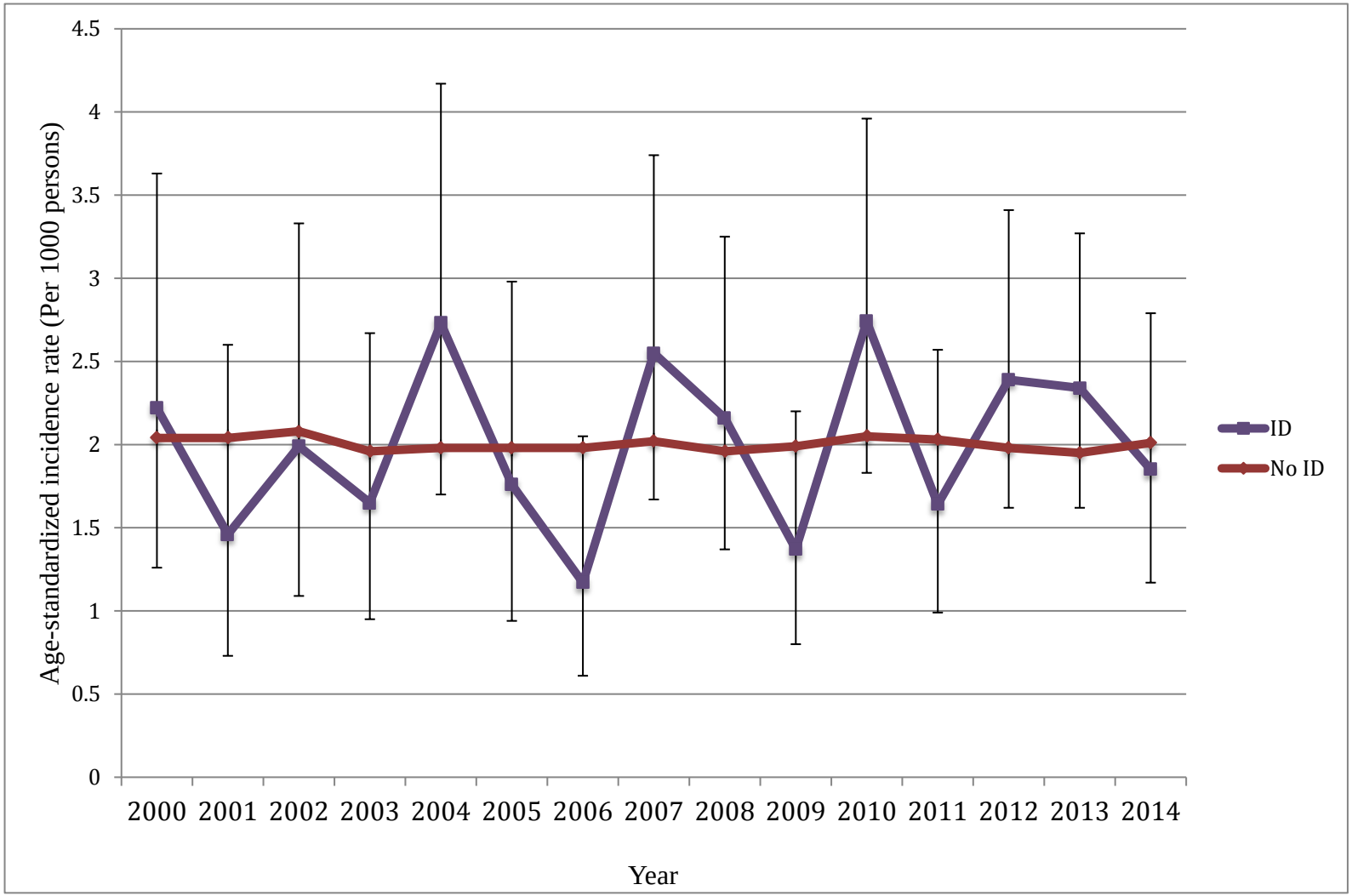
[a] 95% CI: 95% confidence interval

Table 5
Age-specific breast cancer incidence (per 1000) among Ontario females with ID and without ID (Ontario, from 2000-2014)

Age	Population	Incidence	Age-specific incidence per 1000 persons	
			Rate per 1000 persons	95% CI[a]
30-39 years	ID	9/17997	0.50	0.23 - 0.95
	No ID	1907/4686278	0.41	0.39 - 0.43
40 – 49 years	ID	33/20423	1.62	1.11 - 2.27
	No ID	7362/5278722	1.39	1.36 - 1.43
50 – 59 years	ID	43/18162	2.37	1.71 - 3.19
	No ID	10706/4869064	2.2	2.16 - 2.24
60 – 69 years	ID	33/9661	3.42	2.35 - 4.80
	No ID	11403/3400808	3.35	3.29 - 3.42
70+ years	ID	28/6991	4.01	2.77 – 5.78
	No ID	12834/3556668	3.61	3.55 – 3.67

[a] 95% CI: 95% confidence interval

Figure 1.
Trend in breast cancer incidence rates, Ontario females with and without ID, 2000-2014 with 95% CI



Standardized to the Canadian population, Census 2006

Figure 2.
Trend in breast cancer incidence rates, Ontario females with and without ID, 2000-2014 with trendlines

Standardized to the Canadian population, Census 2006

3.5 Discussion

3.5.1 Summary of findings

This is the largest population-based cohort study of ID and breast cancer ever conducted. To date no study has reported on the incidence of breast cancer in Ontario women with ID. The objective was to report on cumulative breast cancer incidence in women with and without ID in Ontario. Baseline characteristics of women with ID identified they were more likely to reside in lower income neighbourhoods and were younger than women without ID. During the study period, a total of 119 516 women diagnosed with breast cancer were identified. Of those women, 330 had ID. The incidence of breast cancer in women without ID remained fairly constant during the 15-year study period, while the incidence in women with ID was more variable. Nonetheless no significant differences were noted between both groups of women.

3.5.2 Results in context of past research

When examining the combined age distribution of women with and without ID in 2000 and 2014, there is evidence of an aging population. When comparing the age profiles in 2000 to those in 2014, there were fewer younger women (<50) and more older women (≥ 50) in 2014. Like the general population of Canada, women with ID are experiencing a demographic shift to an aging population (Statistics Canada, 2016). Despite the pattern of aging over time, the age distribution of women with ID demonstrated that the proportion of women with ID who are young is greater than in women without ID. This finding was consistent with research by Lunsky et al. (2013), which used health as well as social service databases to identify people with ID and

found that the age composition of people with ID in Ontario tended to be younger when compared to people without ID.

The income quintile distributions between women with and without ID were significantly different regardless of the years. Women without ID were roughly evenly distributed throughout the five income quintiles. Women with ID were unevenly distributed across the income quintiles with the highest proportion of women residing in the lowest income quintile. This is consistent with Ontario studies by Lunsky et al. (2013) and Lin et al. (2013), which found that greater than twice the number of adults with ID resided in the lowest than in the highest income quintiles. This finding is also concordant with a British study by Emerson & Hatton (2008), which found the greatest proportion of people in their study with ID resided in the lowest income quintiles. The consistency in the age and income quintile distribution between studies suggests that our sample is representative of women with ID.

In this population study, the results showed that breast cancer incidence in women without ID over the 15-year period did not vary significantly year to year. In women with ID, breast cancer incidence was more variable, likely due to the small sample size. The results demonstrated that breast cancer incidence in women with ID was not significantly different from women without ID. This finding is in accordance with another population level study from Finland by Patja et al. (2001).

The results of the present study were, however, conflicted with a retrospective community sample study from Australia by Sullivan et al. (2003), that found the overall incidence of breast cancer in women with ID from 1982 – 2000 was less than the general population. The differences found may have been a result of the small proportion of

women (n=20) who were diagnosed with breast cancer in the study. Sullivan et al.'s (2003) findings may also be due to the lower life expectancy of women with ID, especially in the earlier years of the study. In fact, Sullivan found that in later years (1995 – 2000) breast cancer was not significantly different in both groups of women, concordant with the present study.

The present study did not show women with ID at a greater or lesser risk of being diagnosed with breast cancer. Even though breast cancer risk factors such as nulliparity are more likely in women with ID (Emerson & Baines, 2011), no excess breast cancer was demonstrated in this study.

A pattern was established in this study that demonstrated women with ID diagnosed with breast cancer tended to be younger than women without ID. This pattern is further confirmed through the age-standardized rate ratios, which were almost always higher than the crude rate ratios indicating women with ID are younger than women without ID. A significant difference ($p<0.05$) was identified in the average age at breast cancer diagnosis in women with and without ID, which were 57 and 61 respectively. This observation may be due to the fact that the age profile of women with ID was younger than that of women without ID. Further calculations of age specific incidence demonstrated breast cancer was comparable in both cohorts throughout all age ranges (Table 5). Nonetheless this finding is strikingly consistent with past research by Satgé et al. (2014), which found the mean age at diagnosis in women with ID to be 56 and 62 in women without ID.

3.5.3 Strengths and limitations

This study used population level data to identify women with and without ID diagnosed with breast cancer. By using administrative health databases, it was possible to identify a relatively large number of women with ID and breast cancer despite women with ID representing only about 1% of the general population. In addition, a high quality cancer registry was used making it unlikely that cases of breast cancer were missed.

This study was subject to some limitations inherent to the use of administrative data. There is a possibility that some women in Ontario with ID were not identified using the algorithm and were misclassified as not having an ID. The likelihood that the cohort of women without ID included a large number of women with ID is quite low given that ID is found in such low rates in the population. It is possible that there are differences in breast cancer incidence according level severity of ID and although a relatively large sample of women with ID was identified, administrative data does not include information on severity.

3.5.4 Implications and future research

The findings of this study have important implications for the detection of breast cancer. The results of the present study indicate women with ID are being diagnosed with breast cancer at comparable rates as women without ID. A non-significant upward trend was indicated by the trendline in Figure 2. Repeating this study in future years and including multiple provinces would be useful to see if this pattern remains the same. In addition, a larger sample size would narrow the confidence intervals of the yearly incidence rates.

In Ontario, breast screening is emphasized for women 50 years of age and older; the data shows that screening women between 40-49 especially in women with ID, may be beneficial as 23% of women with ID versus only 17% in women without ID in this study were diagnosed within that range. Age-specific analyses, however, did not demonstrate significant differences for incidence between women with and without ID in the 40-49 age group. Although the finding was not statistically significant further research is needed to determine whether the results are clinically relevant considering the larger proportion of women with ID diagnosed in that age group. Further research should address whether commencing breast screening earlier in women with ID is beneficial since their age demographic is younger than women without ID.

3.6 Conclusion

The objective of this study was to report cumulative breast cancer incidence in women with and without ID. We found that yearly breast cancer incidence was comparable between women with and without ID. These findings suggest women with ID are at no greater or lesser risk of being diagnosed with breast cancer. Continued surveillance and ensuring screening and prevention strategies reach this population are essential.

4 MANUSCRIPT 2

Breast Cancer Stage at Diagnosis in Women with and without Intellectual Disabilities

4.1 Abstract

Background: Breast cancer stage determines the extent to which the disease has spread and is an important predictor of survival. Stage at diagnosis has not been well researched in women with intellectual disabilities, and to date, no population-level data is available.

Objective: The objectives are to describe and compare breast cancer stage at diagnosis between women with and without intellectual disabilities.

Methods: Women with and without intellectual disabilities diagnosed with breast cancer between 2010 and 2014 were identified using Ontario's administrative database. Logistic regression analyses were used to compare women with ID to those without, reporting the odds of being diagnosed at a later stage (II – IV) versus an early stage (I).

Results: The databases identified 91 women with ID and 29 168 women without ID diagnosed with breast cancer during the study period. In the bivariate logistic regression women with ID were significantly more likely to be diagnosed with a later stage breast cancer (odds ratio1.60; 95% CI=1.03-2.48). When adjusted for age, screening mammography, morbidity, and diabetes, women with ID were 1.3 times more likely to be diagnosed at a later stage (p=0.2).

Conclusion: Women with intellectual disabilities were more likely to be diagnosed with a later stage breast cancer before adjustments for covariates. These findings should be further evaluated in a larger population-level study to determine whether a significant difference is present between both groups of women.

4.2 Introduction

4.2.1 Intellectual disability

The American Psychiatric Association (2013) defines an intellectual disability (ID) as impairments in adaptive functioning and general mental abilities. It affects approximately 0.8% of the Canadian population (Lunsky et al., 2013) and its symptoms must begin in the developmental period of life. Diagnoses for ID are made using intelligence quotient (IQ) tests to measure general mental abilities as well as other standardized tests to determine limitations in adaptive behaviour. Genetic, congenital or acquired factors alongside a variety of other reasons can cause ID (Tasman, Kay, Lieberman, First & Riba, 2015). Down syndrome, fragile X syndrome and fetal alcohol syndrome are just a few of the conditions that are commonly associated with ID (Tasman et al., 2015).

As the life expectancy of people with ID increases they are more likely to experience age related diseases such as breast cancer (Perkins & Moran, 2010).

4.2.2 Breast screening

Breast cancer screening aims to diagnose breast cancer in the early stages of disease progression and has been recommended for many decades (Loberg et al., 2015). Breast cancer screening plays a vital role in relation to stage at breast cancer diagnosis with mammography considered the gold standard screening tool to detect breast cancer (Miller, 2001). It uses x-rays to detect and evaluate changes in the breasts and can help find small breast cancers when they are asymptomatic. It is the most frequently used method to screen for breast cancer in women 50 -74 years of age and aims to reduce the incidence of advanced breast cancer (Cancer Care Ontario, 2015a).

Mammography screening practices are an essential tool for early detection, and in Ontario mammography screening services are available to all women who are eligible for the Ontario Health Insurance Plan (OHIP). Ontario developed the Ontario Breast Screening Program (OBSP) that provides mammographic screening services to women 50 years of age and older (Cancer Care Ontario, 2016). Some benefits of this program include sending patients their screening results and recall notices when they are due for the next screening services, as well; a physician requisition is not required.

Since people with ID tend be poorer, have limited literacy, and communication skills, they are particularly vulnerable to experiencing inequitable access to mammographic screening services (Willis, Kennedy & Kilbride, 2008). For those individuals who rely on caregivers to assist in accessing to screening services, the caregiver's attitude, knowledge and skills further influence the decision to participate in breast screening (Beiser & Stewart, 2005).

Research conducted by Cobigo et al. (2013) on breast screening practices of Ontario women with and without ID found women with ID to be nearly twice as likely not to be screened for breast cancer. The belief that women with ID are not at risk for breast cancer, and thus do not require screening may contribute to decreased screening rates found in the ID population (Cobigo et al., 2013; Ouellette-Kuntz et al., 2015). This disparity may make women with ID more susceptible to being diagnosed at a later stage in their disease progression in comparison to women without ID. Since women with ID have demonstrated decreased participation in screenings services in comparison to women without ID, they may be at a higher risk to be diagnosed at a later stage of breast cancer.

4.2.3 Cancer staging

Cancer staging describes the extent of cancer at diagnosis and is the most important determinant of cancer outcomes (Warner, 2011). Cancer is staged through the tumour, lymph nodes, metastasis (TNM) classification system that describes the extent and behaviour of tumours based on histological characteristics (Compton et al., 2012). Staging consists of indicating the size of the primary tumour and degree of spread, whether cancer has spread to nearby lymph nodes and metastasis to identify if cancer has spread to distant organs. Cancer can be classified into five stages (See Appendix A, Table 1).

4.2.4 Breast cancer stage at diagnosis

A breast cancer diagnosis is determined through the microscopic analysis of breast tissue (American Cancer Society, n.d.). The breast tissue is removed from a suspicious area in the breast. The tissue analysis provides a definitive diagnosis of breast cancer. The breast tissue used for analysis can be obtained through either a needle or surgical biopsy (Schulz-Wendtland, Bautz, & Anders, 2008).

There is a significant lack of research in women with ID and their stage at breast cancer diagnosis. Few epidemiological studies have addressed this gap, and limited research of any type has been performed in this area of healthcare. The only study found was by Satgé et al. (2014), which reported on the breast cancer stage at diagnosis of 11 women with ID. The study sample was retrospectively selected from a single hospital including women treated for invasive breast cancer from 1989 - 2006. The study reported on the tumour grade, tumour size, and disease stage at diagnosis. Women with ID were found to be at a higher risk of having a greater tumour size, metastases to lymph

nodes, and higher tumour grades. This study was not population based and used a small sample; nonetheless, this was the first study of breast cancer stage at diagnosis in women with ID. This study is important because it reported on breast cancer stage at diagnosis in women with ID. Our study will address some of the limitations of the study by Satgé by using population level data to describe breast cancer stage at diagnosis in women with and without ID.

4.2.5 Significance and objectives

Currently no quantitative population level studies have been performed that report on the stage at breast cancer diagnosis in women with ID.

Evidence that women with ID have more advanced breast cancer at diagnosis than women without ID may be indicative of a problem with access to screening and diagnostic procedures. This information would be useful to guide health care decisions about breast cancer management in this population, and potentially identify and address inequities in health service access.

A population-based study performed in Ontario will provide locally relevant results on the stage at diagnosis in women with ID.

The objectives of this research were to: describe the stage at breast cancer diagnosis between women with and without ID, and compare the stage at breast cancer diagnosis between women with and without ID.

4.3 Methods

4.3.1 Study design

This research used a cross-sectional study design to report on breast cancer stage at diagnosis in women with and without ID. The cross-sectional design was common in studies conducted in Ontario that reported breast cancer stage at diagnosis in the general population (Ginsburg et al., 2015, Lipscombe et al., 2015). This study was approved by the institutional review board at Sunnybrook Health Sciences Centre, Toronto, Canada and the University of Ontario Institute of Technology.

4.3.2 Data sources and linkages

In Ontario, health data collected for administrative and billing purposes are housed in administrative health databases. This data is a rich source of information that can be used to answer a variety of research questions. Administrative health databases provide researchers with historical data allowing them to study changes over time at a population level.

The Institute for Clinical Evaluative Sciences (ICES) is a recognized organization that has secure access to large variety of administrative health data in Ontario (ICES, 2016). Data collected by ICES has personal identifiers removed, which are then replaced by a confidential ICES number (IKN). The IKN is consistent though all administrative databases housed at ICES and is provided for all Ontario residents eligible for the Ontario Health Insurance Plan (OHIP) (ICES, 2016). These datasets were linked using unique encoded identifiers and analyzed at ICES.

4.3.3 Data sources

Nine administrative databases retrieved from ICES were accessed in this study including seven health databases, one registry and census data. The databases were the Ontario Mental Health Reporting System (OMHRS), the Canadian Institute of Health Information Discharge Abstract Database (CIHI-DAD), the National Ambulatory Care Reporting System (NACRS), Same Day Surgery (SDS), OHIP, the Ontario Cancer Registry (OCR), Ontario Diabetes Database (ODD), the Registered Persons database (RPDB), and the Canadian census. Clinical and health service data housed in these databases include: mental health problems, inpatient hospital discharges, emergency department visits, same day surgeries, physician claims, cancer diagnoses and diabetes diagnoses (See Appendix B, Table 1).

4.3.4 Study populations

The study included two groups of women diagnosed with breast cancer. One group consisted of women with ID and breast cancer; the second group included women without ID diagnosed with breast cancer.

People with ID were identified from five administrative databases held at ICES using diagnostic codes for ID (See Appendix B, Table 2 and 3).

The Health Care Access Research and Developmental Disabilities research program (H-CARDD) developed a coding algorithm to identify people with ID, which was used in this study (Lunsky et al., 2013). Since ID is often diagnosed and recorded during childhood, the coding algorithm was applied to health databases from their date of inception (Lin et al., 2013). Using the widest time frame possible to maximize the

detection of ID cases is a method that was evaluated and promoted by Lin et al. (2013) and helps to identify people with ID across all ages.

The comparison population of Ontario females without ID was identified using the RPDB.

Once both groups were identified, linkages were performed using the OCR to identify women newly diagnosed with invasive breast cancer (ICD-10 code: C50xx) between January 1, 2010 and December 31, 2014. With permission from Cancer Care Ontario (CCO), information from the OCR was used to identify the breast cancer stage at the time of the first breast cancer diagnosis.

Exclusion criteria

Records of individuals with the following criteria were excluded:

- No/invalid stage information
- In situ (stage 0) breast cancer
- Women with a prior cancer diagnosis
- Women who did not have OHIP coverage in the 365 days prior to a breast cancer diagnosis
- Men

Women with in situ (stage 0) breast cancer were not included in this study to be consistent with previous Ontario research (Lipscombe et al., 2015; Ginsburg et al., 2015). It was also excluded because of the controversy surrounding the diagnosis and treatment of in situ breast cancer (Sakorafas, Farley & Peros, 2008). Due to these factors this study focused on stage I-IV breast cancers, which are more problematic and can spread to nearby lymph nodes and distant organs.

4.3.5 Primary exposure, outcome and other variables

4.3.5.1 Primary exposure

The primary exposure variable is the presence versus absence of ID at the time of breast cancer diagnosis. ID is defined as receiving a diagnosis at any point prior to receiving a breast cancer diagnosis.

4.3.5.2 Primary outcome

The primary outcome was breast cancer stage at the time of the first breast cancer diagnosis between 2010 and 2014, retrieved from CCO's cancer stage data and categorized as stage I, II, III or IV (See Appendix A, Table 1). Stage at breast cancer diagnosis was characterized as a binary variable. Women were either diagnosed with a late stage breast cancer (II-IV) or at an early age (I).

4.3.5.3 Other variables

Demographic information on Ontario residents eligible for OHIP was retrieved from the RPDB. The RPBD includes forward sortation area (FSA) data derived from the first three characters of postal codes (Statistics Canada, 2008). Using the FSA, it was possible to determine the neighbourhood income level of individuals using the Canadian census. Neighbourhood income was categorized into quintiles and provides information about an individual's socioeconomic status (See Appendix B, Table 2).

History of diabetes was obtained from the ODD and was included as a variable because diabetes has been associated with a later stage at breast cancer diagnosis (Lipscombe et al., 2015).

The role of breast cancer screening practices was evaluated because it is one of the most important predictors of cancer stage at diagnosis (Taplin et al., 2004). OBSP is Ontario's organized breast screening program available for women between 50 -74 years of age. Breast screening is available for all women in Ontario with no direct costs through OHIP claims. Women with and without ID diagnosed with breast cancer were coded according to their screening practices (0=no breast cancer screen; 1=yes breast cancer screen). This was done by examining data from OBSP and OHIP for bilateral mammography to identify those who received breast cancer screening in the 3 years to 60 days prior to breast cancer diagnosis (Ginsburg et al., 2015). Breast screening services received between 3 years and 60 days prior to breast cancer diagnosis were classified as screening mammograms. To differentiate between mammograms performed as part of a diagnostic work up rather than screening, the methodology by Ginsburg et al. (2015) was followed. A diagnostic work up is conducted when a woman presents with concerning signs and/or symptoms and is sent for a mammogram. Breast screening services received < 60 days prior to a breast cancer diagnosis were considered pre-diagnostic mammograms and therefore coded as 0 (no breast screen).

The Adjusted Clinical Groups Case-Mix System (ACGs) developed by Johns Hopkins was used to determine the morbidity level for each woman using data from January 1, 2009 – December 31, 2014. This system uses information on age, sex, and number and type of diagnoses to produce a value between 0 (non-users) and 5 (very high morbidity). The Johns Hopkins group uses the term Resource Utilization Band (RUB) when referring to these morbidity levels and the ACG Case-Mix System has been

validated in Canadian populations (Reid, MacWilliam, Roos, Bogdanovic & Black, 1999).

After examining the distribution of variables a decision was made to dichotomize them. This was necessary due to the small cell numbers generated for some of the results in women with ID. Age was categorized into < 50 and ≥ 50. Income was grouped into high (quintiles 3-5) and low (quintiles (1-2). Screening mammogram and diabetes were categorized as yes or no. Lastly morbidity level was classified as either low (1-4) or high (5).

4.3.6 Data analysis

4.3.6.1 Breast cancer stage at diagnosis

In both groups of women, stage at first breast cancer diagnosis during the study period was classified as stage I, II, III or IV. Descriptive demographic information was provided for both cohorts including age, income quintile, screening mammography, prevalent diabetes, and morbidity (RUB).

4.3.6.2 Statistical model

Binary logistic regression analysis using the logit procedure in SAS® software was used to calculate crude and adjusted odds ratios (OR) (SAS Institute, 2016). The primary independent variable was the presence or absence of ID, and the dependent variable was the odds of being diagnosed at a late stage (II-IV) versus an early stage (I) of breast cancer.

An additional logistic regression analysis was performed solely on women with ID, reporting unadjusted and adjusted odds ratios to address the effects of the covariates on that population.

4.3.6.3 Significance Testing

The significance of descriptive demographic information was evaluated using p-values. Two tailed z-tests for proportions were used to calculate p-values comparing women with and without ID. They were also calculated using Z-test for independent sample means to compare mean age in women with and without ID. P-values of less than 0.05 were considered significant.

Statistical significance in the logistic regression analysis was assessed using confidence intervals of 95%. Confidence intervals were used to determine the statistical significance between staging and covariates when comparing women with and without ID diagnosed at later stages. The size of the confidence intervals is directly correlated with the size sample (Baptist du Prel, Hommel, Rohrig & Blettner, 2009). Although confidence intervals describe a 95% probability that the true value is within the range, regardless of the size of the CI, the point estimate based on the data is the best estimate of the actual value (Baptist du Prel et al., 2009). A significant result is demonstrated by a confidence interval that does not include the value 1.00 (Baptist du Prel et al., 2009).

4.4 Results

4.4.1 Baseline characteristics of women with and without ID from 2000 - 2014

The cohort consisted of 29, 259 women diagnosed with invasive breast cancer with and without ID from the Ontario female population (see Figure 1). Within this group, 91 women had ID.

Table 1 shows the baseline demographics and clinical characteristics of women with breast cancer (age, income quintile, prior screening behaviour, prevalent diabetes and morbidity). Statistically significant differences were observed for all characteristics except age group. Women with ID were evenly distributed between low and high income, in contrast to women without ID, where a larger proportion of women diagnosed with breast cancer resided in the highest income quintiles. A greater proportion of women without ID received screening mammograms. The proportion of women with ID with a comorbid diabetes diagnosis was greater than women without ID. Women with ID were more likely to have higher morbidity.

Figure 1.
Study populations of women with and without ID diagnosed with breast cancer

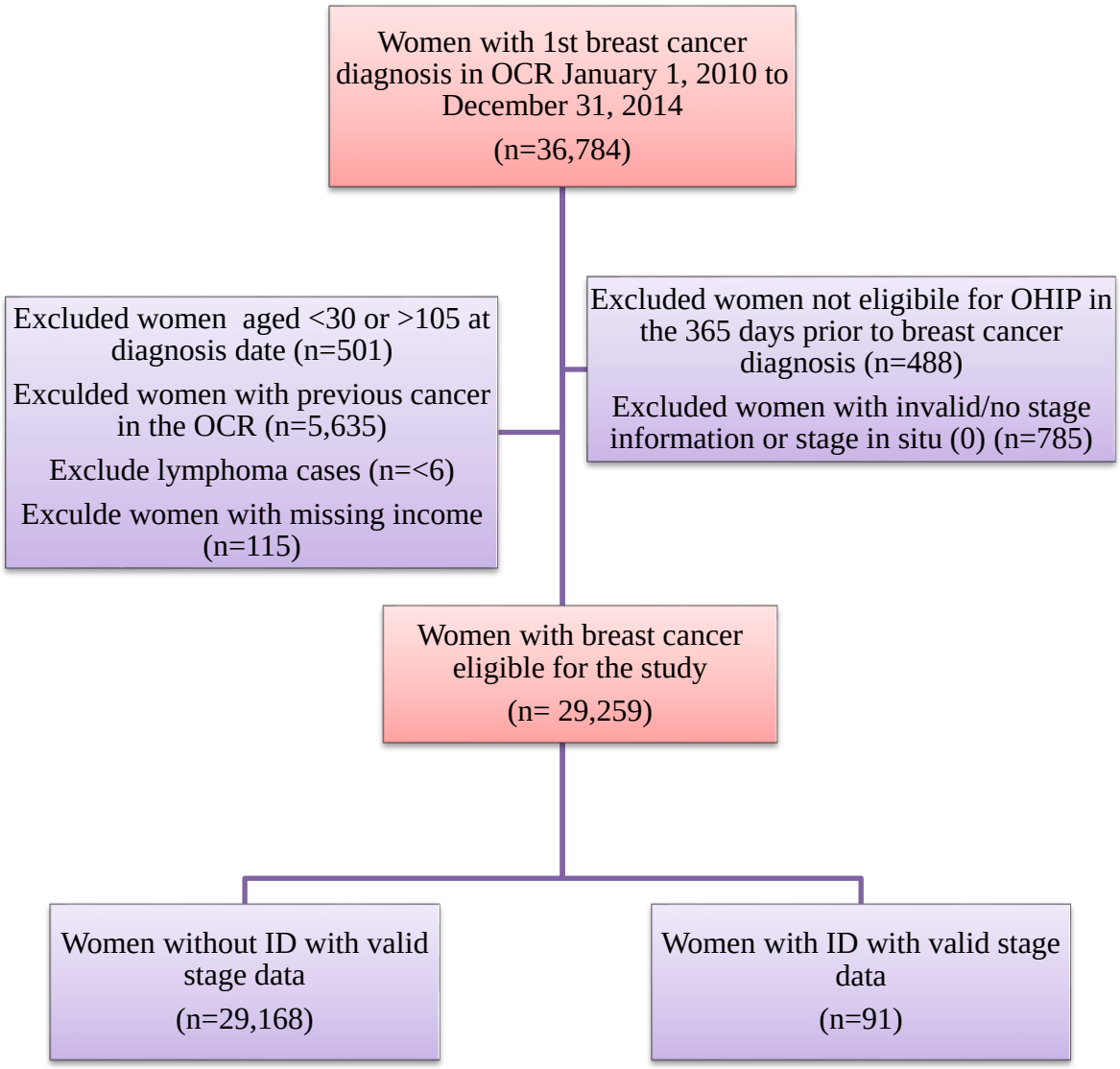


Table 1.
Characteristics of women with and without ID diagnosed with breast cancer (N=29,259) (Ontario, 2010-2014)

	Total with ID	Total without ID	P- value[a]
	N=91	N= 29, 168	
Age			
Mean ± SD	57.10 ± 11.8	60.58 ± 13.3	$p < 0.05$[b]
Age group			
<50	27 (29.7%)	6,458 (22.1%)	$p > 0.05$
≥ 50	64 (70.3%)	22,710 (77.9%)	$p > 0.05$
Neighbourhood income quintile			
1-2	45 (49.5%)	10,676 (36.6%)	$p < 0.05$
3-5	46 (50.5%)	18,492 (63.3%)	$p < 0.05$
Screening mammogram			
Yes	38 (41.8%)	16,042 (55.0%)	$p < 0.05$
No	53 (58.2%)	13,126 (45.0%)	
Previous Diagnosis of Diabetes			
Yes	30 (33.0%)	5,011 (17.2%)	$p < 0.05$
No	61 (67.0%)	24,157 (82.8%)	
Morbidity Level (RUB)			
1-4	23 (25.3%)	10,561 (36.2%)	$p < 0.05$
5	68 (74.7%)	18,607 (63.8%)	$p < 0.05$

[a] According to the two tailed Z test for proportions
[b] According to the Z test for independent sample means

4.4.2 Breast cancer stage at diagnosis in women with and without ID

Table 2 shows the baseline characteristics of women with late versus early stage breast cancer. Significant differences were observed for all baseline characteristics except for morbidity level. A greater proportion of women younger than 50 were diagnosed with a later stage breast cancer, while the opposite was true for women 50 years of age and older. For both women with early and late stage breast cancer a larger proportion of them resided in the highest income quintiles. The majority of women (70%) diagnosed with stage I breast cancer had a screening mammogram prior to being diagnosed in comparison with only 43% of women diagnosed with a late stage breast cancer. In both early and late stage breast cancers, the majority of women (≅64%) resided in the highest morbidity categories.

Figure 2 demonstrates the proportions of women with and without ID diagnosed with breast cancer by stage at diagnosis. The greatest proportion of women with ID were diagnosed with stage II breast cancer (46%), while in women without ID the majority were diagnosed at stage I (44%). This figure demonstrates a greater proportion of women with ID (67%) were diagnosed with a later stage breast cancer when compared to women without ID (60%). When comparing stage IV breast cancer, the results showed 8% of women with ID were diagnosed at the latest stage versus only 4% in women without ID.

4.4.3 Regression analysis results

Women with ID were significantly more likely to present with a later stage breast cancer (II-IV) than women without ID when unadjusted odds ratios were calculated (see Table 3). The unadjusted odds of a woman with ID being diagnosed with either stage II,

III or IV breast cancer was 1.6 times ($p<0.05$) larger than women without ID. Once the odds ratio was adjusted for the covariates, women with ID were no longer significantly more likely to be diagnosed with late stage breast cancer (OR 1.3, $p = 0.2$).

A successive regression analysis was performed on the cohort of women with ID to address the effect of the covariates on a late stage breast cancer. The results are described in Table 4, where non-significant differences in the effects of each covariate were demonstrated.

Table 2.
Characteristics of women with early and late stage breast cancer (N=29,259) (Ontario, 2010-2014)

	Stage I	Stage II-IV	P- value[a]
	N = 12,865	N = 16, 394	
Age group			
< 50	2,037 (15.8%)	4,448 (27.1%)	$p < 0.05$
≥ 50	10,828 (84.2%)	11,946 (72.9%)	$p < 0.05$
Neighbourhood income quintile			
1-2	4,551 (35.4%)	6,170 (37.6%)	$p < 0.05$
3-5	8,314 (64.6%)	10,224 (62.4%)	$p < 0.05$
Screening mammogram			
Yes	8,994 (69.9%)	7,086 (43.2%)	$p < 0.05$
No	3,871 (30.1%)	9,308 (56.8%)	$p < 0.05$
Previous diabetes			
Yes	2,115 (16.4%)	2,926 (17.8%)	$p < 0.05$
No	10,750 (83.6%)	13,468 (82.2%)	$p < 0.05$
Morbidity level			
1-4	4,663 (36.2%)	5,921 (36.1%)	$p > 0.05$
5	8,202 (63.8%)	10,473 (63.9%)	$p > 0.05$

[a] According to the two tailed Z test for proportions

Figure 2.
Proportion of breast cancer patients by stage at diagnosis and intellectual disability (ID N = 91; no ID N = 29,168)

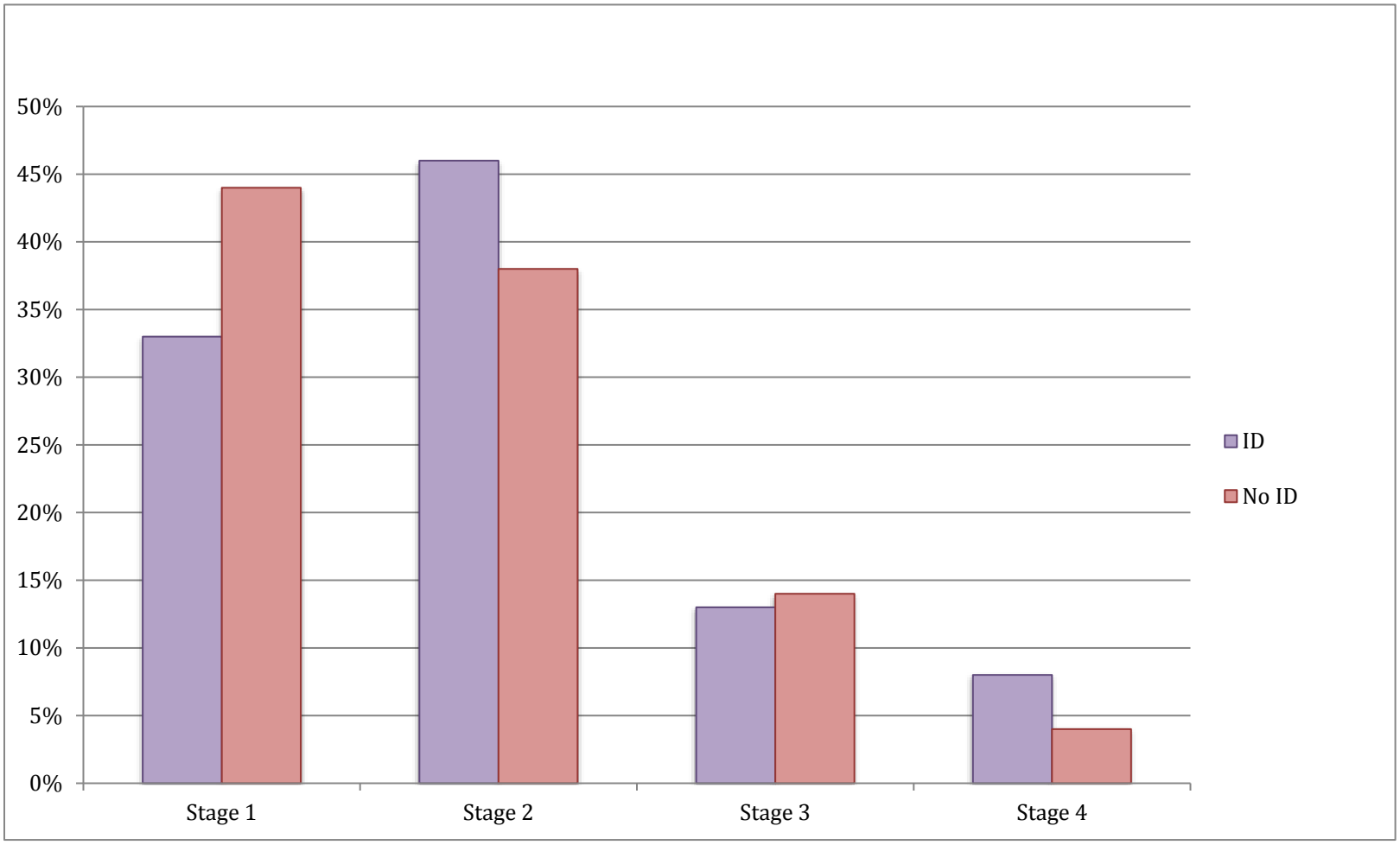


Table 3.
Logistic regression results estimating the unadjusted and adjusted odds ratio for late stage breast cancer in women with ID vs. women without ID, as well as the odds ratios for the covariates

	Logistic regression			
	Stage II-IV vs. I			
	Unadjusted		Adjusted	
	OR[a]	95% CI[b]	OR	95% CI[b]
ID status (ID vs. No ID)	1.60	1.03 – 2.48	1.33	0.85 – 2.11
Age (<50 versus ≥50)	1.98	1.87 - 2.01	1.64	0.57-0.65
Income quintile (low (quintile 1+2) vs. high (quintile ≥3))	1.10	1.05 - 1.16	1.04	0.99-1.10
Screening mammogram (No vs. Yes)	3.05	2.91 -3.20	2.83	2.70 - 2.98
Morbidity (high RUB[c] (5) vs. low RUB (1-4))	1.01	0.96-1.06	1.11	1.05 - 1.16
Diabetes (Yes vs. No)	1.10	1.04 – 1.17	1.16	1.09-1.24

[a] OR: odds ratio
[b] 95% CI: 95% confidence interval
[c] RUB: resource utilization band

Table 4.
Logistic regression results estimating the unadjusted and adjusted odds ratio for advanced stage breast cancer in women with ID by covariates

	Logistic regression			
	Stage II-IV vs. I			
	Unadjusted		Adjusted	
	OR[a]	95% CI[b]	OR[a]	95% CI[b]
Age (<50 versus ≥50)	2.82	0.95-8.42	1.64	0.51-5.55
Income quintile (low (quintile 1+2) vs. high (quintile ≥3))	1.18	0.49-2.83	1.13	0.44-2.90
Screening mammogram (No vs. Yes)	3.08	1.24 -7.60	2.53	0.97-6.62
Morbidity (high RUB[c] (5) vs. low RUB (1-4))	4.39	1.18-16.22	3.68	0.94-14.35
Diabetes (Yes vs. No)	1.28	0.51-3.21	1.019	0.38-2.76

[a] OR: odds ratio
[b] 95% CI: 95% confidence interval
[c] RUB: resource utilization band

4.5 Discussion

4.5.1 Summary of results

This is the only population study of breast cancer stage at diagnosis in women with ID. The objective was to report and compare breast cancer stage at diagnosis in women with and without ID. Of the 29, 259 women diagnosed with invasive breast cancer, 91 women had an ID. The majority of women with ID were diagnosed with stage II breast cancer; in contrast, the majority of women without ID were diagnosed at stage I. A logistic regression analysis was performed to determine the odds of women with ID being diagnosed at a late (II-IV) versus early (I) stage breast cancer. The unadjusted odds ratio showed that, compared to women without ID, women with ID were significantly more likely to be diagnosed at a later stage. When adjusted for covariates (age, income quintile, screening mammogram, morbidity and prevalent diabetes) however, the odds ratio comparing the two groups of women was not statistically significant.

4.5.2 Results in context of past research

Significant differences were noted in the mean ages at diagnosis between both groups of women. Women with ID were diagnosed at a mean age of 57 and women without ID were diagnosed at a mean age of 61. Prior research conducted in France found the mean ages to be 56 in women with ID and 62 in women without ID (Satgé et al., 2014). However, an Australian study by Sullivan et al. (2003) found the mean age at diagnosis to be 49 in women with ID. The lower age at diagnosis found in the Australian study may be due to its inclusion criteria that allowed for younger women in the sample as well as its inclusion of in situ breast cancer. Nonetheless, these three studies have

demonstrated that women with ID are diagnosed at a younger age in comparison to women without ID. The age specific breast cancer incidence calculations performed in manuscript 1, demonstrated that the differences in age can be accounted for by the difference in the age distributions between women with and without ID.

Overall, women in this study were predominantly diagnosed with stage I or II breast cancer. The majority of women with ID were diagnosed with stage II breast cancer, while the majority of women without ID were diagnosed with stage I breast cancer. The only other study to look at stage at diagnosis in women with ID was a small hospital based study conducted by Satgé et al. (2014). In accordance with the present study, Satgé found that the largest proportion of women with ID were diagnosed at stage II. In the present study, the proportion of women with ID diagnosed with stage II breast cancer was 46%, while Satgé found the proportion to be 73%. Though there is a discrepancy in the results, our finding is likely more accurate owing to our larger sample size (n=91 vs. Satgé n=11).

In an unadjusted odds ratio comparing women with and without ID, women with ID were significantly more likely to be diagnosed with a late stage breast cancer. These results are again consistent with the research by Satgé et al. (2014). The French study found a significant unadjusted odds ratio of 3.2 representing the risk of being diagnosed with stage II versus stage I and an odds ratio of 10.2 comparing Stage III versus stage I. This is considerably higher than the present study with an of 1.6 comparing stage II-IV versus stage I. Both studies demonstrated that women with ID are at an increased risk of being diagnosed with a later stage breast cancer. The study by Satgé also reported on various components of breast cancer stage. They reported that, women with ID had

greater tumour sizes and were more likely to have metastases and lymph node involvement.

Although Satgé found that women with ID were more likely to be diagnosed at later stage, significant differences were not noted in the histologically types of breast cancer. Thus women with ID were not diagnosed with more aggressive cancers. Histology was not assessed in the present study since women with ID are very heterogeneous and different syndromes may present with different physiological differences. Thus the focus remained on health service access issues and their association with stage at diagnosis.

Prior population level research on other minority and vulnerable populations have demonstrated an increased risk of being diagnosed with a later stage breast cancer. An Ontario study by Ginsburg et al. (2015) found that South Asian women had a significant adjusted odds ratio of 1.3 comparing stage II-IV to stage I breast cancer. In the United States (USA), researchers found some visible minorities (Black, South Asian & Hispanic) were at a greater risk of presenting with a later stage breast cancer relative to non-Hispanic whites (Li, Malone &Daling, 2003; Iqbal, Ginsburg, Rochon, Sun & Narod, 2015; Warner et al., 2012). The odds ratios in the studies ranged from 1.25-3.6, demonstrating that minority and vulnerable populations are at a greater risk of being diagnosed at a later stage. The magnitudes of the odds ratios in some of the aforementioned studies are comparable with that of the present study (Li et al., 2015; Ginsburg et al., 2015). It is possible that some minority and vulnerable populations are experiencing similar barriers to early diagnosis as those with ID.

Though it was not our primary objective, it was instructive to look at other variables strongly associated with late stage breast cancers. Breast screening plays an integral role in relation to breast cancer stage at diagnosis (Miller, 2001) and, of all the covariates in this study, it showed the strongest association with the outcome: women were close to 3 times more likely to be diagnosed with a later stage breast cancer if they did not participate in routine screening.

In addition, the current study found that women with ID were less likely to have obtained a screening mammogram. This is consistent with previous research that found that women with ID are less likely to participate in breast screening when compared to women without ID (Cobigo et al., 2013; Sullivan et al., 2001). For instance, Cobigo et al. (2013) demonstrated that less than 50% of Ontario women with ID participated in breast screening. Screening practices may be lower in women with ID due to challenges associated with their disability. It may be technically challenging to perform optimal mammograms exacerbated by communication challenges and possible comorbid physical disabilities. Decreased screening among Ontario women generally, and in women with ID specifically, contribute to their likelihood of receiving a later stage diagnosis; however, women with ID are starting at a lower screening take-up rate and at least matching the rate in the general population would lead to more equity in terms of health service access and potential outcomes. The results of this study have demonstrated that more attention needs to be given to women with ID so that earlier diagnoses can be achieved.

Among all women, screening practices, high morbidity, and the prevalence of diabetes were significantly associated with being diagnosed at a later stage. The

influence of these risk factors contributed to why women with ID were diagnosed at a later stage as can be seen in the changes in crude to adjusted odds ratios for the primary independent variable. There was a decrease in the unadjusted odds ratio from 1.6 to 1.3 when comparing women with and without ID after controlling for other variables. This suggests that the associations found between the covariates (i.e. age, income quintile, breast screening practices, morbidity and diabetes) and breast cancer stage at diagnosis can explain some of the variation in staging between women with and without ID. In our opinion, an adjusted odds ratio of 1.3 still suggests that having an ID is an independent predictor of late stage breast cancer diagnosis, but the lack of statistical power due to the low number of women with ID in the sample resulted in a non-significant result. This finding needs to be corroborated with a larger sample, an issue dealt with in the limitation section of this manuscript.

Additional analyses were performed solely on women with ID in order to identify potential factors associated with being diagnosed at a later stage. There was a consistent pattern between the model with all women and the model among only those with ID in that the odds ratios for all of the covariates were very comparable, except for morbidity. The morbidity variable, however may have been largely influenced by a small cell size among women with ID with low morbidity used in the odds ratio calculation. Overall, these results demonstrate that the factors that result in all women being diagnosed at a later stage are consistent with those that affect women with ID alone. Thus, factors including preventive and early detection initiatives that are addressed in women without ID should be tailored to meet the needs of people with ID and support their inclusion in prevention efforts.

4.5.3 Strengths and limitations

Population level data was used to identify women with and without ID diagnosed with breast cancer and their stage at diagnosis. Considering only about 1% of the population has ID, administrative data allowed us to identify a relatively large number of women with ID diagnosed with breast cancer (Lunsky et al., 2013).

This study has several limitations. There is a possibility that the algorithm did not identify some women with ID, resulting in a misclassification error. Previous research has found that women with milder disabilities are probably underrepresented, as they are more likely to go unidentified in administrative databases (Iezzoni, 2002). It is not uncommon for people with mild ID to go undiagnosed since they often function reasonably well in society (British Institute of Learning Disabilities, n.d.; Thambirajah, 2007). In addition due to the limitations of administrative data, we were unable to identify the severity of the ID which is a potentially important risk factor. Although the data was adjusted for a variety of covariates that influence breast cancer stage, this study did not include other factors such as family history of breast cancer, and lifestyle factors.

After adjusting for covariates, this study did not find a statistically significant difference between women with and without ID regarding breast cancer stage. This may be the result of type II error (i.e. failing to reject the null hypothesis that is false, also known as a false negative). A post hoc power analysis found the power of this study to be 0.59; thus, there was a 41% chance of type II error in this study. A power of 59% is less than the standard 80% power that is considered adequate to report a difference when one exists (Hylown Consulting, n.d.). A significant effect was only found between the

primary independent variable and outcome when examining the crude odds ratio and this is possibly due to type II error.

4.5.4 Implications and future research

This study is important because, it demonstrates that women with ID are significantly more likely to be diagnosed with a later stage breast cancer (before adjustments with covariates). Prior research on minority and vulnerable populations demonstrated significant results with odds ratios comparable to the present study. A study of stage at diagnosis in women with ID across all or multiple provinces would be beneficial to increase the amount of women with ID in the study sample. A larger study would increase the statistical power and potentially provide more conclusive results on the risk of being diagnosed at a later stage.

The covariates that contribute to being diagnosed with breast cancer at a later stage are, being < 50, not participating in regular screening, having a high morbidity, and prevalent of diabetes. Greater proportions of women with ID were found in all of those covariates when compared to women without ID.

In Ontario, women are encouraged to begin breast screening at 50 (Cancer Care Ontario, 2015b). This threshold may not be beneficial for women with ID, as 30% of them in this study were diagnosed before the age of 50. Large population studies are required to further establish whether having ID is an independent predictor for advanced stage breast cancer and to establish benefits of identifying them as high risk.

The lower breast screening usage in women with ID highlights the need for improved access and utilization of breast screening services, seeing as it is the greatest predictor of stage at diagnosis. Lower screening usage may vary by the severity of the

disability, as women with comorbid physical disabilities are not easily accommodated by mammography. In addition to the technical challenges, women with ID may have difficulty understanding the procedure.

Standard recruitment strategies may not be suitable for women with ID and self-referral is unlikely unless they are encouraged by an advocate or family member (Sullivan, Slack-Smith & Hussain, 2004). Since women with ID often have limited knowledge about breast cancer, further research is needed to identify whether using patient navigators could be a useful tool for women with ID to provide individualized assistance and facilitate timely access breast screening services (Dohan & Schrag, 2005; Natale-Pereira, Enard, Nevarez & Jones, 2011). Navigators can be used to help increase compliance with breast screening services. The support of a patient navigator may help decrease anxiety associated with medical examinations and increase patient satisfaction. Patient navigators would prepare the women for the exam by empowering them and providing emotional and informational support (Dohan & Schrag, 2005; Fowler, Steakley, Garcia, Kwok & Bennett, 2006; Marriott, Turner, Ashby & Rees, 2015; Meade et al., 2014). They can help bridge the gap between health care professionals and women with ID as communication can often be challenging (Dohan & Schrag, 2005; Marriott et al., 2015; Mcilfatrick, Taggart & Truesdale-Kennedy, 2011; Meade et al., 2014; Natale-Pereira et al., 2011). Patient navigators may be a very useful tool to help reduce disparities and improve the uptake of mammographic screening in women with ID. It is imperative that further research is performed in this area to identify if implementing patient navigators improves outcomes for women with ID.

Caregivers need to be properly educated and supported as they play an integral role in the health of people with ID (Krahn et al., 2006). It is important that caregivers understand the importance of breast screening and early detection in women with ID as their attitude and knowledge greatly influence participation in secondary prevention strategies (Lunsky et al., 2013). Thus it is not only important to empower the patient but also the caregiver as women with ID often heavily rely on them to help navigate through the healthcare system. They can be used independently or in addition to patient navigators to help support people with ID.

It is essential that research be performed to identify barriers that restrict access to breast screening for women with ID to help improve the number of women who actively participate in breast screening. Reducing barriers to breast screening services should in turn contribute to a reduction in women with ID being diagnosed with breast cancer at a later stage.

4.6 Conclusion

Our study found that ID was associated with later breast cancer stage at diagnosis when considering the unadjusted odds ratio. When adjusted for covariates, women with ID were no longer more likely to be diagnosed at a later stage, suggesting some of the variation in stage between both groups was explained through the associations found between the covariates and breast cancer staging. The lack of statistical significance for the multivariate results in this study was possibly due to type II error. The small sample of women with ID and breast cancer resulted in a lack of power to detect an effect where one may exist. Therefore, larger population-level studies are needed to evaluate whether a significant association is present between women with ID and later stage breast cancer diagnosis.

5 THESIS CONCLUSION

5.1 Thesis Conclusion

5.1.1 Introduction

Women with ID have impairments in both general mental abilities and adaptive functioning (American Psychiatric Association, 2013). They are more disadvantaged and are more likely to be diagnosed with various health conditions (Lunsky et al., 2013). Women with ID have higher morbidity when compared to women without ID (Lunsky et al., 2013). Previous research has demonstrated that the life expectancy of people with ID is increasing in parallel to those without ID (Bittles et al., 2002; Emerson & Baines, 2011; Kapell, et al., 1998; Perkins & Moran, 2010). Their increased life expectancy increases the likelihood that they will be diagnosed with an age related health concern such as cancer. In women, breast cancer is a significant contributor to the morbidity and mortality of the general population (Canadian Cancer Statistics, 2016). However, breast cancer has not been well studied in women with ID and its impact is not well understood. As the life expectancy of women with ID increases, it becomes increasingly important to identify if any disparities exist between women with and without ID in relation to breast cancer.

5.1.2 Summary of results

Manuscript 1 addressed the first objective: To describe and compare breast cancer incidence in women with and without ID. Using administrative databases women with and without ID diagnosed with breast cancer between 2000 and 2014 were identified. When compared to women without ID, a greater proportion of women with ID were diagnosed with breast cancer at < 50. Women without ID diagnosed with breast cancer predominately resided in the higher income quintiles, in contrast, the greatest

proportion of women with ID resided in the lowest income quintile. Yearly cumulative breast cancer incidence was calculated and no statistical difference was found between the two cohorts after adjusting for age. Thus, the present study did not demonstrate any disparities in breast cancer incidence between women with and without ID.

Manuscript 2 addressed the second objective: To describe and compare breast cancer stage at diagnosis in women with and without ID. Women diagnosed with breast cancer were classified as having either an early (I) or late stage (II-IV) cancer. Administrative databases were used to identify women with and without ID diagnosed with breast cancer between 2010 and 2014 and their stage at diagnosis. The largest proportion of women with ID were diagnosed with breast cancer at stage II, in contrast to women without ID who were predominately diagnosed at stage I. Unadjusted and adjusted odds ratios were calculated to determine the odds of being diagnosed at a later stage if you have an ID vs. no ID. Adjusted odds ratios addressed the effect of the covariates on being diagnosed at a later stage. Women with ID were significantly more likely to be diagnosed at a later stage before adjustments for covariates. Adjusted odds ratios demonstrated women with ID were not significantly more likely to be diagnosed at a later stage.

5.1.3 Future research

This thesis made a significant contribution the body of Canadian research on the health of women with ID. No prior Canadian research had been performed to identify and compare breast cancer incidence and stage at diagnosis between women with and without ID. The findings of this study were important because they described that breast

cancer incidence in both populations is comparable but disparities may be present as women with ID may be diagnosed at later stages when compared to women without ID.

The model of healthcare disparities and disability described in this thesis is a multi-faceted tool that recognized the importance of environmental and personal factors and how their interactions can affect the health status of people with ID. Unfortunately, in this research, environmental factors could not be studied due to the limitations inherent in the use of administrative data. In the context of this research environmental factors could include, physical, social and attitudinal factors.

Important differences in breast cancer staging were not detected due to the small sample. Larger population studies including multiple provinces would make it possible to determine whether a significant difference is present in stage at diagnosis between women with and without ID.

Prior and current research have highlighted the need for improved access and utilization of breast screening services in women with ID. It is essential that future research be performed to identify barriers that restrict access to breast screening services in women with ID to improve utilization.

Lastly, we recommend future research on other cancers, specifically those with screening programs in place, to identify any disparities in the incidence of various cancers as well as the stage at diagnosis between people with and without ID.

5.1.4 Conclusion

In conclusion, this thesis found that the incidence of breast cancer was comparable between women with and without ID. This finding demonstrates that women with ID are at no greater or lesser risk of being diagnosed with breast cancer when

compared to women without ID. Although they are being diagnosed at comparable rates, disparities may exist within the stage at diagnosis. Women with ID were significantly more likely to be diagnosed at a later stage in an unadjusted odds ratio, nonetheless when adjusted for covariates the finding was not significant. The findings of this research fill a gap in the literature, as stage at diagnosis had never been studied in women with ID at the population level. This study recommends a larger population study be performed to confirm whether significant differences are observed between women with and without ID in terms of stage at breast cancer diagnosis.

6 THESIS REFERENCES

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APPENDIX A

Table 1: Tumour, lymph node and metastasis (TNM) Classification – Breast Cancer

Stage	Definition
Stage 0	Breast cancer in situ o Tumour confined to original site o Non-invasive
Stage 1	Invasive breast cancer o Small cancer (<2mm) or tumour (< 2cm) o No lymph node involvement or spread to other organs
Stage II	Invasive breast cancer o Cancers (>2mm) with lymph node involvement (1-3 nodes) OR o Tumour (<2cm) with lymph node involvement (1-3 nodes) OR o Tumour (2cm < tumour < 5cm) with lymph node involvement OR o Tumour (>5cm) with no lymph node involvement
Stage III	Invasive breast cancer o Cancer with 4-9 lymph nodes OR o Tumour (>5cm) with lymph node involvement (1-3 nodes) OR with cancer cells found in the lymph nodes (0.2mm< cancer <2mm)
Stage IV	Invasive breast cancer o Spread to distant organs and distant lymph nodes o Metastatic

APPENDIX B

Table 1: Administrative databases housed at the Institute for Clinical Evaluative Sciences

Administrative database	Definition
Ontario Mental Health Reporting System (OMHRS)	Contains data about mental health conditions
Canadian Institute for Health Information-Discharge Abstract Database (CIHI-DAD)	Contains administrative, clinical and demographic data on inpatient hospital discharges
National Ambulatory Care Reporting System (NACRS)	Contains data on emergency room visits
Same Day Surgery (SDS)	Contains data on day surgery visits
The Ontario Health Insurance Plan (OHIP)	Contains data on physician claims for insured services provided to residents of Ontario
Registered Persons Database (RPDB)	Contains demographic information on Ontario residents eligible for health insurance coverage
Ontario Cancer Registry (OCR)	Contains data on cancer diagnoses including data on stage at diagnosis
Canadian Census	Contains demographic data such as postal codes
Ontario Diabetes Database	Contains data on diabetes diagnoses
Ontario Breast Screening Program Database	Contains data on breast screening utilization

Table 2: Administrative health databases and codes used to identify individuals with intellectual disabilities

Administrative data	**Year**	**Codes to identify intellectual disabilities**	**Notes**
Discharge Abstract Database	1988	Discharges with any diagnosis listed in Table 3	• In any diagnostic field • For all facilities submitting to DAD, SDS and NACRS • From inception of database to December 31, 2015
Same Day Surgery Database	1991		
National Ambulatory Care Reporting System	2002		
Ontario Mental Health Reporting System	2005	• Q3 = 1 • Or Q2aa, Q2ab or Q2ac in 299 to 299.80 • Or Q2b in 317 to 319.99 • Or l11a-l11f = any diagnosis of Qxxx as listed in Table 3	• For all facilities submitting to OMHRS • From inception of database to December 31, 2015
Ontario Health Insurance Plan	1991	299, 319	• For all providers submitting to OHIP • From June 1991 – December 31, 2015

Table 3: Codes associated with intellectual disability codes in the International Classification of Diseases, 9th and 10th editions

Code	Label
ICD-9	
299-299.99	Pervasive developmental disorders
317-317.99	Mental Retardation
318-318.99	Mental Retardation
319-319.99	Mental Retardation
758.0-758.39	Chromosomal anomalies for which a developmental disability is typically present
758.8-758.89	Other conditions due to chromosome anomalies (do not include 758.81)
758.9	Conditions due to anomaly of unspecified chromosome
759.5	Tuberous sclerosis
759.81	Other and unspecified congenital anomalies: Prader-Willi syndrome
759.821	Other and unspecified congenital anomalies: de Lange syndrome
759.827	Other and unspecified congenital anomalies: Seckel syndrome
759.828	Other and unspecified congenital anomalies: Smith-Lemli-Opitz syndrome
759.83	Other and unspecified congenital anomalies: Fragile X syndrome
759.874	Other and unspecified congenital anomalies: Beckwith-Wiedemann syndrome
759.875	Other and unspecified congenital anomalies: Zellweger syndrome
759.89	Other and unspecified congenital anomalies: other
760.71	Fetal alcohol syndrome
760.77	Fetal hydantoin syndrome
ICD-10	
F700	Mild mental retardation with the statement of no, or minimal, impairment of behaviour
F701	Mild mental retardation, significant impairment of behaviour requiring attention or treatment
F708	Mild mental retardation, other impairments of behaviour
F709	Mild mental retardation without mention of impairment of behaviour
F710	Moderate mental retardation with the statement of no, or minimal, impairment of behaviour
F711	Moderate mental retardation, significant impairment of behaviour requiring attention or treatment
F718	Moderate mental retardation, other impairments of behaviour
F719	Moderate mental retardation without mention of impairment of behaviour

F720	Severe mental retardation with the statement of no, or minimal, impairment of behaviour
F721	Severe mental retardation, significant impairment of behaviour requiring attention or treatment
F728	Severe mental retardation, other impairments of behaviour
F729	Severe mental retardation without mention of impairment of behaviour
F730	Profound mental retardation with the statement of no, or minimal, impairment of behaviour
F731	Profound mental retardation, significant impairment of behaviour requiring attention or treatment
F738	Profound mental retardation, other impairments of behaviour
F739	Profound mental retardation without mention of impairment of behaviour
F780	Other mental retardation with the statement of no, or minimal, impairment of behaviour
F781	Other mental retardation, significant impairment of behaviour requiring attention or treatment
F788	Other mental retardation, other impairments of behaviour
F789	Other mental retardation without mention of impairment of behaviour
F790	Unspecified mental retardation with the statement of no, or minimal, impairment of behaviour
F791	Unspecified mental retardation, significant impairment of behaviour requiring attention or treatment
F798	Unspecified mental retardation, other impairments of behaviour
F799	Unspecified mental retardation without mention of impairment of behaviour
F840	Childhood autism
F841	Atypical autism
F843	Other childhood disintegrative disorder
F844	Overactive disorder associated with mental retardation and stereotyped movements
F845	Asperger's syndrome
F848	Other pervasive developmental disorders
F849	Pervasive development disorder, unspecified
Q851	Tuberous sclerosis
Q860	Fetal alcohol syndrome
Q861	Fetal hydantoin syndrome
Q871	Aarskog, Prader-Willi, deLange, Seckel, etc.
Q8723	Rubinstein-Taybi syndrome
Q8731	Sotos syndrome
Q878	Other
Q900-Q939	All Down syndrome types
Q971	Female with more than three X chromosomes
Q992	Fragile X syndrome

Q998	Other specified chromosome abnormalities

Figure 3. Developmental disabilities and related codes included in the International Classification of Diseases, 9th and 10th editions. Reprinted from the " Atlas on the primary care of adults with developmental disabilities in Ontario," by Y. Lunsky, J.E. Klein-Geltink and E.A. Yates, 2013, Retrieved from https://www.camh.ca/en/research/news_and_publications/reports_and_books/Documents/HCARDD_Atlas%20-%20Rev_WEB_2014.pdf. Copyright 2013 by the Institute of Clinical Evaluative Sciences.

APPENDIX C

Table 1: Relevance of the studies included in the literature review

Literature Review	
Title	Summary
Incidence of breast cancer in the general population	
Retrospective Cohort Studies	
Canadian Cancer Statistics 2016 Country: Canada	Breast cancer is the most diagnosed cancer in Canadian women. Following fluctuations in breast cancer incidence, since 2004 the incidence of breast cancer has stabilized.
Kachuri, L., De, P., Ellison, L. F., Semenciw, R. (2013) Cancer incidence, mortality and survival trends in Canada, 1970 – 2007 Country: Canada	The study reported cancer incidence in Canada. The incidence of breast cancer in Canada rose between 1970 and 1988 at a rate of 0.9% yearly. After which it began to decline at a rate of 0.7% yearly.
Australian Institute of Health and Welfare. (2013) Cancer in Australia: Actual incidence data from 1991 to 2009 and mortality data from 19991 to 2010 with projections to 2012 Country: Australia	This study used Australian databases to report on cancer incidence between 1991 and 2010. After an increase in breast cancer incidence between 1991 and 1995, incidence rates stabilized.
Molinié, F., Vanier, A., Woronoff, A. S., Guizard, A. V., Delafosse, P., Velten, M., . . . Tretarre, B. (2014) Trends in breast cancer incidence and mortality in France 1990-2008.	Population level French registries were used to report on the incidence of breast cancer between 1990 and 2008. From 1990 – 2003 the incidence of breast cancer increased, but stabilized after 2006.

Country: France	
Kohler, B. A., Sherman, R. L., Howlader, N., Jemal, A., Ryerson, A. B., Henry, K. A., . . . Penberthy, L. (2015) Annual Report to the Nation on the Status of Cancer, 1975-2011, Featuring Incidence of Breast Cancer Subtypes by Race/Ethnicity, Poverty, and State. Country: United States of America	Using population level data acquired from registries, the study reported that the incidence of breast cancer remained stable between 2002 and 2011
Summary of studies on the incidence of breast cancer in the general population	
All of the abovementioned studies employed a retrospective cohort methodology using administrate databases or registries to report on breast cancer trends over time. All the studies demonstrated that the incidence of breast cancer has stabilized. This suggests that in the present study I should see a stable trend of breast cancer incidence in the general population in accordance with the above studies. The studies were useful to inform the methods used in the present study.	
Incidence of breast cancer in subpopulations	
Retrospective Cohort Studies	
Marrett, L. D., & Chaudhry, M. (2003) Cancer incidence and mortality in Ontario First Nations, 1968-1991 Country: Canada	The study reported on cancer incidence and mortality amongst Ontario First Nations (FN) people from 1968 – 1991 in comparison to the Ontario population. Women registered under the Indian act were identified and linked to the Ontario Cancer Registry. The results demonstrated breast cancer incidence in First Nations people was significantly lower when compared with the general population. The reduced rate of breast cancer may be attributed to a combination of both FN women generally having their first child at a

	younger age and having more children than women in the general population.
Ali, R., Barnes, I., Kan, S. W., & Beral, V. (2010) Cancer incidence in British Indians and British whites in Leicester, 2001-2006. Country: England	Both cancer registries and hospital databases were used to identify cases of breast cancer in British Indians and British whites. The incidence of breast cancer was lower in British Indians when compared to British whites.
Boehmer, U., Miao, X., Maxwell, N. I., & Ozonoff, A. (2014) Sexual minority population density and incidence of lung, colorectal and female breast cancer in California. Country: United States of America	Survey data linked with the California Cancer registry identified sexual minorities (gay, lesbian, bisexual) with incident lung, colorectal and breast cancer. The study revealed two associations. Lesbians had a higher incidence of breast cancer, whereas being bisexual was associated with a lower incidence of breast cancer.
Summary of studies on the incidence of breast cancer in subpopulations	
The studies on subpopulations used a consistent methodology. The studies used either registry or survey data to identify the subpopulation. Once identified the subpopulations were linked to cancer registries to identify incident breast cancers. A limitation of reporting on subpopulations is the potential for misclassification error. These studies informed my research as they used consistent methodologies of identifying subpopulations and linking them to cancer registries.	
Incidence of breast cancer in people with intellectual disabilities	
Retrospective Cohort Studies	

Patja, K., Eero, P., & Iivanainen, M. (2001) Cancer incidence among people with intellectual disability Country: Finland	People with ID were identified using a nation-wide survey administered to the Finnish population. Once identified they were linked to the Finish cancer registry to identify incident cancers in the study period. The incidence of breast cancer in people with and without ID was comparable.
Sullivan, S. G., Glasson, E. J., Hussain, R., Petterson, B. A., Slack-Smith, L. M., Montgomery, P. D., & Bittles, A. H. (2003) Breast cancer and the uptake of mammography screening services by women with intellectual disabilities Country: Australia	The Disability Services Commission of Western Australia was used to identify people with ID. Once identified they were linked to the Western Australia Cancer Registry. This study found the incidence of breast cancer to be lower in the ID population.
Janicki, M. P., Dalton, A. J., Henderson, C. M., & Davidson, P. W. (1999) Mortality and morbidity among older adults with intellectual disability: health services considerations Country: United States of America	The study reported on mortality and morbidity in people with ID 40 and older who died between 1984 -1993. The main causes of death in people with ID were cardiovascular, respiratory and neoplastic disease. Although this study does not report on breast cancer incidence it demonstrated the trend that the life expectancy of people with ID is increasing.
Summary of studies on the incidence of breast cancer in people with intellectual disabilities	

As people with intellectual disabilities are living longer into the age group of people being diagnosed with breast cancer, it is important to understand the impact in that population. The above studies used different methods to identify people with intellectual disabilities (e.g. survey, database). Once identified they were linked to cancer registries to determine incident breast cancer. These studies informed my research as they have conflicting results on the incidence of breast cancer in people with ID. The limitations of both the study by Patja and Sullivan are the small sample sizes, which limit the power of the study to make statistically significant observations.	
Breast cancer stage at diagnosis in the general population	
Retrospective Cohort Studies	
Anderson, W. F., Reiner, A. S., Matsuno, R. K., & Pfeiffer, R. M. (2007) Shifting breast cancer trends in the United States Country: United States of America	This study examined five decades of breast cancer incidence, rates and age distributions. A 110% increase was observed in the incidence rates of early stage tumours between 1973 and 2003. A 2.9% decrease was observed in the incidence rates of late stage tumours. The mean age during the entire study period for women diagnosed at an early stage was 44 and for women diagnosed at later stages was 73.
Henley, S. J., King, J. B., German, R. R., Richardson, L. C., & Plescia, M. (2010) Surveillance of screening-detected cancers (colon and rectum, breast, and cervix) - United States, 2004-2006 Country: United States of America	Data acquired from registries and databases were used to determine the incidence rates for late-stage cancers. The study population was restricted to women between the ages of 50 – 74. The incidence of late stage breast cancers was lowest among women 50 – 59 and highest among women 60 – 79 years of age. Between 2004 and 2006 one third of breast cancers were diagnosed at a late stage where treatment is less effective.

McPhail, S., Johnson, S., Greenberg, D., Peake, M., & Rous, B. (2015) Stage at diagnosis and early mortality from cancer in England Country: England	An English study reported stage at diagnosis of breast, colon, lung, prostate and ovarian cancer in 2012 using administrative data. The majority of participants presented at either stage I or II breast cancer.
Summary of studies on breast cancer stage at diagnosis in the general population	
These studies were valuable as they demonstrated that the majority of cancers in the general population are diagnosed at earlier stages. As well the study by Anderson demonstrated an important shift to younger ages at diagnosis. This stresses the importance of including women under the age of 50 in my study.	
Breast cancer stage at diagnosis in subpopulations	
Retrospective Cohort Studies	
Newman, L. A., & Alfonso, A. E. (1997) Age-related differences in breast cancer stage at diagnosis between black and white patients in an urban community hospital Country: United States of America	Retrospective reviews of hospital and physician records paired with cancer registry data were used to determine the age and stage at diagnosis in black and white patients. Black patients were significantly more likely to be diagnosed at a younger age and a more advanced stage. The mean age at diagnosis for black patients was 56, while the mean age for white patients was 63.
Deshpande, A. D., Jeffe, D. B., Gnerlich, J., Iqbal, A. Z., Thummalakunta, A., & Margenthaler, J. A. (2009). Racial disparities in breast cancer survival: an analysis by age and stage Country: United States of America	Administrative data was used to identify the study cohorts of Black and White women diagnosed with breast cancer. During the study period of 1988 – 2003, Black women were more likely to be diagnosed at more advanced stages when compared to White women. They were also more likely to be diagnosed with breast cancer before the age of 50.

Hensley Alford, S., Schwartz, K., Soliman, A., Johnson, C. C., Gruber, S. B., & Merajver, S. D. (2009) Breast cancer characteristics at diagnosis and survival among Arab-American women compared to European- and African-American women Country: United States of America	This study compared breast cancer in Arab, White and Black women. Arab women were identified in a registry using a name algorithm. The overall mean age at diagnosis was 60 and the majority of breast cancer cases were diagnosed at a local stage. Both Black and Arab women were more likely to be diagnosed at a younger age and a more advanced stage of cancer.
Cross Sectional Studies	
Ginsburg, O. M., Fischer, H. D., Shah, B. R., Lipscombe, L., Fu, L., Anderson, G. M., & Rochon, P. A. (2015) A population-based study of ethnicity and breast cancer stage at diagnosis in Ontario Country: Canada	This study examined the association between ethnicity and stage at diagnosis. The ethnicities studied were Chinese and South Asian women compared to the general population. Using Ontario's cancer registry all women diagnosed with breast cancer between 2005 and 2010 were identified. Surname algorithms were used to specifically identify Chinese and South Asian women. South Asian were more likely to be diagnosed at a later stage, while Chinese women were more likely to be diagnosed at an earlier stage.
Lipscombe, L. L., Fischer, H. D., Austin, P. C., Fu, L., Jaakkimainen, R. L., Ginsburg, O., . . . Paszat, L. (2015) The association between diabetes and breast cancer stage at diagnosis: a population-based study Country: Canada	This Ontario study used administrative data to compare women with and without diabetes and their breast cancer stage at diagnosis. The results demonstrated that the majority of women were diagnosed at either stage I or II. Nonetheless women with diabetes were significantly more likely to be diagnosed at a more advanced stage.
Summary of breast cancer stage at diagnosis in subpopulations	

<table>
<tr><td colspan="2">The studies demonstrated that some visible minorities (Black, South Asian, Arab) are more likely to be diagnosed at a later stage when compared to the general population.

Both cross sectional studies performed in Ontario using administrative databases informed the methodology used in manuscript 2. A cross sectional design was implemented to be consistent with prior Ontario research. The studies by Ginsburg and Lipscombe demonstrated how administrative databases could be used to identify subpopulations, which can be further linked to the Ontario Cancer Registry.</td></tr>
<tr><td colspan="2">Cancer stage at diagnosis in people with intellectual disabilities</td></tr>
<tr><td colspan="2">Prospective Qualitative Study</td></tr>
<tr><td>Tuffrey-Wijne, I., Bernal, J., Hubert, J., Butler, G., & Hollins, S. (2009)

People with learning disabilities who have cancer: an ethnographic study

Country: England</td><td>The goal of this study was to provide awareness about the needs and experiences of people with ID that have a cancer diagnosis through participant observation. This study explored the impact of cancer, their experience of care and barriers to healthcare access. The mean age of participants was 53 years. Although in the majority of cases people with ID were diagnosed at late stages, the types of cancer were not included.</td></tr>
<tr><td colspan="2">Case Control</td></tr>
<tr><td>Satgé, D., Sauleau, E. A., Jacot, W., Raffi, F., Azéma, B., Bouyat, J. C., & El Hage Assaf, N. (2014)

Age and stage at diagnosis: a hospital series of 11 women with intellectual disability and breast carcinoma

Country: France</td><td>This study provided detailed information about 11 female patients with ID diagnosed with breast cancer. The study assessed histology, tumour grade, age, tumour size and disease stage at diagnosis. The study found that the mean age of diagnosis within the ID sample was 55.64 whilst in the non-disabled population the mean age at diagnosis was 62.35. In an unadjusted OR women with ID had a 3.2 times higher risk of being diagnosed at stage II</td></tr>
</table>

	and 10.2 times higher risk of being diagnosed with stage III. The study showed that women with ID had larger tumours at diagnosis; lymph node involvement and blood metastases were more frequent.
Summary of cancer stage at diagnosis in people with intellectual disabilities	
The prospective qualitative study informed my research as the results showed the majority of people with ID in their study were diagnosed at late stages. The study by Satgé was the sole study found focused on breast cancer stage at diagnosis in women with intellectual disabilities. The limitation of the studies was that they were not population based and few patients were included. The findings were not representative of the populations of interest.	