Tier 1 Genomic Applications: A Kentucky State Needs Assessment

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ABSTRACT OF DISSERTATION

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The College of Public Health

University of Kentucky

2015
TIER 1 GENOMIC APPLICATIONS: A KENTUCKY STATE NEEDS ASSESSMENT

ABSTRACT OF DISSERTATION

A Dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Public Health in the College of Public Health at the University of Kentucky

By:
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ABSTRACT OF DISSERTATION

TIER 1 GENOMIC APPLICATIONS: A KENTUCKY STATE NEEDS ASSESSMENT

Paper 1: An Assessment of Kentucky Cancer Registry Data for Appropriate Referral to Genetic Services for Hereditary Breast and Ovarian Cancer Syndrome and Lynch Syndrome, 2009-2012

BACKGROUND: It is estimated that over 1 million people in the United States have Hereditary Breast and Ovarian Cancer syndrome (HBOC) or Lynch syndrome (LS). Evidence-based guidelines for identifying individuals with HBOC and LS are available, and the CDC has developed a toolkit to provide guidance for the implementation of programs to increase identification of patients appropriate for cancer genetic services. However, most individuals with HBOC and LS remain undiagnosed. While some state public health departments have pioneered programs in public health genetics, many states, including Kentucky, have conducted little work in this area. This study utilizes Kentucky Cancer Registry data to estimate the number of cases of breast, ovarian, fallopian tube, colorectal and endometrial cancers diagnosed between 2009-2012 that would meet guidelines for referral to genetic services in order to determine the state’s need for public health genetics programs that target hereditary cancer syndromes.

METHODS: Kentucky Cancer Registry data for all diagnoses of breast, ovarian, fallopian tube, colorectal and endometrial cancers between 2009-2012 was obtained. Evidence-based guidelines from NCCN, EGAPP, and ACMG/NSGC
were applied to the data to determine the number of cases that met criteria for referral to genetic services. Descriptive statistics were performed to generate count data and referral groups were compared using chi-square statistics. The most recent year of data (2012) was used to analyze the distribution of cases across Kentucky counties and Area Development Districts (ADDs).

RESULTS: Of the 28,109 cases of breast, ovarian, fallopian tube, colorectal, and endometrial cancer diagnosed in Kentucky between 2009-2012, 15,477 (55.1%) were determined to meet guidelines for referral including 4229 cases of breast cancer, 1057 cases of ovarian and fallopian tube cancers, 9815 colorectal cancers and 376 endometrial cancers. Chi-square analysis indicated that cases in the referral group were more likely to be from individuals identified as black (p=0.0005), individuals with late stage caners (p<0.0001), individuals from Appalachian counties (p=0.0006) and individuals who are deceased (p<0.0001). Analysis of cases by county show that 10% (12/120) Kentucky counties and 60% of ADDs have genetic counseling services.

DISCUSSION: This study represents the first analysis of Kentucky Cancer Registry data to identify cancer cases appropriate for referral to genetic services and has identified that a significant number of cases each year would be appropriate for referral. Identification of patients with HBOC and LS allow for the appropriate planning for cancer prevention, screening, and treatment in both index cases and their relatives. Population-based programs for the identification and referral of patients who would benefit from genetic services should be considered in Kentucky. In order to accommodate additional referrals that would likely result, efforts should be made to expand the genetic counseling workforce in Kentucky.
Paper 2: Utilizing Medicaid Claims Data to Assess the Use of Genetic Testing for Hereditary Breast and Ovarian Cancer Syndrome in Kentucky and Characteristics that Influence Genetic Testing Completion

BACKGROUND: Hereditary Breast and Ovarian Cancer syndrome (HBOC) is a genetic condition that causes a significantly increased risk for breast, ovarian and other cancers. Genetic testing of the BRCA1 and BRCA2 genes has been available commercially for nearly 20 years; however, many individuals with HBOC remain unaware of their increased cancer risks. Factors that affect referral to and uptake of genetic counseling and testing have been previously reported including race, age, physician type, marital status, increased risk for breast cancer, and knowledge of genetics. This study utilizes Kentucky Medicaid Claims data to examine how many individuals diagnosed with breast, ovarian or fallopian tube cancer actually received genetic testing and to determine the specific socio-demographic factors associated with obtaining genetic testing in Kentucky.

METHODS: A cross-section of Kentucky Medicaid Claims data for the years 2009-2012 for individuals diagnosed with breast, ovarian or fallopian tube cancer was utilized in this study to determine how many individuals appropriate for genetic counseling and testing based on select NCCN guidelines actually received this testing. Descriptive statistics were performed to generate count data. T-test and chi-square tests were used to determine difference between individuals who had a claim for genetic testing and individuals who did not. Logistic regression was performed to determine variables that affected whether a person had genetic testing while controlling for possible confounders.

RESULTS: This study found 3144 patients with a Medicaid claim between 2009-2012 who had a diagnosis of breast cancer and were age 50 or younger, male breast cancer, ovarian or fallopian tube cancer. Of these individuals, 241 (7.7%) also had a claim for genetic testing. Of individuals who were appropriate for referral, 43.61% lived within 50 miles of a full-time, on-site genetic counseling clinic, and distance from a genetic counseling clinic was not found to be
significantly associated with genetic testing. Logistic regression results showed that the odds of having genetic testing decreased by 13.2% for every 5 years increase in patient age (OR=0.868, p<0.0001). Being diagnosed with female breast cancer (OR=9.137, p<0.0001), and having an appointment with a gynecologist (OR=1.816, p=0.0083) or oncologist (OR=3.599, p<0.0001) were all statistically significantly associated with an increase in the odds of receiving genetic testing.

DISCUSSION: This study was the first to use Medicaid Claims data in Kentucky to determine the use of genetic testing among individuals who meet evidence-based guidelines for referral to genetic services. This study found a low uptake of genetic testing in this population (7.7%), although this is likely an underestimate of the number of individuals who had genetic testing given that this was a cross-sectional data set where individuals may have had genetic testing outside of the study time frame. Given the results of this study, strategies need to be considered by the public health workforce for increasing the number of individuals at-risk for hereditary cancer syndromes who are referred to and receive cancer genetic services. Continued research of the utilization of genetic testing in Kentucky and barriers to referral and uptake of genetic testing need to be done to further inform program development.
KEYWORDS: Public Health Genomics; Hereditary Breast and Ovarian Cancer Syndrome; Colorectal neoplasms, Hereditary Nonpolyposis; Tier One Genomic Applications; Bidirectional Cancer Registry Reporting, Kentucky

Andrea L. Durst

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TIER 1 GENOMIC APPLICATIONS: A KENTUCKY STATE NEEDS ASSESSMENT

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2015

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TIER 1 GENOMIC APPLICATIONS: A KENTUCKY STATE NEEDS ASSESSMENT

Andrea Lynette Durst, MS, CGC

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CHAPTER 1

INTRODUCTION

A. INTRODUCTION

The Centers for Disease Control and Prevention (CDC) has designated genetic counseling, family health history, and/or genomic testing for a number of genetic diseases as Tier 1 Genomic Applications. These applications are based on analytic validity, clinical validity, clinical utility and existing evidence-based guidelines indicating that the use or test is ready for population-based implementation \(^1,2\). Inherited genetic syndromes with Tier 1 Applications include Hereditary Breast and Ovarian Cancer (HBOC), Lynch syndrome (LS), Familial Hypercholesterolemia (FH), and diseases included on the Newborn Screening (NBS) Recommended Uniform Screening Panel (RUSP), among others \(^2\). The CDC recently published a Genomic Applications Toolkit that contains best
practice examples for addressing the Tier 1 Genomic Applications at the level of local and state health departments. Phase 1 approaches focus on several broad activities including identifying individuals appropriate for testing, informing policy, conducting surveillance, and providing education. These Phase 1 approaches can be used to prepare a state for cascade screening, which is the main Phase 2 approach. Cascade screening is the process of identifying individuals appropriate for genetic counseling and testing by systematically offering services to the relatives of index cases found to have one of the included genetic disorders. To date, few states have started the process of developing programs to address Tier 1 Genomic Applications.

Two of the genetic conditions with tier 1 genomic applications are HBOC and LS, which are the primary focus of this dissertation. It is estimated that 1/500 to 1/300 individuals in the general population have a BRCA1 or BRCA2 mutation, either of which causes HBOC. Approximately 5% of female breast cancer (9.5% of breast cancers diagnosed under age 50), 25% or more of male breast cancers, up to 18% of ovarian cancers, and up to 30% of fallopian tube cancers are due to mutations in BRCA1 and BRCA2.

LS is caused by mutations in one of five known genes: MLH1, MSH2, MSH6, PMS2, and EPCAM. LS has a population prevalence as high as 1 in 440 and is responsible for an estimated 2-4% of colorectal cancer diagnoses. Individuals with LS have an increased risk for colorectal, endometrial, ovarian, stomach, small bowel, hepatobiliary tract, urinary tract, brain and central nervous system, and skin cancers over the person’s lifespan.
Although individuals with HBOC and LS have a significantly increased lifetime risk for certain cancers, there are steps that can be taken to prevent cancer or diagnose it early when people know that they are at increased risk. Individuals with HBOC or LS can undergo preventive surgery, pursue increased screening for certain cancers, and/or take medications to reduce cancer risk\textsuperscript{12–15}. Furthermore, family members of individuals with HBOC or LS may also be at very high risk for cancer and could benefit greatly from knowing this information and pursuing preventive measures. Thus, utilizing the CDC Toolkit to implement genomics programs to increase the use of this primary prevention measure may have a significant impact on reducing cancer incidence and deaths. Currently, genetic risk assessment and testing for HBOC and LS are not offered to all appropriate patients. A recent study found that physicians correctly identified only 41\% of women at high risk for HBOC and referred them for genetic counseling and testing\textsuperscript{16}. In a study conducted in Louisville, Kentucky, clinic appointments were reviewed over a one year period, identifying over 500 women who were appropriate for genetic counseling for HBOC, but had not been previously referred.\textsuperscript{17}

All states in the United States have been involved with the provision of public health genetic services since 1985, when Mississippi became the last state to implement a state newborn screening program\textsuperscript{18}. More recently, some states have been working on state needs assessments, planning, and program implementation to further incorporate genomics into state public health programs\textsuperscript{19}. To date, Kentucky has not implemented any official programs in
local or state health departments to address the CDC Tier 1 Genomic Applications. However, Kentucky does have a number of assets that can be utilized to prepare for and implement Phase 1 programs. One example is the robust Kentucky Cancer Registry that collects data on every case of cancer diagnosed in the state. Guidelines from the National Comprehensive Cancer Network (NCCN), Evaluation of Genomic Applications in Practice and Prevention (EGAPP) workgroup, the American College of Medical Genetics (ACMG), and the National Society of Genetic Counselors (NSGC) for identifying individuals at risk for hereditary cancer syndromes could be used to screen the Kentucky Cancer Registry data already being collected\textsuperscript{12–14,20}. This could lead to bidirectional cancer registry reporting, which involves a two-way exchange of information between the state cancer registry and reporting institutions in the state including hospitals and physician offices, being implemented through the Kentucky Cancer Registry office and the Kentucky Department of Public Health. In a bidirectional cancer registry reporting system, an algorithm developed from national guidelines is applied to data already being collected by the state cancer registry to identify individuals who are potentially at increased risk for HBOC and LS. Information about patients who are potential candidates for genetic counseling and testing, as well as educational information, is reported back to cancer registrars, physicians, hospital administrators, and/or patients to assist providers in referring patients and their relatives to appropriate services for genetic risk assessment and testing\textsuperscript{21}. 

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There are a number of barriers to implementing Phase 1 programs from the CDC Genomics Application Toolkit in Kentucky. First, funding for public health genetics and genomics projects is limited, and implementation would likely require significant staff hours and materials costs. At this time, Kentucky has few individuals in the Kentucky Department of Public Health with experience in genetics, and furthermore, the state does not have an adequate supply of genetics professionals to provide appropriate services to new individuals who are identified for genetic risk assessment. In addition, many public health providers, healthcare providers, and lay people know very little about inherited genetic conditions and the importance of genetic counseling and testing. Educational materials and programs would need to be developed in order to prepare the public health and medical workforce for a public health program that addresses screening for HBOC, LS, or other disorders with tier 1 genomic applications. Finally, there have been few previous studies in Kentucky that have attempted to quantify the number of individuals at risk for HBOC, LS and the other conditions included in the Tier 1 Genomic Applications.

B. PROBLEM STATEMENT

Genetic counseling and/or testing for HBOC and LS has been available for approximately twenty years. The provision of these services has traditionally been based on a medical provider-patient model where patients are referred for counseling and testing by a physician or other health care provider. In order for this to occur, personal and family history should be collected for each patient and
addressed by the health care provider. Individuals referred for services are typically seen on an individual basis by a genetic counselor and/or other provider.

Given the growing body of knowledge regarding HBOC and LS, the type of people who are appropriate for counseling and testing is growing, and the importance of family history in recognizing these syndromes, while still important in many situations, has been shifting to broader population-based models for identification of at-risk individuals \(^7,8,22,23\). This shift in thinking about patient identification for genetic services is likely to assist in the identification of individuals who are appropriate candidates for genetic counseling and testing by increasing provider and public awareness about the disease. However, a shift to a public health model will require a significant amount of preparation and planning as most public health departments and programs have had little experience with genetics and genomics outside of state newborn screening programs.

The recognition that genetics and genomics is becoming an important aspect of public health is reflected in the addition of genomic goals to the Healthy People 2020 goals for first time. Healthy People 2020 goals are evidence-based goals for health improvement in the United States over a ten year period. The Healthy People 2020 goal in genomics is to, “Improve health and prevent harm through valid and useful genomic tools in clinical and public health practices” \(^24\). A specific objective of the goal relating to HBOC is to, “Increase the proportion of women with a family history of breast and/or ovarian cancer who receive genetic counseling,” from 34.6% to 38.1% (10% increase) \(^24\). Select state and national
public health organizations are now taking steps toward implementing programs in an effort to meet these goals.

In order to implement public health genomic programs in the near future, states must assess their current strengths, weaknesses, opportunities and goals regarding public health genetics. Data will be required to identify the needs of the state’s population, disparities in access to genetic services, and the capacity of the state to assure the provision of services to residents. Currently, Kentucky lacks public health genetics capacity outside of the state newborn screening program and has little available data regarding public health genetics activities. Furthermore, the state is currently serviced by only 19 genetic counselors, or 1 genetic counselor per 232,000 individuals. While other states have pursued data collection studies and implemented programs to increase education, surveillance of, and access to genetic counseling and testing among their residents, Kentucky has done little to collect the data needed to assess the needs and capacity of the state to identify individuals appropriate for genetic services encompassed by the CDC Tier 1 Genomic Applications and to assure access to those services.

C. PURPOSE OF DISSERTATION

To date, the presence of genetics and genomics in public health has been exemplified by state newborn screening programs, which screen nearly all infants born in the U.S. for severe inherited diseases including metabolic, endocrine, hemoglobin and other disorders. However, evidence-based guidelines for
identifying and diagnosing other genetic diseases, including HBOC and LS, across the lifespan have recently been developed where public health programs could play an important role in implementation\textsuperscript{12–14}. The CDC has recognized that these genetic diseases have Tier 1 Genomic Applications, and is calling on state and local health departments to take action in the areas of policy, education, surveillance, and clinical intervention as the first steps to developing public health programs regarding these diseases \textsuperscript{1}.

This dissertation will encompass the first steps in a Kentucky state needs assessment for implementing Tier 1 Genomic Applications. The dissertation will provide information on two of the three Public Health Core Functions—assessment and assurance—with a focus on HBOC and LS. The results of the dissertation will provide information on Kentucky’s strengths, opportunities and barriers to implementing public health based programs to promote genetic counseling and testing. This will allow for future informed program planning to address HBOC, LS, and other Tier 1 Genomic Applications to best meet the unique needs of Kentuckians. Specifically, the first study will address public health surveillance by utilizing Kentucky Cancer Registry data to assess individuals diagnosed with breast, ovarian, fallopian tube, colorectal and endometrial cancers in Kentucky to determine how many of these individuals would be appropriate for referral to cancer risk assessment services based on select NCCN, USPSTF (United States Preventive Services Task Force), EGAPP, and ACMG/NSGC guidelines \textsuperscript{12–14}. This analysis will provide the first estimate of how many individuals diagnosed with these cancers in Kentucky may benefit.
from HBOC and LS genetic counseling and testing. It will also examine the potential contribution of HBOC and LS to late stage cancers and the distribution of at-risk individuals across the state. Study two will utilize Medicaid data to determine what characteristics might influence an individual’s access to genetic testing for HBOC. The study will detect potential barriers to and disparities in care that may be encountered as larger public health programs that aim to identify and refer individuals to genetic services are developed.

Aggregated together, the results of the two studies encompassed in this dissertation will provide some of the groundwork needed for Kentucky to begin to address public health genetics and genomics in the state. More work will need to be done, but this dissertation should provide the preliminary information needed to begin to build the funding and infrastructure for further assessment and program implementation. Addressing inherited causes of common diseases in Kentucky could contribute significantly to reducing diagnoses of and/or deaths from these diseases.

D. RESEARCH QUESTIONS

This dissertation focuses on the following research questions as the basis for conducting the first steps of a Kentucky state needs assessment for the implementation of Tier 1 Genomic Applications:

1. How many patients diagnosed with breast, ovarian, fallopian tube, colorectal, and endometrial cancer in Kentucky between January 2009 and December 2012 meet certain NCCN, EGAPP, or ACMG/NSGC guidelines for genetic risk assessment referral? (Assessment)
2. What is the contribution of breast, ovarian, fallopian tube, colorectal and endometrial cancers that are likely due to HBOC or LS to the incidence of late stage cancers and cancer mortality in Kentucky? (Assessment)
3. What is the availability of genetic counseling services to individuals at risk for HBOC and LS? (Assurance)
4. What characteristics influence whether an individual diagnosed with breast, ovarian, or fallopian tube cancer in Kentucky who is eligible for genetic testing receives genetic testing of the \textit{BRCA1} and \textit{BRCA2} genes? (Assessment)

\textbf{E. RESEARCH HYPOTHESES}

\textbf{Study 1: An Assessment of Kentucky Cancer Registry Data for Appropriate Referral to Genetic Services for Hereditary Breast and Ovarian Cancer syndrome and Lynch syndrome, 2009-2012}

Hypothesis: There are not a significant number of individuals diagnosed with breast, ovarian, fallopian tube, colorectal, and endometrial cancers who are appropriate for genetic counseling and testing services in Kentucky, and currently the available genetic services are sufficient to meet this need.

\textbf{Study 2: Utilizing Medicaid Claims Data to Assess the Use of Genetic Testing for Hereditary Breast and Ovarian Cancer Syndrome in Kentucky and Characteristics that Influence Genetic Testing Completion}

Hypothesis: There are no significant differences between individuals who are appropriate for genetic testing for HBOC and receive vs. do not receive testing.
F. SCOPE AND IMPORTANCE

It has been recognized by the CDC that involvement of state and local health departments in public health genomics will be vital for the appropriate identification and care of individuals at risk for genetic diseases over the lifespan. The information generated from this dissertation will yield the first surveillance data in Kentucky regarding the need for public health genomics programs for HBOC and LS. The results of these studies will also contribute to the growing body of state specific literature on public health genomics issues. Although needs assessment for public health genomics has been done in other states, specific information about the population of Kentucky will lay the groundwork for further research and program implementation locally. This is fundamentally important to the health of Kentucky residents, especially given that the state has highest cancer incidence rate among the fifty states and District of Columbia. Furthermore, in March 2014, Kentucky Governor Steve Beshear announced the KY Health Now goals, which include reducing Kentucky cancer deaths by 10% by 2019. A significant proportion of certain cancers are caused by genetic conditions with Tier 1 genomic applications, with HBOC being responsible for approximately 5% of female breast cancer (9.5% of breast cancers diagnosed under age 50) and 18% of ovarian cancers and LS being responsible for 2-4% of colon cancers. Identifying individuals at risk for these diseases can allow for prevention of disease, appropriate treatment, or early diagnosis through increased screening. Focusing on primary prevention in the individuals most at risk for these common diseases would be expected to
significantly contribute towards meeting the KY Health Now goals, especially when combined with other efforts in the state to decrease environmental and lifestyle risks.

G. LIMITATIONS AND DELIMITATIONS

Each of the studies included in this dissertation have unique limitations, which are discussed in subsequent chapters. More broadly, the studies are secondary data analyses, which are associated with specific limitations including not having access to some important data points that could make the study more robust and the researchers not having direct control over data quality. However, the secondary data is being obtained from two high quality data sets—the Kentucky Cancer Registry and Kentucky Medicaid Claims—which help to minimize these concerns.

This dissertation includes two studies that represent the beginning of a needs assessment in Kentucky for public health genomics, but is not comprised of all the necessary components for a complete state needs assessment. Furthermore, the dissertation focuses on HBOC and LS, and additional research will need to be done to address other diseases with Tier 1 Genomic Applications.

An additional delimitation of this dissertation is lack of generalizability. The data involved in each study is specific to the state of Kentucky, so results may not be able to be generalized to needs in other states. This is an appropriate approach to this project as public health genetic and genomic programs have traditionally been developed and implemented on a state-by-state basis, allowing states to tailor programs to coincide with state health initiatives and to reflect the
needs of the state’s population. Although the results of this study cannot be
generalized outside of Kentucky, the methods used in each of the studies can
certainly be applied in other states as part of a needs assessment for public
health genomic programs.

H. ADVANCE ORGANIZER FOR DISSERTATION

The chapters of this dissertation are organized to reflect the two papers
generated by the research project, each of which has a self-contained literature
review, methods, results, and discussion section. The present chapter (Chapter
I) provides an introduction to the body of work encompassed in subsequent
chapters. Chapter II is the paper generated from Study 1, An Assessment of
Kentucky Cancer Diagnoses for Appropriate Referral to Genetic Services for
Hereditary Breast and Ovarian Cancer, 2009-2012. Chapter III contains the
paper from Study 2, Characteristics that Influence Genetic Testing Completion
for Hereditary Breast and Ovarian Cancer in Kentucky. Chapter IV provides a
summary of the conclusions from the body of research as well as
recommendations for future research and public health program implementation.
I. REFERENCES


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CHAPTER 2

PAPER 1: AN ASSESSMENT OF KENTUCKY CANCER REGISTRY DATA FOR APPROPRIATE REFERRAL TO GENETIC SERVICES FOR HEREDITARY BREAST AND OVARIAN CANCER SYNDROME AND LYNCH SYNDROME, 2009-2012

A. INTRODUCTION

Hereditary Breast and Ovarian Cancer syndrome (HBOC) and Lynch syndrome (LS) are two hereditary cancer syndromes that cause an increased lifetime risk for specific cancers in affected individuals. It is estimated that over one million people in the United States have HBOC or LS. HBOC caused by mutations in the BRCA1 and BRCA2 genes is associated with up to a 71% lifetime risk for breast cancer and up to a 46% lifetime risk for ovarian, fallopian tube and primary peritoneal cancer. HBOC is responsible for approximately 5% of female breast cancer (9.5% of breast cancers diagnosed under age 50), 25% or more of male breast cancers, up to 18% of ovarian cancers, and up to 30% of fallopian tube cancers. LS causes a 45% or greater lifetime risk for colorectal cancer as well as increased risks for other cancers including endometrial,
ovarian, stomach, hepatobiliary tract, urinary tract, small bowel, and brain/central nervous system cancers\textsuperscript{7,8}. Approximately 2-4\% of colorectal cancers are due to LS\textsuperscript{7}.

Individuals who have already been diagnosed with cancer that is found to be due to HBOC or LS are at a significantly increased risk for developing a second cancer in the future. Their relatives are at risk for also having the inherited cancer syndrome, with first degree relatives (parents, siblings, children) having a 50\% chance to inherit the disease-causing, germ-line mutation, and second degree relatives (grandparents, aunts, uncles, nieces, nephews, grandchildren, etc.) having a 25\% chance to inherit the mutation. Other, more distant family members are also at risk for carrying the same genetic mutation. Therefore, the identification of index cases in families with HBOC or LS has the potential to not only help the individual best manage his or her cancer risk in the future, but also to help additional family members prevent cancer or take steps to diagnose cancer at the earliest possible stage through increased screening. The process of systematically identifying at-risk relatives of an index case has been termed cascade screening, and is recommended by the CDC as the method for Phase II implementation of the Tier 1 Genomic Applications.\textsuperscript{9}

Identifying individuals and their family members with a significantly increased risk for cancer is a way of utilizing a primary prevention measure to reduce cancer incidence and deaths. While individuals with HBOC and LS have significantly increased lifetime cancer risks compared to the general population, there are preventive measures including surgical interventions, increased
screening, and medications that can be taken to reduce their cancer risks or diagnose a cancer at the earliest possible stage.

Several organizations have published national guidelines for the identification of individuals at risk for HBOC and LS. In 2013 the U.S. Preventive Services Task Force (USPSTF) released guidelines for identifying unaffected women with a family history of breast or ovarian cancer who are appropriate for genetic counseling and testing. In 2009, the Evaluation of Genomic Applications in the Practice and Prevention (EGAPP) workgroup published guidelines on identifying individuals newly diagnosed with colorectal cancer who have Lynch syndrome. The American College of Medical Genetics (ACMG) and the National Society of Genetic Counselors (NSGC) recently published joint guidelines for referral to genetic counseling for multiple hereditary cancer syndromes, including HBOC and LS. The National Comprehensive Cancer Network (NCCN) releases regularly updated guidelines for the identification of individuals with and without cancer who are at risk for HBOC or LS. Despite these available guidelines, most individuals with HBOC and LS remain undiagnosed.

HBOC and LS have been designated by the CDC as conditions with Tier 1 Genomic Applications, which are family history and genetic testing applications with significant evidence, validity and utility to support implementation into public health practice. The CDC has released a toolkit for local and state health departments to help these entities implement programs for the education, identification, and screening of individuals at increased risk for HBOC, LS, and other conditions. The toolkit outlines two phases of implementation, with Phase
I implementation including bi-directional cancer registry reporting, providing guidance for evidence-based policy making, developing data collection tools and tracking data on the implementation of Tier 1 Genomic Applications, and providing education and outreach to providers and the public.\(^9\) Phase II implementation focuses on cascade screening programs\(^9\).

Existing data sources represent an important resource that can be utilized to advance the implementation of Tier 1 Genomic Applications. One existing data source, state cancer registries, contains important information that has the potential to be used to identify individuals who are at risk for HBOC and LS. In the U.S., each state maintains a central cancer registry that collects detailed information on each case of cancer that is diagnosed in the state for public health purposes. Typically, a standard set of information about each diagnosis of cancer is reported from cancer registries at healthcare institutions to the state cancer registry. This results in a comprehensive, population-based dataset that can be used to address state and national surveillance and research questions regarding cancer. Bidirectional cancer registry reporting is a process where an algorithm developed from national guidelines is applied to the data already being collected by the state cancer registry to identify specific sets of individuals who are at increased risk for HBOC and LS\(^{13}\).

Several states have already utilized cancer registry data in implementing Phase I recommendations, specifically in the creation of bidirectional cancer registry programs\(^9,^{14,15}\). Michigan, Connecticut, Colorado, and Oregon have used cancer registry data in the implementation of bidirectional cancer registry
reporting programs to identify individuals diagnosed with cancer who were at risk for having HBOC and/or LS\textsuperscript{13}. This information was then reported back to institutions, physicians and/or patients. Although bidirectional cancer registry reporting programs will vary by state depending on resources, state law, and infrastructure, all programs will begin with an analysis of cancer registry data in order to identify those patients who are potentially at risk for HBOC and/or LS.

There are some states that have pioneered programs for addressing the CDC Tier 1 Genomic Applications, established public health genetics and genomics programs, and secured funding for public health genetics programs\textsuperscript{15}. In contrast, most states, including Kentucky, have conducted little work in this area. A data analysis to determine the impact of a bidirectional cancer registry reporting program has not been conducted in Kentucky. The first step to program implementation is a demonstration of need, and this study aims to estimate the number of cases of newly diagnosed breast, ovarian, fallopian tube, colorectal and endometrial cancers that would meet certain national guidelines for genetic risk assessment referral for HBOC and LS. This study will provide information regarding the current need for genetic counseling and testing for HBOC and LS in Kentucky and provide preliminary information for use in the planning and implementation of public health programs to increase awareness and utilization of cancer genetic services.
B. MATERIALS AND METHODS

Data Source

The data set analyzed for this study was obtained from the Kentucky Cancer Registry located in Lexington, KY. The Kentucky Cancer Registry is the state cancer registry, which collects data on each case of cancer diagnosed in the state of Kentucky. Beginning in 1994, Kentucky state law KRS 214.556 requires all Kentucky hospitals, their associated outpatient facilities, and other health care facilities that diagnose or treat cancer patients to report every case of cancer diagnosed to the registry\textsuperscript{16}. Each year, the registry receives data on the over 28,000 primary cancer cases diagnosed in Kentucky residents\textsuperscript{16}. Quality control is addressed through a number of measures including the re-abstraction of a subset of cases by cancer registrars employed by the registry\textsuperscript{16}. This process increases the validity and reliability of the data to represent an accurate picture of cancer diagnoses in Kentucky. However, threats to validity and reliability may include incomplete or inaccurate information recorded in patient medical records, cases not reported to or identified by the registry, and/or mistakes in abstracting that cannot be detected through the extensive edit checks implemented in software applications used to capture registry data. Complete, population-based data is currently available in the Kentucky Cancer Registry through 2012.

The data subset used in this study was obtained from the Kentucky Cancer Registry after completing the appropriate application for release of data and obtaining IRB approval from the University of Kentucky IRB. Breast, ovarian, and colorectal cancer cases were selected based on cancer site and year of
diagnosis. Fallopian tube and endometrial cancers were selected based on cancer site, histology and year of diagnosis. The final data subset contained case based information. While individual patients may have had multiple cancers diagnosed during the study period, this could not be determined from the data set, and each diagnosis was considered separately. The cross sectional data subset included 28,109 observations, which represent all cases of breast (n=14,812), ovarian (n=1036), fallopian tube (n=121), colorectal (n=9815) and endometrial (n=2325) cancers diagnosed in Kentucky from 2009-2012.

Data Analysis

The data set was reviewed and then loaded into SAS version 9.3 and R version 3.1.3, which were used to conduct the data analysis. The data set contains no missing data values. Descriptive statistics were run to generate count data to measure the number of individuals newly diagnosed with breast, ovarian, fallopian tube, colorectal and endometrial cancer each year who would be appropriate for referral to genetic services. Chi-square analyses were used to determine whether there were statistically significant differences between cases that did and did not meet the referral guidelines examined in this study.

The following national guidelines were used to identify which cases were appropriate for genetic counseling and testing:

_Hereditary Breast and Ovarian Cancer syndrome (NCCN Criteria)¹¹_

- Women diagnosed with breast cancer ≤ 50y
- Women diagnosed with triple negative breast cancer
- Women diagnosed with epithelial ovarian or fallopian tube cancer at any age
- Men diagnosed with breast cancer at any age

*Lynch syndrome*

- Any individual diagnosed with colorectal cancer (EGAPP)\(^7\)
- Endometrial cancer diagnosed at age < 50\(^{10}\)

The data set was then subdivided into four sub-sets based on these criteria:

1) Breast cancer cases that were diagnosed at age 50 or younger, breast cancer cases diagnosed in a male, or breast cancer cases that were triple negative (ER, PR and HER2 negative) at any age, 2) Ovarian cancer cases excluding histologies that are known not to be associated with hereditary breast and ovarian cancer syndrome (mucinous tumors, germ cell tumors, neuroendocrine tumors and benign tumors \(^{6,17}\)) or fallopian tube cancer cases, 3) Colorectal cancer cases, and 4) Endometrial cancer cases under age 50. Additional descriptive statistics were generated for each sub-set of data.

The numbers of cancer diagnoses meeting the above stated criteria for appropriate referral to genetic counseling and/or testing in 2012 were calculated for each county in Kentucky as well as the 15 Kentucky Area Development Districts (ADDs). The locations of cancer genetic counseling clinics and outreach services were obtained through key informant interviews with genetic counselors in the state of Kentucky. This information was used to determine the number of
genetic counselors in the state as well as which counties and ADDs had access to genetic counseling services.

C. RESULTS

A total of 28,109 breast, ovarian, fallopian tube, colorectal and endometrial cancer cases diagnosed between 2009-2012 were included in the original data set. Of these cancers, 4847 (17.2%) were diagnosed at or before age 50. In this data set, 92.7% of cancer cases were diagnosed in individuals whose race was identified as white, 6.8% in individuals identified as black, and 0.53% in individuals of other races. Cancer stage at diagnosis was also evaluated using the variable best stage group, which is derived from the collaborative stage and incorporates both pathological and clinical stages18. While the majority of cancers (70.1%) were diagnosed at an early stage (Stage 0, 1 or 2) as defined by the best stage group (a calculated registry value from the pathological and clinical TNM stage groups), this varied by cancer type with early stage diagnoses occurring more often in breast (83.18% of cancers) and endometrial (75.57%) cancers and less often in colorectal (53.57%) and ovarian/fallopian tube (31.72%) cancers. Cases diagnosed in Appalachian counties comprised 27.98% of all cancer diagnoses in the data set. Descriptive statistics for the full data set are summarized in Table 1.
Table 1: Full sample demographics

<table>
<thead>
<tr>
<th>Age at dx</th>
<th>Breast (n=14,812)</th>
<th>Ovarian/FT (n=1157)</th>
<th>Colorectal (n=9,815)</th>
<th>Endometrial (n=2,325)</th>
<th>Total (n=28,109)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>&lt; 35 years</td>
<td>225</td>
<td>1.52%</td>
<td>34</td>
<td>2.94%</td>
<td>98</td>
</tr>
<tr>
<td>35-50 years</td>
<td>2919</td>
<td>19.71%</td>
<td>180</td>
<td>15.56%</td>
<td>1015</td>
</tr>
<tr>
<td>51-65 years</td>
<td>5806</td>
<td>39.20%</td>
<td>421</td>
<td>36.39%</td>
<td>3269</td>
</tr>
<tr>
<td>&gt; 65 years</td>
<td>5862</td>
<td>39.58%</td>
<td>522</td>
<td>45.12%</td>
<td>5433</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>84</td>
<td>14728</td>
</tr>
<tr>
<td>N</td>
<td>0.57%</td>
<td>99.43%</td>
</tr>
<tr>
<td>%</td>
<td>0.00%</td>
<td>100.00%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Race</th>
<th>White</th>
<th>Black</th>
<th>Other</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>13596</td>
<td>1075</td>
<td>82</td>
<td>59</td>
</tr>
<tr>
<td>N</td>
<td>91.79%</td>
<td>7.26%</td>
<td>0.55%</td>
<td>0.40%</td>
</tr>
<tr>
<td>%</td>
<td>94.90%</td>
<td>4.49%</td>
<td>0.52%</td>
<td>0.09%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year of Diagnosis</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>3637</td>
<td>3631</td>
<td>3698</td>
<td>3846</td>
</tr>
<tr>
<td>%</td>
<td>24.55%</td>
<td>24.51%</td>
<td>24.97%</td>
<td>25.97%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cancer Stage</th>
<th>Stage ≤ 2</th>
<th>Stage 3 or 4</th>
<th>Other/Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>12320</td>
<td>2077</td>
<td>415</td>
</tr>
<tr>
<td>%</td>
<td>83.18%</td>
<td>14.02%</td>
<td>2.80%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Appalachia County</th>
<th>Appalachian</th>
<th>Non-Appalachian</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>3757</td>
<td>11055</td>
</tr>
<tr>
<td>%</td>
<td>25.36%</td>
<td>74.64%</td>
</tr>
</tbody>
</table>

When the previously described evidence-based guidelines for referral to genetic services are applied to this data set, 15,477 (55.1%) of the 28,109 cases were determined to be appropriate for referral. Of the 14,812 cases of breast cancer diagnosed between 2009 and 2012, 4229 (28.55%) were included in the final data set because they were found to be diagnosed at or younger than age
50, to have triple negative breast cancer, or to be male. Of the 1157 women who were diagnosed with ovarian and fallopian tube cancer in 2009-2012, 1057 (91.36%) were included in the data sent, including 936 ovarian cancers with histologies consistent with a possible hereditary ovarian cancer and all fallopian tube cancers (121 cases). In the original data set, 2325 women were diagnosed with endometrial cancer, and 376 (16.17%) were diagnosed at or under age 50, thus meeting criteria for inclusion in the final data set. All cases of colorectal cancer are appropriate for referral based on the EGAPP guidelines and included in the final data set. Cases identified as being appropriate for referral to genetic services are summarized in Table 2.

Table 2: Cancer Cases Appropriate for Referral to Genetic Services

<table>
<thead>
<tr>
<th></th>
<th>Breast</th>
<th>Ovarian/FT</th>
<th>Colorectal</th>
<th>Endometrial</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Cases</td>
<td>3637</td>
<td>292</td>
<td>2515</td>
<td>522</td>
</tr>
<tr>
<td>Appropriate Referrals</td>
<td>1054</td>
<td>256</td>
<td>2515</td>
<td>94</td>
</tr>
<tr>
<td>Percent</td>
<td>28.98%</td>
<td>87.67%</td>
<td>100.00%</td>
<td>18.01%</td>
</tr>
<tr>
<td>2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Cases</td>
<td>3631</td>
<td>282</td>
<td>2416</td>
<td>543</td>
</tr>
<tr>
<td>Appropriate Referrals</td>
<td>1008</td>
<td>259</td>
<td>2416</td>
<td>79</td>
</tr>
<tr>
<td>Percent</td>
<td>27.76%</td>
<td>91.84%</td>
<td>100.00%</td>
<td>14.55%</td>
</tr>
<tr>
<td>2011</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Cases</td>
<td>3698</td>
<td>280</td>
<td>2414</td>
<td>588</td>
</tr>
<tr>
<td>Appropriate Referrals</td>
<td>1065</td>
<td>256</td>
<td>2414</td>
<td>95</td>
</tr>
<tr>
<td>Percent</td>
<td>28.80%</td>
<td>91.43%</td>
<td>100.00%</td>
<td>16.16%</td>
</tr>
<tr>
<td>2012</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Cases</td>
<td>3846</td>
<td>303</td>
<td>2470</td>
<td>672</td>
</tr>
<tr>
<td>Appropriate Referrals</td>
<td>1102</td>
<td>286</td>
<td>2470</td>
<td>108</td>
</tr>
<tr>
<td>Percent</td>
<td>28.65%</td>
<td>94.39%</td>
<td>100.00%</td>
<td>16.07%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Cases</td>
<td>14812</td>
<td>1157</td>
<td>9815</td>
<td>2325</td>
</tr>
<tr>
<td>Appropriate Referrals</td>
<td>4229</td>
<td>1057</td>
<td>9815</td>
<td>376</td>
</tr>
<tr>
<td>Percent</td>
<td>28.55%</td>
<td>91.36%</td>
<td>100.00%</td>
<td>16.17%</td>
</tr>
</tbody>
</table>
Cases that were identified as appropriate for referral to genetic services were further analyzed to determine the race, sex (where applicable), stage (best stage group), year of diagnosis, vital status and Appalachian county designation of identified cases. The demographics of the cases meeting criteria for referral for each cancer type are summarized in Table 3. These demographics represent in part the referral criteria used in this study. For example, 74.34% of breast cancer cases included in the referral data set where diagnosed at or under age 50, which is mainly due to one of the criteria for referral being age of diagnosis with breast cancer at or under age 50. Furthermore, 62.06% of ovarian and fallopian tube cancers were diagnosed at stages 3 or 4, which is likely representative of ovarian and fallopian tube cancers in general being fast-growing, aggressive cancers that are often diagnosed at later stages. Alternately, the cases for the three other cancer types had less than half of the cases diagnosed at stages 3 or 4: breast cancer (16.34% stage 3 or 4), colorectal cancer (38.28%), and endometrial cancer (9.57%).

When compared to the entire study sample, a higher percentage of cases that were identified as appropriate for referral were diagnosed at or under the age of 50 (31.08% vs. 17.24% in the entire study sample) given that young age is a criteria for referral for both breast and endometrial cancers. The majority of the cases included in this analysis were from individuals who identified as being white, both in the entire data set (92.17%) and in those appropriate for referral (91.52%).
Table 3: Characteristics of Cancer Cases Appropriate for Genetic Referral by Cancer Type

<table>
<thead>
<tr>
<th>Age at dx</th>
<th>Breast (n=4229)</th>
<th>Ovarian/FT (n=1057)</th>
<th>Colorectal (n=9815)</th>
<th>Endometrial (n=376)</th>
<th>Total (n=15477)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 35 years</td>
<td>225 (5.32%)</td>
<td>21 (1.99%)</td>
<td>98 (1.00%)</td>
<td>46 (12.23%)</td>
<td>390 (2.52%)</td>
</tr>
<tr>
<td>35-50 years</td>
<td>2919 (69.02%)</td>
<td>156 (14.76%)</td>
<td>1015 (10.34%)</td>
<td>330 (87.77%)</td>
<td>4420 (28.56%)</td>
</tr>
<tr>
<td>51-65 years</td>
<td>619 (14.64%)</td>
<td>385 (36.42%)</td>
<td>3269 (33.31%)</td>
<td>n/a</td>
<td>4273 (27.61%)</td>
</tr>
<tr>
<td>&gt; 65 years</td>
<td>466 (11.02%)</td>
<td>495 (46.83%)</td>
<td>5433 (55.35%)</td>
<td>n/a</td>
<td>6394 (41.31%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>84 (1.99%)</td>
<td>0 (0.00%)</td>
<td>5107 (52.03%)</td>
<td>0 (0.00%)</td>
<td>5191 (33.54%)</td>
</tr>
<tr>
<td>Female</td>
<td>4145 (98.01%)</td>
<td>1057 (100.00%)</td>
<td>4708 (47.97%)</td>
<td>376 (100.00%)</td>
<td>10286 (66.46%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Race</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>3764 (89.00%)</td>
<td>1010 (95.55%)</td>
<td>9033 (92.03%)</td>
<td>358 (95.21%)</td>
<td>14165 (91.52%)</td>
</tr>
<tr>
<td>Black</td>
<td>403 (9.53%)</td>
<td>40 (3.78%)</td>
<td>669 (6.82%)</td>
<td>15 (3.99%)</td>
<td>1127 (7.28%)</td>
</tr>
<tr>
<td>Other</td>
<td>33 (0.78%)</td>
<td>6 (0.57%)</td>
<td>49 (0.50%)</td>
<td>1 (0.27%)</td>
<td>89 (0.58%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>29 (0.69%)</td>
<td>1 (0.09%)</td>
<td>64 (0.65%)</td>
<td>2 (0.53%)</td>
<td>96 (0.62%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cancer Stage</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage ≤ 2</td>
<td>3460 (81.82%)</td>
<td>299 (28.29%)</td>
<td>5272 (53.71%)</td>
<td>306 (81.38%)</td>
<td>9337 (60.33%)</td>
</tr>
<tr>
<td>Stage 3 or 4</td>
<td>691 (16.34%)</td>
<td>656 (62.06%)</td>
<td>3757 (38.28%)</td>
<td>36 (9.57%)</td>
<td>5140 (33.21%)</td>
</tr>
<tr>
<td>Other/Unknown</td>
<td>78 (1.84%)</td>
<td>102 (9.65%)</td>
<td>786 (8.01%)</td>
<td>34 (9.04%)</td>
<td>1000 (6.46%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Appalachia County</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Appalachian</td>
<td>1020 (24.12%)</td>
<td>307 (29.04%)</td>
<td>3011 (30.68%)</td>
<td>121 (32.18%)</td>
<td>4459 (28.81%)</td>
</tr>
<tr>
<td>Non-Appalachian</td>
<td>3209 (75.88%)</td>
<td>750 (70.96%)</td>
<td>6804 (69.32%)</td>
<td>255 (67.82%)</td>
<td>11018 (71.19%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vital Status</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive</td>
<td>3752 (88.72%)</td>
<td>551 (52.13%)</td>
<td>6066 (61.80%)</td>
<td>354 (94.15%)</td>
<td>10723 (69.28%)</td>
</tr>
<tr>
<td>Deceased</td>
<td>477 (11.28%)</td>
<td>506 (47.87%)</td>
<td>3749 (38.20%)</td>
<td>22 (5.85%)</td>
<td>4754 (30.72%)</td>
</tr>
</tbody>
</table>

When comparing the cases that met criteria for referral to those cases that did not meet criteria, cases identified as being appropriate for referral had a higher proportion of individuals who were identified as black than in those cases that did not meet criteria for referral (7.37% in the referred group vs. 6.31% in the non-referred group, $\chi^2=12.025$, $p=0.0005$). Cases that were identified as appropriate for referral were more likely to be stage 3 or 4 cancers (n=5140,
than all cancers analyzed in the study (n=6853, 24.38%). Cases appropriate for referral to genetic services were statistically significantly more likely to be stage 3 or 4 cancers than cases that were determined to not be appropriate for referral (35.50% in the referred group vs. 14.17% in the non-referred group, $\chi^2=1567.35$, $p<0.0001$). Individuals represented by the cases included in the referral data set were slightly more likely to be from Appalachian counties than in the data set as a whole (28.81% of referrals vs. 27.98% of all cases) and were statistically significantly more likely to be from Appalachian counties than those cases not identified as appropriate for referral (28.81% in the referred group vs. 26.96% in the non-referred group, $\chi^2=11.88$, $p=0.0006$). Individuals represented by the cases in the referral data set were less likely to be living (69.28%) than those determined to be not appropriate for referral (84.75%) ($p<0.0001$), which could be in part due to the fact that cases in the referral data set were more likely to be later stage cancers (stage 3 or 4). These results are summarized in Table 4.
Table 4: Comparison of Cases Appropriate for Referral to Cases Not Appropriate for Referral

<table>
<thead>
<tr>
<th></th>
<th>Referral</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>n=28,109</td>
<td>n=12,632</td>
<td>n=15,477</td>
</tr>
<tr>
<td>Age at dx</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 35 years</td>
<td>403 (1.43%)</td>
<td>13 (0.10%)</td>
<td>390 (2.52%)</td>
</tr>
<tr>
<td>35-50 years</td>
<td>4444 (15.81%)</td>
<td>24 (0.19%)</td>
<td>4420 (28.56%)</td>
</tr>
<tr>
<td>51-65 years</td>
<td>10654 (37.90%)</td>
<td>6381 (50.51%)</td>
<td>4273 (27.61%)</td>
</tr>
<tr>
<td>&gt; 65 years</td>
<td>12608 (44.85%)</td>
<td>6214 (49.19%)</td>
<td>6394 (41.31%)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5191 (18.47%)</td>
<td>0 (0.0%)</td>
<td>5191 (33.54%)</td>
</tr>
<tr>
<td>Female</td>
<td>22918 (81.53%)</td>
<td>12632 (100.0%)</td>
<td>10286 (66.46%)</td>
</tr>
<tr>
<td>Race*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>25907 (92.17%)</td>
<td>11742 (92.95%)</td>
<td>14165 (91.52%)</td>
</tr>
<tr>
<td>Black</td>
<td>1918 (6.82%)</td>
<td>791 (6.26%)</td>
<td>1127 (7.28%)</td>
</tr>
<tr>
<td>Other</td>
<td>148 (0.53%)</td>
<td>59 (0.47%)</td>
<td>89 (0.58%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>136 (0.48%)</td>
<td>40 (0.32%)</td>
<td>96 (0.62%)</td>
</tr>
<tr>
<td>Cancer Stage*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage ≤ 2</td>
<td>19716 (70.14%)</td>
<td>10379 (82.16%)</td>
<td>9337 (60.33%)</td>
</tr>
<tr>
<td>Stage 3 or 4</td>
<td>6853 (24.38%)</td>
<td>1713 (13.56%)</td>
<td>5140 (33.21%)</td>
</tr>
<tr>
<td>Other\Unknown</td>
<td>1540 (5.48%)</td>
<td>540 (4.27%)</td>
<td>1000 (6.46%)</td>
</tr>
<tr>
<td>Appalachia County*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appalachian</td>
<td>7864 (27.98%)</td>
<td>3405 (26.96%)</td>
<td>4459 (28.81%)</td>
</tr>
<tr>
<td>Non-Appalachian</td>
<td>20245 (72.02%)</td>
<td>9227 (73.04%)</td>
<td>11018 (71.19%)</td>
</tr>
<tr>
<td>Vital Status*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alive</td>
<td>21429 (76.24%)</td>
<td>10706 (84.75%)</td>
<td>10723 (69.28%)</td>
</tr>
<tr>
<td>Deceased</td>
<td>6680 (23.76%)</td>
<td>1926 (15.25%)</td>
<td>4754 (30.72%)</td>
</tr>
</tbody>
</table>

In order to better characterize the annual need for cancer genetic counseling services for individuals with newly diagnosed cases of breast, ovarian, fallopian tube, colorectal and endometrial cancers across the state of Kentucky, the most recent year of data (2012) was used to look at distribution of cases appropriate for genetic referral among Kentucky counties (n=3966). Of the 120 Kentucky
counties, all counties had at least 1 individual diagnosed with one of the cancers examined in this study who met criteria for referral to genetic counseling. The five counties with the highest number of cases identified as appropriate for referral in 2012 were 1) Jefferson County (n=729, 18.38% of appropriate cases identified in the state), 2) Fayette County (n=255, 6.43%), 3) Kenton County (n=108, 2.72%), 4) Hardin County (n=106, 2.67%) and 5) Boone County (n=100, 2.52%), which is expected as these five counties are included in the six highest populated counties in the state. Of these 5 counties, 3 (Jefferson, Fayette, and Kenton) have full time genetic counseling services available in the county, Boone county has services available in a bordering county, and Hardin County has services available through outreach programs. Overall, residents in 12/120 counties (10%) have access to genetic counseling services in their county. A summary of cases by county is included in Figure 1.

Appropriate cases for referral in 2012 were also examined by area development district (ADD). The state of Kentucky is made up of 15 ADD’s, which are planning and developing districts made up of multiple counties\textsuperscript{19}. The counties in each ADD work together to attain economic growth, improve the quality of life, and provide services to their residents. The Kentuckiana Regional Planning and Development Agency (KIPDA) has the highest number of cancer cases identified as appropriate for referral to genetic counseling services (n=933) and is made up of Jefferson, Bullitt, Oldham, Trimble, Henry, Shelby and Spencer Counties. The Bluegrass ADD contains the second highest number of cases appropriate for referral (n=699) and is made up of Anderson, Franklin,
Woodford, Mercer, Boyle, Lincoln, Garrard, Jessamine, Fayette, Scott, Harrison, Bourbon, Nicholas, Clark, Madison, Powell, and Estill counties. Of the 15 ADD’s in Kentucky, only 3 have full time, on-site genetic counselors providing cancer genetic counseling services (KIPDA, Bluegrass and Northern Kentucky) with an additional 6 ADD’s having cancer genetic counseling services available via outreach clinics or telemedicine (Cumberland Valley, Gateway, Green River, Kentucky River, Lincoln Trail, and Pennyrile). Of individuals identified in this study as being appropriate for referral for cancer genetic counseling services, 75% (2973/3966) can access these services with a genetic counselor in their ADD. However, even in ADD’s with a genetic counselor, some patients may have to drive an hour or more to access services. The number of appropriate cases for referral to genetic services in each ADD are shown in Figure 2.
This study represents the first analysis of Kentucky Cancer Registry data for identifying cases that would be appropriate for referral to genetic services due to being at risk for HBOC or LS. The study shows that over the four year period between 2009-2012, 15,477 (55.06%) of the 28,109 cases of breast, ovarian, fallopian tube, colorectal or endometrial cancer in Kentucky were appropriate for referral to genetic services based on meeting at least one of the NCCN, EGAPP, and ABGC/NSGC criteria examined by this study.

Analysis of the Kentucky Cancer Registry data shows that cancer cases appropriate for referral to genetic services had overrepresentation of late stage
(stage 3 and 4) cancers and cancer deaths when compared to the breast, ovarian, fallopian tube, colorectal and endometrial cancers that were not appropriate for referral during the study time period. In cases appropriate for referral to genetic services, 33.21% were late stage cancers, and 30.72% of cases were from individuals now deceased. Increasing the number of individuals referred for genetic services in the state of Kentucky and then focusing on testing the relatives of patients with positive genetic test results through cascade screening has the potential to result in more individuals being identified as having HBOC and LS before cancer develops. These Individuals can be offered increased screening and preventive services to either prevent a cancer from developing or improve the chances that a cancer is diagnosed at the earliest possible stage if it were to form. Based on the information from this study, this could subsequently contribute to a decrease in late stage cancers and cancer deaths in Kentucky. A public health focus on increasing genetic counseling and testing services for individuals at risk for hereditary cancer syndromes in Kentucky would not only contribute to the achievement of national goals in public health genetics, such as the Healthy People 2020 goals, but also to state health goals. Recently, Kentucky’s Governor released the KY Health Now goals, which call for a reduction in cancer deaths in the state by 10% by 2019\textsuperscript{20}. While individuals with a hereditary cancer syndrome such as HBOC and LS will make up a small percentage of all cancers diagnosed, identifying them offers an opportunity for primary prevention in those at the highest risk to develop cancer.
This study also showed that cancer cases identified as appropriate for referral to genetic services had a higher proportion of individuals identified as black (7.28%) than those cases determined not to be appropriate for referral (6.26%, p=0.0005); however, it is important to note that the vast majority of the cases in both groups were individuals identified as white. This finding is likely influenced by a number of factors including that African American women are more likely to be diagnosed with triple negative breast cancer, which is one of the criteria for a case to be a referral. Furthermore, African American women in Kentucky have a higher incidence of invasive breast cancer diagnosis than white women in Kentucky\textsuperscript{21}. There was also a higher proportion of individuals living in Appalachian-designated counties in the cases appropriate for referral (28.81%) than in those cases determined not to be appropriate for referral (26.69%, p=0.0006). Although these differences between referral and non-referral cases are small, but significant, it is important to consider these differences given that these represent two underserved populations. These results can provide important information to genetics providers and public health departments in the state to further validate the development of programs to increase patient identification and referrals. Previous studies have often shown disparities in the access to and use of genetic services by minority groups, specifically African Americans\textsuperscript{22–24}. Few studies have been done to look at genetic counseling in the Appalachian population, but a 2007 study did find that living in an Appalachian county was not associated with intent to seek cancer genetic services\textsuperscript{25}. However, individuals in Appalachian counties likely face a number of barriers to
accessing healthcare services such as cost, transportation, child care, obtaining time off from work, lower education levels, etc. that could hinder their chances of obtaining genetic services. Furthermore, only 4 of the 54 Kentucky counties designated as Appalachian counties by the Appalachian Regional Commission (Madison, Whitley, Rowan, and Perry counties) have genetic counseling services through outreach or telemedicine. Given that individuals from Appalachian counties were overrepresented in the cases appropriate for referral and currently have limited access to genetic counseling services, public health departments should look to expand access to genetic counseling in these areas of Kentucky.

While the differences between groups may change with the use of additional criteria for case referral that are not included in this study, additional criteria would only increase cases where individuals were African American or living in Appalachian counties. This would further support the need for expanding genetic counseling services to underserved populations.

The identification and referral of patients diagnosed with cancer who are at risk for HBOC and LS is important for determining the best plan for additional cancer screening and preventive measures in the future, and may also have implications for treatment of an individual's current cancer diagnosis. Additionally, relatives of individuals who are identified as having HBOC or LS are also at risk for having the condition and its associated increased risk for cancer. However, many patients and their relatives who are at risk for HBOC and LS remain unaware of their risk and are not appropriately referred to genetic services by their medical providers. One recent study found that physicians
correctly identified only 41% of women at high risk for HBOC and referred them for genetic counseling and testing\textsuperscript{26}. A study conducted in Michigan showed that in 2012 only an estimated 23.4% of women who had a relative diagnosed with breast cancer at or under age 50 had a family member who had undergone genetic counseling, and this number was lower for women with a family history of ovarian cancer, where only 15.9% reported that a family member had had genetic counseling\textsuperscript{27}. Individuals who are not appropriately referred for genetic services represent a missed opportunity to provide preventive services to those who are at the highest risk for a future diagnosis of cancer.

The CDC has proposed methods for state and local health departments to use to increase the identification of individuals at risk for HBOC and LS in their states\textsuperscript{28}. One method of improving identification is through bidirectional cancer registry reporting. The analysis and results of this study will provide helpful information for Kentucky public health departments and genetics providers for taking the first steps towards public health genetics program planning.

One major obstacle to implementing a population based screening program such as bi-directional reporting with the cancer registry is having the genetics professional capacity to handle the resulting case load. Our results indicate that a significant number of individuals per year would be appropriate for genetic services. In 2012, the most recent year in the study, 3966 cases were identified by this analysis as appropriate for referral. If even half of these individuals who were identified as meeting criteria for genetic services would see a genetic counselor, this would be an estimated 1983 patients newly diagnosed with
cancer each year who would utilize genetic counseling based on the 2012 data from this study. Based on the National Society of Genetic Counselors (NSGC) 2012 Professional Status Survey, genetic counselors specializing in cancer see an average of 6 new patients per week\textsuperscript{29}. In order to cover just the patients identified in this study for genetic counseling services, 6.4 full time cancer genetic counselors would need to be employed in the state. If we estimate a 10\% rate for positive genetic test results among these patients, this would result in approximately 198 new patients each year identified with HBOC or LS.

In addition to the index cases identified through bidirectional cancer registry reporting or another population-based program, family members of those index cases who have positive test results will also need access to cancer genetic counseling services. A Kentucky study that looked at automatic referral for certain groups of patients diagnosed with breast and ovarian cancer in one healthcare system found that for each index patient found to have a \textit{BRCA1} or \textit{BRCA2} mutation, there was an average of 5.6 first degree relatives who would have a 50\% risk for also carrying the mutation\textsuperscript{30}. Similarly, a study looking at relatives of index patients who were identified as having LS reported that 249 relatives of 33 index patients identified with LS underwent testing, or over 7 relatives per index patient\textsuperscript{31}. In that study, 109 of these relatives tested positive (greater than 3 relatives per index case), and cascade screening could be used to continue to systematically screen additional relatives. Considering the 198 newly diagnosed cancer patients per year estimated to be found to have HBOC and LS using the criteria examined in this study, 1109 first degree relatives at
50% risk would be identified (estimating 5.6 first degree relatives per index case), many of whom will be unaffected carriers of HBOC or LS and unaware that they may have a significantly increased risk for cancer.

In order to also provide services to these at-risk, first degree family members, 3.6 additional full time genetic counselors would need to be employed, for a total of 10 cancer genetic counselors just to provide services to individuals newly diagnosed with breast, ovarian, fallopian tube, colorectal and endometrial cancers each year and their first degree relatives. This model to estimate the number of genetic counselors needed to provide services as a result of a bidirectional cancer registry reporting program is summarized in Figure 3.

The number of genetic counselors needed to provide cancer genetic counseling in this state will likely far exceed the 10 estimated by this analysis due to the limitations of this data analysis resulting in an underestimate of the individuals in Kentucky appropriate for cancer genetic services each year. In addition to patient care, genetic counselors would likely also need to increase participation in provider and public education in order to prepare for a population screening program. Genetic counselors specializing in cancer also often see patients for other hereditary cancer syndromes as well as patients with concerns other than hereditary cancer. The “Find a Counselor” search function on the NSGC website and personal communications with genetic counselors in Kentucky indicate that there are 10.5 genetic counselors currently providing cancer genetic counseling services in the state. These genetic counselors are located in the three major cities in Kentucky: Louisville, Lexington, and
Covington and provide outreach services to other areas (clinics and outreach summarized in Appendix A). If population based public health genetics programs for the identification of individuals with HBOC and LS are to be successfully implemented in the state of Kentucky, it is imperative to support the growth of cancer genetic counselors and cancer genetic counseling clinics in the state.

Analysis of cases by county and ADD indicate that there is a need for cancer genetic counseling services throughout the state. Currently, only 10% of Kentucky counties have cancer genetic counseling services available within the county. However, when larger ADD’s are considered, residents in 9 of the 15 districts encompassing 75% of cases meeting guidelines for referral, have access to these services. If a population based program were to be implemented, it would be important for the Kentucky Department for Public Health and local health departments in the 6 ADDs without access to cancer genetic counseling services to determine the best way to offer services in these areas. Applying the same model for estimating the number of patients and their first degree relatives (FDRs) who would access genetic counseling services as outlined in Figure 3 for the individual ADDs can help public health leaders identify the best placement of additional genetic counselors.

Figure 3: Model for Estimating Genetic Counseling Workforce Needed in KY to Provide Services to Patients Identified Through Bidirectional Screening Program
<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
</table>
| 1983 | • **3966** cases identified in 2012 appropriate for referral  
  • Estimate half of appropriate patients elect to pursue genetic services |
| 198 | • Estimate a 10% positive rate for HBOC or LS in referred patients |
| 1109 | • Estimate 5.6 1<sup>st</sup> degree relatives per positive patient who will need genetic services |
| 3092 | • Estimated number of patients each year who will need genetic services as a result of a public health program aimed at increasing identification of at-risk individuals (1109 + 1983) |
| 10 | • Cancer genetic counselors see an average of 6 patients per week (312 patients per year)  
  • 10 genetic counselors would be required to see these patients |

The number of estimated patients and FDRs that would present annually in each ADD are summarized in Table 5. Based on this information, an additional 1.17 full time genetic counselors in Barren River and Lake Cumberland ADDs would be able to cover the patients identified through the proposed population based program, which improve overall access to services in Kentucky because these are the ADDs that currently do not have genetic counseling services with the largest number of appropriate cases for genetics referral. Furthermore, they are located in the southern part of the state where services are sparse. Although
there are fewer cases in the ADDs in the eastern part of Kentucky, the ADDs Fivco, Big Sandy, and/or Buffalo Trace would also benefit from the addition of a genetic counselor to expand services to this underserved area. While these genetic counselors would cover the patients identified through a bidirectional cancer registry screening program, additional patients who meet national guidelines not included in this study would also be appropriate for referral, which further increases the need for genetic counseling in these areas. Furthermore, given that over 40% of Kentucky residents live in rural areas, alternative methods of delivery of services, such as telemedicine, should be considered across the state\textsuperscript{33}. Currently, several genetic counseling centers in Kentucky are offering telemedicine services, which could be used as models for setting up additional services in the state.

While bidirectional cancer registry reporting is an important method for identifying index cases who have been diagnosed with cancer in families with HBOC and LS, it will not identify all individuals who meet national guidelines for referral to genetic counseling and/or testing\textsuperscript{1}. The major limitation of this study is that it likely provides a conservative estimate of the number of individuals newly diagnosed with these cancers who would be appropriate for a genetics referral for evaluation of HBOC or LS. This is due to this data not including individuals who would meet other criteria for referral to genetic services, including having a known mutation in the family, being diagnosed with multiple primary cancers, being of Ashkenazi Jewish heritage, or having a significant family history of cancer \textsuperscript{11}. The analysis also did not look at individuals with cancers other than
breast, ovarian, fallopian tube, colorectal, and endometrial cancer that are associated with HBOC and LS. Additional cancers that are associated with these syndromes include pancreatic, prostate, stomach, small bowel, urinary tract, hepatobiliary tract, brain, and other cancers\textsuperscript{4,34}.

Table 5: Annual Estimated Patients & First Degree Relatives (FDR) by ADD

<table>
<thead>
<tr>
<th>ADD</th>
<th>Referral Cases 2012</th>
<th>Estimated Annual Pts &amp; FDR*</th>
<th># GCs Needed**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barren River</td>
<td>243</td>
<td>190</td>
<td>0.61</td>
</tr>
<tr>
<td>Big Sandy</td>
<td>144</td>
<td>112</td>
<td>0.36</td>
</tr>
<tr>
<td>Bluegrass</td>
<td>699</td>
<td>545</td>
<td>1.75</td>
</tr>
<tr>
<td>Buffalo Trace</td>
<td>68</td>
<td>53</td>
<td>0.17</td>
</tr>
<tr>
<td>Cumberland Valley</td>
<td>176</td>
<td>137</td>
<td>0.44</td>
</tr>
<tr>
<td>Fivco</td>
<td>117</td>
<td>91</td>
<td>0.29</td>
</tr>
<tr>
<td>Gateway</td>
<td>83</td>
<td>65</td>
<td>0.21</td>
</tr>
<tr>
<td>Green River</td>
<td>180</td>
<td>140</td>
<td>0.45</td>
</tr>
<tr>
<td>Kentucky River</td>
<td>142</td>
<td>111</td>
<td>0.36</td>
</tr>
<tr>
<td>KIPDA</td>
<td>933</td>
<td>728</td>
<td>2.33</td>
</tr>
<tr>
<td>Lake Cumberland</td>
<td>223</td>
<td>174</td>
<td>0.56</td>
</tr>
<tr>
<td>Lincoln Trail</td>
<td>293</td>
<td>229</td>
<td>0.73</td>
</tr>
<tr>
<td>Northern Kentucky</td>
<td>309</td>
<td>241</td>
<td>0.77</td>
</tr>
<tr>
<td>Pennyrile</td>
<td>158</td>
<td>123</td>
<td>0.39</td>
</tr>
<tr>
<td>Purchase</td>
<td>198</td>
<td>154</td>
<td>0.49</td>
</tr>
</tbody>
</table>

*Using model outlined in this paper

Estimated cases & FDR = \((\# \text{cases})(.5) + (\#\text{cases})(.5)(.1)(5.6))

**Using model outlined in this paper

GCs = (Estimated cases & FDR)/312

Additional groups who were not included in this study are individuals with a significant family history of cancer who have not been diagnosed with cancer themselves, individuals without cancer with a known mutation in the family, and individuals who were diagnosed with breast, ovarian, fallopian tube, colorectal or endometrial cancer prior to 2009 or after 2012 who meet criteria for referral to
genetic services but were never offered these services. The latter of these
groups likely represents a significant number of individuals who are at risk for
HBOC or LS in Kentucky, given that this study shows that an average of 3869
patients each year are appropriate for referral using a subset of national
guidelines. A recent study of one Kentucky hospital’s cancer center screened
patient appointment lists to identify women who had been diagnosed with breast
cancer under age 50 or ovarian cancer at any age who had not previously been
referred for genetic counseling services\(^3\). In one year, 521 patients were
identified for referral, with a mean number of years since diagnosis of 5.3 years
for women with breast cancer and 2.7 years for women with ovarian cancer \(^3\).
This study illustrates that in addition to the women identified in this data analysis
who have new diagnoses of breast or ovarian cancer, a significant number of
individuals with past diagnoses are also appropriate for referral to genetic
services but have not received them. This study was conducted at a cancer
center with an established genetic counseling program, and it is posited that
hospitals and physician offices that do not employ full time genetic counselors
would have a higher percentage of patients appropriate for a genetic risk
assessment who have not been referred.

The EGAPP recommendations for offering testing for LS to every patient
diagnosed with colorectal cancer were released in January 2009\(^7\). Prior to this
recommendation, standard practice for identifying patients for referral to genetic
services for LS involved the use of clinical criteria that relied on family history
information. However, as many as 28% of patients with LS would not meet the
previously established clinical criteria for patient identification\textsuperscript{31}. Even after the publication of the EGAPP guidelines, uptake of universal screening programs of colorectal cancers for LS has been slow. A study surveying a sample of National Cancer Institute-designated Comprehensive Cancer Centers, Community Hospital Cancer Programs, and Community Hospital Comprehensive Cancer Programs found that 15.9\% of responding institutions (11/69) were performing universal IHC screening on colorectal tumors in 2009\textsuperscript{35}. A later study that surveyed genetic counselors working in a cancer setting found that 27.4\% of respondents (29/106) indicated that their institution was universally screening colorectal tumors for LS as of 2011\textsuperscript{36}. Barriers to universal IHC screening implementation were identified and included cost, assembling stakeholders, and obtaining approval from appropriate medical staff\textsuperscript{36}. This delayed implementation of screening programs based on the EGAPP guidelines indicate that all individuals with colorectal cancer are not currently being offered screening and/or testing for LS in Kentucky and that there are likely significant numbers of patients diagnosed before the time period examined in this study who would be still be appropriate for referral for genetic services to discuss options for evaluation. Individuals who are at risk for hereditary cancer syndromes other than HBOC and LS would also benefit from referral to genetic services, thus further increasing the need for genetic services above what is discussed in this study. Finally, while bidirectional cancer registry reporting will identify index cases, cascade screening to identify at-risk family members will need to be conducted
through other methods. Thus, it is important that providers remain vigilant in identifying patients via the ascertainment of a detailed family health history\textsuperscript{1}.

Another limitation of this study is that Kentucky Cancer Registry data can only provide information on who is appropriate for referral to genetic services, but not who has been offered or pursued these services. In fact, there is no state-wide data source to obtain this information. Rather, it would have to be collected from individual institutions.

In conclusion, this study shows that there is a significant, ongoing need for cancer genetic counseling services in the state of Kentucky. At this time, the genetic counselors employed in Kentucky would likely not able to effectively see the volume of patients that would result from such a program. Thus, simultaneous attention needs to be given to growing the genetic counseling workforce and developing public health genetics programs for HBOC and LS. Through these programs, Kentucky and other states can ensure that the residents are obtaining appropriate referrals to cancer genetic counseling that could prove life-saving to themselves and their relatives.
REFERENCES


CHAPTER 3:
PAPER 2: UTILIZING MEDICAID CLAIMS DATA TO ASSESS THE USE OF GENETIC TESTING FOR HEREDITARY BREAST AND OVARIAN CANCER SYNDROME IN KENTUCKY AND CHARACTERISTICS THAT INFLUENCE GENETIC TESTING COMPLETION

A. INTRODUCTION

Breast cancer is the most common cancer diagnosed in women in the U.S. and the second leading cause of cancer death in women\(^1\). Although far less common, ovarian cancer is the fifth leading cause of cancer death in women\(^1\). A small, but significant subset of breast and ovarian cancers are due to Hereditary Breast and Ovarian Cancer (HBOC) syndrome, which is a genetic condition that, most often, is associated with mutations in the \textit{BRCA1} and \textit{BRCA2} genes. HBOC due to \textit{BRCA1} and \textit{BRCA2} mutations causes increased lifetime risks for breast (up to 90%), ovarian (up to 62%), and other cancers\(^2\). It is estimated that approximately 5% of female breast cancer (9.5% of breast cancers diagnosed under age 50), 25% or more of male breast cancers, and up to 18% of ovarian cancers are due to HBOC \(^3\)\(^–\)\(^6\).

Individuals who have been diagnosed with cancer and found to have a \textit{BRCA1} or \textit{BRCA2} mutation are at increased risk for developing a second
cancer. Results of genetic testing can provide important information for the surgical management of high risk women newly diagnosed with breast cancer\textsuperscript{7--11}. Genetic testing also has important implications for the medical treatment of cancer, especially with the recent FDA approval of Lynparza (olaparib) for the treatment of women with a \textit{BRCA1} or \textit{BRCA2} mutation and ovarian cancer\textsuperscript{12}. Furthermore, it is preferable to complete \textit{BRCA1} and \textit{BRCA2} genetic testing in a family first in an individual who has already been diagnosed with cancer\textsuperscript{13}. The American Society of Clinical Oncology recommends that patients diagnosed with cancer who meet specific criteria be offered genetic testing for hereditary cancer syndromes including HBOC, and the Commission on Cancer requires that genetic counseling and testing services be available to patients either on-site or through referral as part of their accreditation program\textsuperscript{14,15}.

After an index case of HBOC is identified in a family, other relatives can typically be identified who are at risk for carrying the same genetic mutation and increased risk for cancer. Testing can then systematically be offered to these relatives to identify high-risk individuals who would benefit from increased screening and prevention for breast and ovarian cancer. Interventions available for individuals found to have a \textit{BRCA1} or \textit{BRCA2} mutation include prophylactic removal of the breasts and/or ovaries, earlier and additional screening for breast cancer, and taking medications that can reduce the risk of cancer\textsuperscript{2,4}. These interventions have been shown to be effective at reducing cancer risk and/or diagnosing a cancer earlier in individuals with \textit{BRCA1} and \textit{BRCA2} associated HBOC.
There is extensive literature on disparities in the referral of patients for genetic counseling and/or testing and the uptake of genetic testing, which has been a concern since testing was first implemented. Many of these studies have focused on racial disparities in genetic testing for HBOC. An early study by Armstrong, et al. found that Caucasian women had 4.1 times the odds of undergoing genetic counseling for \textit{BRCA1} and \textit{BRCA2} than non-Caucasian women\textsuperscript{16}. A case-control study of women with a family history of breast or ovarian cancer undergoing genetic counseling between 1999 and 2003 determined that African American women were significantly less likely to have genetic counseling than Caucasian women even after controlling for other factors that affect uptake (adjusted OR=0.28, 95% CI 0.09-0.89)\textsuperscript{17}. However, a study of women referred for genetic counseling between 2001 and 2008 found no difference in the uptake of genetic testing by race among individuals who received genetic counseling\textsuperscript{18}. Continued documentation of racial disparities in access to genetic counseling for hereditary cancer syndromes led Hall et al. to state that, "Increasing testing access and volume in racial/ethnic minority and underserved populations must be a national priority if mounting disparities in genetic testing utility and utilization are to be eliminated."\textsuperscript{19} Other patient socio-demographic factors found to influence uptake of genetic counseling or testing include age, referral source, marital status, increased breast cancer risk, and knowledge of genetics\textsuperscript{16,20,21}.

Provider barriers can also affect whether a patient appropriate for genetic counseling and/or testing is referred for genetic services. Awareness of genetic
services has been found to be essential to provider referral, and many studies have called for increased education of physicians about genetic counseling and testing for hereditary cancer\textsuperscript{22-24}. One study of a national sample of primary and tertiary care physicians found that referrals were highest for patients who initiated the conversation about genetic risk for breast and ovarian cancer themselves (OR 5.52; 95% CI, 3.97-7.67)\textsuperscript{22}. Concerns about insurance coverage for testing and the fear of genetic discrimination have also traditionally impacted physician referral as illustrated in multiple studies that were conducted before and after the Genetic Information Nondiscrimination Act (GINA) was passed in May 2008\textsuperscript{22-25}.

Early studies of the referral and uptake of $BRCA1$ and $BRCA2$ genetic testing indicated that lack of provider knowledge and lack of clinical guidelines for referring patients were barriers to patients receiving this testing\textsuperscript{23,24,26}. More recently, several organizations have published evidence-based guidelines for identifying individuals appropriate for genetic risk assessment, counseling, and testing. The National Comprehensive Cancer Network (NCCN) has issued guidelines for identifying individuals diagnosed with breast, ovarian, and fallopian tube cancers who are appropriate candidates for genetic testing\textsuperscript{2}. The American College of Medical Genetics (ACMG) and National Society of Genetic Counselors (NSGC) have issued joint guidelines for identifying individuals with a variety of hereditary cancer syndromes, including HBOC, and the U.S. Preventive Services Task Force (USPSTF) published guidelines specifically for identifying unaffected, at-risk women appropriate for genetic counseling\textsuperscript{27}.  

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However, many individuals with HBOC are not appropriately referred and remain undiagnosed despite these national guidelines for patient identification\textsuperscript{25,28,29}.

Genetic testing for HBOC has been identified by the Centers for Disease Control and Prevention (CDC) as a Tier 1 Genomic Application based on analytic validity, clinical validity, clinical utility and existing evidence-based guidelines indicating that the use or test is ready for population-based implementation\textsuperscript{30,31}. Recently, the CDC has released a toolkit for local and state health departments to help these entities implement programs for the education, identification, and screening of individuals at increased risk for HBOC and other Tier 1 Genomic disorders \textsuperscript{32}. As states begin the process of developing and implementing these programs, special attention should be paid to disparities in genetic counseling and testing specific to the state. While previous studies certainly provide a starting point for considering and addressing disparities, the majority of these studies looking at disparities in genetic counseling and testing for HBOC based on patient socio-demographic factors have been institution specific, and studies of provider-perceived barriers have largely been conducted through institutional or national surveys\textsuperscript{22–24,26}.

Utilizing data already being collected by states can be helpful in both assessing need for genetic counseling and testing services and in identifying state-specific disparities. In this study, Kentucky Medicaid Claims data is utilized to identify genetic testing disparities in an already underserved population. The use of this data set allows for assessment of disparities when
insurance coverage is not an issue as Kentucky Medicaid has covered genetic testing in full for patients meeting clinical criteria for HBOC over the time period included in this secondary data analysis. Furthermore, genetic testing of the \textit{BRCA1} and \textit{BRCA2} genes has been available commercially in the U.S. for nearly 20 years. This testing had been performed exclusively by Myriad Genetics, Inc. until June 2013 when the Supreme Court decision of \textit{Association of Molecular Pathology, et al v. Myriad Genetics, Inc., et al.} invalidated some of the patents held by Myriad on the \textit{BRCA1} and \textit{BRCA2} genes, prompting other laboratories to begin offering testing\textsuperscript{33}. A single laboratory offering this testing simplifies the search for individuals who have undergone testing in the Medicaid Claims data set. Utilizing a secondary data source also represents a cost-effective way for an initial analysis to be completed in a state, such as Kentucky, where there is no funding or dedicated staff for public health genetics and genomics outside of newborn screening.

The aims of the current study are to 1) determine how many individuals with Kentucky Medicaid diagnosed with breast, ovarian, and fallopian tube cancer who were appropriate for genetic counseling and testing for HBOC received genetic testing; and 2) determine the socio-demographic and provider factors that predict receipt of genetic testing. Information about the factors that predict whether a particular patient receives genetic testing can then be used by public health and genetics professionals to begin to address the particular disparities in access to genetic counseling and testing services present in Kentucky. To our knowledge, this is the first study utilizing state Medicaid data to conduct a needs
assessment for cancer genetic counseling and testing services and identify state-specific disparities in access to these services.

B. METHODS

This study consists of a secondary data analysis of Kentucky Medicaid data for individuals diagnosed with breast (including male breast), ovarian, or fallopian tube cancer from 2009-2012. Data were obtained from the Kentucky Medicaid Claims Database using ICD-9 codes corresponding to these diagnoses of cancer. ICD-9 codes included 174.* (malignant neoplasm of female breast), 175.* (malignant neoplasm of male breast), 183.0 (malignant neoplasm of ovary), and 183.2 (malignant neoplasm of fallopian tube). The data set was obtained after University of Kentucky and the Kentucky Cabinet for Health and Family Services IRB approval.

The following NCCN criteria for referral to genetic services for HBOC were used to determine which individuals included in the Kentucky Medicaid data set would be appropriate candidates for referral:

- Women diagnosed with breast cancer ≤ 50y
- Women diagnosed with ovarian or fallopian tube cancer
- Men diagnosed with breast cancer at any age

Given that this is a cross-sectional data set, information was not available on the age at diagnosis with cancer. Thus, women diagnosed with breast cancer included in the data set were considered appropriate for genetic testing if their youngest age at the time of a claim in the database was age 50 or younger. All individuals diagnosed with ovarian, fallopian tube, and male breast cancer were
considered appropriate for referral. CPT codes that designate genetic testing were used to determine those individuals in the subset of records identified as being appropriate for genetic counseling and/or testing who actually were tested. These CPT codes included: 83891 (isolation or extraction of highly purified nucleic acid), 83898 (amplification of patient nucleic acid), 83904 (mutation identification by sequencing), 83909 (separation by high resolution technique), and 83912 (interpretation and report). In 2012, additional CPT codes were introduced for genetic testing of the \textit{BRCA1} and \textit{BRCA2} genes, including: 81211 (\textit{BRCA1}, \textit{BRCA2} gene analysis; full sequence analysis and common duplication/deletion variants in \textit{BRCA1}), 81212 (\textit{BRCA1}, \textit{BRCA2} gene analysis; 185delAG, 5385insC, 6174delT variants (the three common mutations found in the Ashkenazi Jewish population)), 81213 (\textit{BRCA1}, \textit{BRCA2} gene analysis; uncommon duplication/deletion variants), 81214 (\textit{BRCA1} gene analysis; full sequence analysis and common duplication/deletion variants), 81215 (\textit{BRCA1} gene analysis; known familial variant), 81216 (\textit{BRCA2} gene analysis; full sequence analysis), and 81217 (\textit{BRCA2} gene analysis; known familial variant). These were also used to determine individuals who had undergone genetic testing in 2012. Although Healthcare Common Procedure Coding System (HCPCS) codes were introduced for genetic testing during the time period included in this secondary data analysis, they did not appear in the data set and as a result were not used to identify individuals undergoing genetic testing.

Variables included in the data set received from the Kentucky Medicaid Claims database and utilized in this study were: Medicaid ID number, age at
claim, gender, ethnicity, patient geographical coordinates (latitude/longitude), billing provider, place of service, category of service, provider specialty, procedure codes, date of claim, ICD-9 Codes, patient survival, and presence of CPT codes for genetic testing (83891, 83898, 83904, 83909, 83912, 81211, 81213). The Medicaid claims data set contained multiple entries per Medicaid recipient, and information was condensed to create one entry per individual meeting the above stated criteria for genetic testing. For individuals who had conflicting information coded into the database for fixed characteristics, such as race, sex, and ethnicity, the description that occurred most commonly in the data set was used and applied to the unique entry for that individual. For demographic information that was claim dependent such as including whether services were received in an Appalachian county, final entries were coded based on where the majority of services were received. Age was determined using the age at claim for the earliest claim in the database for any given individual. Cancer type was determined using ICD-9 codes included with each claim. The database contained the first four ICD-9 codes per claim, and cancer type was determined first by the primary diagnosis code, and then by secondary diagnosis codes if one of the ICD-9 codes examined in this study was not present. Data cleaning identified several individuals with both breast and ovarian (or fallopian tube) cancers, and the unique entry for those Medicaid ID numbers were coded based on the first cancer to appear in the database.

Basic descriptive statistics are reported for the data subset of individuals determined to be appropriate for referral to genetic services. Independent
sample t-test (for continuous variables) and Chi-square tests (for categorical variables) were used to determine differences between individuals who did and did not receive genetic testing. Logistic regression was then performed to evaluate which demographic and provider variables were associated with the outcome variable of whether an individual received genetic testing while controlling for other variables in the model. All independent variables of interest were included in the first model, and the final model was obtained by excluding some variables that were not significant. Breslow-Day tests were used to determine possible variable interactions.

Multiple diagnostics were assessed for the final model including convergence criterion, the likelihood ratio to determine if the overall model was significant, Hosmer and Lemeshow Goodness of fit test to determine if the fitted model was an adequate fit, and the r-square value.

The locations of cancer genetic counseling services were obtained through key informant interviews with genetic counselors in the state of Kentucky. All statistical analyses were completed using SAS v.9.3 and R version 3.1.3.

C. RESULTS

A total of 3144 unique individuals included in the Kentucky Medicaid Claims Database between 2009 and 2012 were identified as meeting criteria for genetic testing for HBOC based on the criteria outlined previously. Of these individuals, 1849 had female breast cancer and a claim in the database at or under age 50. There were 74 individuals diagnosed with male breast cancers included in the
data set and 1221 individuals diagnosed with ovarian or fallopian tube cancers. Of note, 34 individuals in the data set had ICD-9 codes for both female breast and ovarian/fallopian tube cancer. For the purpose of this study, which utilized only one observation per individual included in the database, these individuals had their cancer type classified based on which diagnosis appeared on the earliest claim. Of these 3411 unique individuals, 241 (7.7%) had a claim for genetic testing between 2009 and 2012. These results are summarized in Table 1.

Table 1: Appropriate Referrals and Genetic Testing by Cancer Type

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Appropriate Referral (n=3144)</th>
<th>Genetic Testing (n=241)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast (Female)</td>
<td>1849</td>
<td>226 (12.2%)</td>
</tr>
<tr>
<td>Breast (Male)</td>
<td>74</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Ovarian/FT</td>
<td>1221</td>
<td>15 (1.2%)</td>
</tr>
</tbody>
</table>

Given that genetic testing is often associated with multiple CPT codes for one test, the 241 individuals who had genetic testing claims between 2009 and 2012 had a total of 1402 claims with one of the CPT codes for genetic testing. Of these 77.03% of the claims were paid. Myriad Genetic Laboratories was the provider for the majority of claims (87.23%) with other claims being filed by hospitals and other independent labs.

The average age at the time of claim of individuals who were appropriate for genetic testing is 48.46 years (sd=13.31). Individuals who had a claim for genetic testing were statistically significantly younger than individuals who were appropriate for genetic testing but did not have a claim between 2009 and 2012.
for this testing ($t=13.63$, $p<0.0001$). When looking specifically at average age by cancer type, women diagnosed with breast cancer who had testing were statistically significantly younger than women who did not have testing ($t=4.6$, $p<0.0001$). A significant difference in mean age was not found for women diagnosed with ovarian or fallopian tube cancer ($t=1.61$, $p=0.1087$). These results are summarized in Table 2.

Table 2: Mean Age of Patient by Cancer Type and Genetic Testing

<table>
<thead>
<tr>
<th></th>
<th>No Genetic Testing</th>
<th>Genetic Testing</th>
<th>t-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Cancer Types</td>
<td>49.05 (13.50)</td>
<td>41.37 (7.83)</td>
<td>13.63</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Breast (Female)</td>
<td>43.01 (6.80)</td>
<td>40.79 (6.60)</td>
<td>4.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ovarian/FT</td>
<td>56.72 (15.95)</td>
<td>50.07 (16.28)</td>
<td>1.61</td>
<td>0.1087</td>
</tr>
</tbody>
</table>

Study demographics show that 83.11% of individuals in this data set who were identified as appropriate for referral for genetic testing are white, 9.73% are black and 0.97% are of other race. Of the individuals appropriate for referral to genetic services who identified as white, 7.85% had a claim for genetic testing, and 10.13% of individuals who were appropriate for referral and identified as black had a claim for genetic testing. Of individuals found to be appropriate for referral to genetic testing, 26.40% received the majority of their services between 2009 and 2012 in Appalachian counties, 71.02% received the majority of their services in Non-Appalachian counties, and 2.54% only had claims from out of state. Chi-square testing indicated a statistically significant difference between Appalachian county designation and genetic testing ($\chi^2=86.66$, $p<0.0001$). Of the 830 individuals in this data set who received the majority of services in Appalachian counties, 59 (7.10%) had a claim for genetic testing compared to
6.90% (154 of 2233) of individuals who received the majority of services in non-Appalachian counties. Individuals who had a claim from a gynecologist were more than twice as likely to receive genetic testing (15.2%) as those who did not see a gynecologist (7.4%). Individuals who saw an oncologist during the study period were nearly 3 times more likely to receive genetic testing (16.4%) as those who did not see an oncologist (5.7%). Distance from a genetic counseling clinic was calculated using longitude and latitude data of the patients and the cancer genetic counseling clinics in Kentucky. Distance to the closest clinic was then categorized and reported for just the full-time cancer genetic counseling clinics (Main) and for all cancer genetic counseling clinics (including outreach and telemedicine clinics). These data show that the majority of individuals who had genetic testing lived within 50 miles of a main cancer genetic counseling clinic (41.91%). However, chi-square analysis did not show a statistically significant difference between distance from genetic counseling clinics and genetic testing. All study demographics and descriptive statistics are summarized in Table 3.

Table 3: Patients for Genetic Services Referral Demographics

<table>
<thead>
<tr>
<th></th>
<th>Total (n=3144)</th>
<th>Genetic Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No (n=2903)</td>
</tr>
<tr>
<td>Age* Mean (sd)</td>
<td>48.46 (13.31)</td>
<td>49.05 (13.50)</td>
</tr>
<tr>
<td>Sex* Male</td>
<td>106 (3.37%)</td>
<td>106 (3.65%)</td>
</tr>
<tr>
<td></td>
<td>3038 (96.63%)</td>
<td>2797 (96.35%)</td>
</tr>
<tr>
<td>Race* White</td>
<td>2613 (83.11%)</td>
<td>2408 (82.95%)</td>
</tr>
<tr>
<td>Black</td>
<td>306 (9.73%)</td>
<td>275 (9.47%)</td>
</tr>
<tr>
<td>Other</td>
<td>31 (0.97%)</td>
<td>30 (1.03%)</td>
</tr>
<tr>
<td>Not Reported</td>
<td>194 (6.17%)</td>
<td>190 (6.54%)</td>
</tr>
<tr>
<td>Ethnicity*</td>
<td>Non-Hispanic</td>
<td>Hispanic</td>
</tr>
<tr>
<td>-------------------</td>
<td>--------------</td>
<td>----------</td>
</tr>
<tr>
<td></td>
<td>2933 (93.29%)</td>
<td>17 (0.54%)</td>
</tr>
<tr>
<td></td>
<td>2697 (92.90%)</td>
<td>16 (0.55%)</td>
</tr>
<tr>
<td></td>
<td>236 (97.93%)</td>
<td>1 (0.41%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Appalachian County*</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>830 (26.40%)</td>
<td>771 (26.56%)</td>
<td>59 (24.48%)</td>
</tr>
<tr>
<td>No</td>
<td>2233 (71.02%)</td>
<td>2079 (71.62%)</td>
<td>154 (63.90%)</td>
</tr>
<tr>
<td>Out of state</td>
<td>80 (2.54%)</td>
<td>52 (1.79%)</td>
<td>28 (11.62%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Distance from Genetic Counseling Clinic (Main)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 50 miles</td>
<td>1371 (43.61%)</td>
<td>1270 (43.75%)</td>
<td>101 (41.91%)</td>
</tr>
<tr>
<td>51-100 miles</td>
<td>1042 (33.14%)</td>
<td>962 (33.14%)</td>
<td>80 (33.20%)</td>
</tr>
<tr>
<td>101-150 miles</td>
<td>561 (17.84%)</td>
<td>517 (17.81%)</td>
<td>44 (18.26%)</td>
</tr>
<tr>
<td>&gt;150 miles</td>
<td>170 (5.41%)</td>
<td>154 (5.30%)</td>
<td>16 (6.64%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Distance from Genetic Counseling Clinic (Any)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 50 miles</td>
<td>2806 (89.25%)</td>
<td>2588 (89.15%)</td>
<td>218 (90.46%)</td>
</tr>
<tr>
<td>51-100 miles</td>
<td>331 (10.53%)</td>
<td>309 (10.64%)</td>
<td>22 (9.13%)</td>
</tr>
<tr>
<td>101-150 miles</td>
<td>3 (0.10%)</td>
<td>2 (0.07%)</td>
<td>1 (0.41%)</td>
</tr>
<tr>
<td>&gt;150 miles</td>
<td>4 (0.13%)</td>
<td>4 (0.14%)</td>
<td>0 (0%)</td>
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<table>
<thead>
<tr>
<th>Vital Status*</th>
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<tbody>
<tr>
<td>Alive</td>
<td>2244 (71.37%)</td>
<td>2037 (70.17%)</td>
<td>207 (85.89%)</td>
</tr>
<tr>
<td>Deceased</td>
<td>900 (28.63%)</td>
<td>866 (29.83%)</td>
<td>34 (14.11%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Claim from Gynecologist*</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>105 (3.34%)</td>
<td>89 (3.07%)</td>
<td>16 (6.64%)</td>
</tr>
<tr>
<td>No</td>
<td>3039 (96.66%)</td>
<td>2814 (96.93%)</td>
<td>225 (93.36%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Claim from Oncologist*</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>579 (18.42%)</td>
<td>484 (16.67%)</td>
<td>95 (39.42%)</td>
</tr>
<tr>
<td>No</td>
<td>2565 (81.58%)</td>
<td>2419 (83.33%)</td>
<td>146 (60.58%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year First in Database*</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>1322 (42.05%)</td>
<td>1277 (43.99%)</td>
<td>45 (18.67%)</td>
</tr>
<tr>
<td>2010</td>
<td>646 (20.55%)</td>
<td>598 (20.60%)</td>
<td>48 (19.92%)</td>
</tr>
<tr>
<td>2011</td>
<td>607 (19.31%)</td>
<td>528 (18.19%)</td>
<td>79 (32.78%)</td>
</tr>
<tr>
<td>2012</td>
<td>569 (18.10%)</td>
<td>500 (17.22%)</td>
<td>69 (28.63%)</td>
</tr>
</tbody>
</table>

* Chi-square analysis shows statistically significant association between variable and Genetic Testing (p < 0.05)

Logistic regression was performed to assess which independent variables of interest contributed to whether recipients of Kentucky Medicaid received genetic testing. The results of this analysis showed that a number of variables were
associated with the outcome variable of whether individuals had received genetic testing. Of note, increasing age was associated with a decrease in the odds of an individual having genetic testing with a 13.2% decrease in the odds of having genetic testing for every 5 year increase in age (p<0.0001). Individuals diagnosed with female breast cancer had 9.137 times the odds of having genetic testing when compared to those diagnosed with ovarian or fallopian tube cancers (p<0.0001). Patients who saw a gynecologist during the time span of the study had 1.81 times the odds of having genetic testing than patients who did not see a gynecologist (p=0.0083) after controlling for other variables in the model. Patients who saw an oncologist during the time span of the study had 3.599 times the odds of having genetic testing than those who did not see this type of specialist (p<0.0001). In this sample, we did not find a statistically significant difference in genetic testing by race.

Several potential interaction variables were identified utilizing Breslow-Day tests, and included Appalachian*gynecology, Appalachian*oncology, and vital status*cancer type. When included in the model, these interaction variables caused a quasi-separation of data points, and as a result were ultimately excluded from the final regression model. The odds ratios and confidence intervals for variables included in the final regression model are summarized in Table 4.

Diagnostic tests for the logistic regression were used to determine the fit of the model. The measure of deviance indicated that the model was a good fit (p=1.0) but the Pearson Goodness of Fit indicated that the model may not be a
good fit (p=0.0114). The R-squared value indicates that the model explains 22.06% of the variance in the outcome variable, genetic testing. Convergence criterion were satisfied.

Table 4: Logistic Regression Results for Genetic Testing Outcome

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Odds Ratio</th>
<th>95% Confidence Limits</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.972</td>
<td>0.960-0.985</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Cancer Type</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovarian/FT ref</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female Breast</td>
<td>9.137</td>
<td>6.155-13.562</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male Breast &lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001 to &gt;999.999</td>
<td>0.9765</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White ref</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>0.873</td>
<td>0.633-1.206</td>
<td>0.4102</td>
</tr>
<tr>
<td>Other</td>
<td>0.276</td>
<td>0.065-1.170</td>
<td>0.0807</td>
</tr>
<tr>
<td>Not Reported</td>
<td>0.309</td>
<td>0.148-0.646</td>
<td>0.0018</td>
</tr>
<tr>
<td><strong>Year First in Database</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2009 ref</td>
<td></td>
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</tr>
<tr>
<td>2010</td>
<td>2.611</td>
<td>1.931-3.564</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>2011</td>
<td>5.075</td>
<td>3.811-6.759</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>2012</td>
<td>5.212</td>
<td>5.212-3.871</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Claim from a Gynecologist</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>No ref</td>
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</tr>
<tr>
<td>Yes</td>
<td>1.816</td>
<td>1.166-2.828</td>
<td>0.0083</td>
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<td><strong>Claim from an Oncologist</strong></td>
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<tr>
<td>Yes</td>
<td>3.599</td>
<td>2.886-4.488</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Appalachian County</strong></td>
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<tr>
<td>No ref</td>
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<tr>
<td>Yes</td>
<td>1.24</td>
<td>0.973-1.580</td>
<td>0.082</td>
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<tr>
<td>Out of State</td>
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<td>6.137-14.260</td>
<td>&lt;0.0001</td>
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</tbody>
</table>

D. DISCUSSION

This study was the first to use Medicaid Claims data to determine the use of genetic testing among individuals who have been diagnosed with breast,
ovarian, and fallopian tube cancers in Kentucky. This data set was chosen because there is currently no data set at the state level that includes information on whether individuals who are appropriate for referral to genetic services are actually referred and receive those services. While this data set does not provide complete information on individuals receiving genetic testing, it does provide a limited view into the use of genetic testing in Kentucky. Furthermore, this data represents a sample of individuals in the Commonwealth of Kentucky who would have had full coverage for genetic testing because Kentucky Medicaid provides full coverage for genetic testing given that a patient meets nationally established clinical criteria for testing. This was the case during the entire study period, thus eliminating insurance coverage as a confounding factor that may be important to consider in other data sets.

The study shows that between 2009 and 2012, 3144 Medicaid recipients who had been diagnosed with breast, ovarian or fallopian tube cancer met clinical criteria for referral for genetic counseling and testing. Of these, 214 (7.7%) actually had a claim for genetic testing over the same time period. This study certainly shows room for improvement in patient referral to and uptake of genetic testing services in the state of Kentucky among Medicaid recipients. However, this number is likely an underestimate of the individuals who received genetic testing. Because cross-sectional data was used, it is likely that some individuals included in this data set underwent genetic testing either prior to or after the study period. In addition, a number of individuals may have been referred for genetic services by their healthcare provider, but decided not to
proceed with genetic counseling and/or genetic testing after the referral.

Furthermore, individuals utilizing Medicaid are often not continuously enrolled, and a proportion of those identified in this data set as being appropriate for referral for genetic testing may have had genetic testing while uninsured or on a health insurance plan other than Medicaid.

Despite the likelihood that the number of individuals appropriate for genetic services who received genetic testing shown by the results of this study is an underestimate, the data does show that a significant number of individuals are not undergoing the appropriate genetic testing. Genetic testing for HBOC and other hereditary cancer syndromes not assessed in this study is important for creating a future cancer screening and prevention plan for individuals who have already been diagnosed with cancer. Individuals who are found to have HBOC have a significantly increased risk of developing a second cancer in the future. However, there are surgical, screening, and medication options available for those who are found to have HBOC that can either prevent a second cancer from forming or increase the chances that cancer is found at an early stage if it were to develop. More recently, genetic test results have also become important to treatment planning of individuals with a new diagnosis of cancer, specifically related to surgical interventions for women with breast cancer and treatment with PARP (poly ADP ribose polymerase) inhibitors in women diagnosed with ovarian cancer. In addition, genetic testing is important in cancer prevention in the family members of an index case, and it represents an important method of primary cancer prevention among those most at risk.
The logistic regression analysis completed in this study found that a number of variables were associated with the genetic testing outcome. These variables included patient age (earliest age of patient recorded in the data set) cancer type, year the patient first appears in the database, and having a claim from a gynecologist and/or oncologist. For every 5 years of increased in patient age, there was a 13.2% decrease in the odds that that person had had genetic testing (p<0.0001). One explanation for this may be that providers are more likely to think of genetic counseling services for women who are very young at the time of diagnosis, but may be less likely to refer patients who are diagnosed closer to age 50 even though they still meet criteria and should be referred.

Furthermore, women with breast cancer had greater than 9 times the odds of having had genetic testing than women diagnosed with ovarian or fallopian tube cancer (p<0.0001). This could be due to a number of factors including physicians being more knowledgeable about the benefit of genetic testing for women with breast cancer. Furthermore, women with ovarian cancer are typically diagnosed at later stages of cancer development, and physicians may be less likely to refer and/or patients less likely to follow through with the referral due to other health concerns. Individuals who had seen a gynecologist or oncologist during the 4 year study period had significantly higher odds of having genetic testing than those who did not see these physician specialties. However, only 3.34% (105/3144) of those appropriate for a referral saw a gynecologist, and only 18.42% (379/3411) saw an oncologist. These logistic regression results may indicate that Kentucky providers need to be provided with information
regarding referral to cancer genetic counseling services. Based on the results of this study, future educational efforts in Kentucky may have more of an impact if they were focused on primary care and other specialty providers.

Of note, this study did not find a statistically significant association between patient race and having a claim for genetic testing during the study period. Although a number of studies have found racial disparities in genetic counseling and testing\textsuperscript{16,17}, at least one other more recent study did not find this association\textsuperscript{18}. The current study provides further information regarding race and genetic testing, and indicates that this disparity, though seen early in the availability of genetic testing for hereditary cancer syndromes, may be decreasing over time. However, this finding may also be due in part to race not being reported for 6.17\% of individuals included in this sample and/or that the population of Kentucky is predominantly composed of individuals who identify as white. Additional studies will need to be completed in order to determine if disparities in genetic testing due to race are decreasing.

This study does show that an individual's odds of having genetic testing improve in the later years included in the data set. While this shows that appropriate patients are likely currently being referred more often to genetic services, the percent of individuals receiving genetic testing remains concerning. There are a number of reasons why such a small percentage of appropriate patients for referral to genetic services are actually undergoing genetic testing. For example, patients may not be referred because providers are unaware of availability of cancer genetic counseling services. Previous studies have shown
that lack of provider knowledge about the availability of cancer genetic counseling services is a barrier to care, even when the genetic counseling service is located within a provider’s organization\textsuperscript{22–24}.

Correspondence with cancer genetic counseling clinics in Kentucky indicate that only 12/120 (10%) counties in Kentucky have cancer genetic counseling services being offered in the county either directly or through outreach and/or telemedicine. Currently, Kentucky does not maintain an active list of cancer genetic counseling services in the state, which means that providers must take extra steps to determine where to refer appropriate patients. As information on cancer genetic counseling clinics was collected as part of this study, a list will be submitted to the Kentucky public health genetics coordinator. Additional studies will be needed in order to determine if lack of knowledge about genetic counseling services is a barrier to Medicaid providers in the state. If this is the case, then state-level educational programs for Medicaid providers and development of resources to aid in education and physician referral need to be considered by the Kentucky Department for Public Health and state genetics providers.

Another potential barrier to referral may be lack of knowledge about insurance coverage of testing. Even though Medicaid has covered genetic testing of the \textit{BRCA1} and \textit{BRCA2} genes for a number of years, this fact may not be widely known outside of providers who regularly provide genetic services or refer to genetic services. Given that this dataset is looking at an underserved
population, cost of genetic testing would likely be a concern of both providers and patients when considering referral or following through on a referral.

Focusing on increasing referrals among the Kentucky population receiving Medicaid will only grow in importance in the future given the 2014 Medicaid expansion in Kentucky. As stated previously, additional educational programs should be considered for providers in the state to increase the awareness of genetic counseling services and clinical guidelines for referral. This study also provides evidence to support the implementation of strategies outlined in the CDC’s Tier 1 Genomic Applications Toolkit for increasing the number of patients who are identified as appropriate for genetic counseling. Strategies suggested in the toolkit that could be considered by Kentucky include bidirectional cancer registry reporting, which is a process where the cancer registry uses national guidelines for referral of individuals diagnosed with cancer to genetic counseling services to identify cases that should be referred and then sending this information as well as educational materials on hereditary cancer syndromes back to reporting institutions to help in patient identification. Other strategies could include evaluating the policies of Medicaid insurance providers to determine if clear guidelines for coverage of genetic testing are in place and readily available to healthcare providers and developing methods to assess the awareness and use of genetic testing among the general population in Kentucky, such as developing new questions for the state Behavioral Risk Factor Surveillance System (BRFSS) about genetic testing.
The limitations of this study are due mainly to the data set used for this secondary data analysis. First, the Kentucky Medicaid Claims database is only as complete and as accurate as the information being submitted by providers. It is possible that there are claims for genetic testing for Medicaid members that are not included in the data set requested. During the data cleaning process, a number of entries were found with misinformation (for example, a patient is coded as being female when all other claims for the same individual indicate that the person is a male). Considerable effort to correct these type of entries was made, but misinformation may still exist in the data set. As stated previously, there are a number of factors that make it likely that the estimate of the number of appropriate individuals for genetic referral who received genetic testing (7.7%) is an underestimate. However, the number of individuals appropriate for referral to genetic services for HBOC is also likely an underestimate. The three clinical criteria used in this study to identify appropriate patients (individuals diagnosed with breast cancer under age 50, all individuals diagnosed with male breast cancer, and all individuals diagnosed with ovarian or fallopian tube cancer) will miss a number of members who are appropriate for genetic services including those with a family history of breast, ovarian, or other cancers, those with a known BRCA1 and BRCA2 mutation in the family, those with triple negative breast cancer diagnoses and those diagnosed with multiple cancers. However, there is currently no state-level data that contains the type of information needed to identify some of these individuals who are appropriate for referral, and utilizing this Medicaid data provides a useful first step to assessing the need for
increased education, programs, and genetic services to ensure that at-risk individuals are being referred to cancer genetic services.

While this study provides useful information for a Kentucky state-wide needs assessment regarding cancer genetic counseling and testing, it only addresses the issue in one set of individuals. Additional research will need to be done to ascertain the use of genetic testing by individuals with insurance coverage from other companies. This will provide a more comprehensive picture of genetic testing in Kentucky and would be useful for future program development by the Kentucky Department of Public Health and genetics providers. The results of this study will not be generalizable to all other states given the specific and limited nature of the data used for this secondary data analysis, but may be generalizable to states with similar population demographics and availability of genetic counseling services. Other researchers can use this study as an example to begin examining the use of cancer genetic counseling services in their own states. It is only through the generation of evidence that the need for increased education and programming for public health genetic issues will make its way to the agenda of healthcare facilities, policy makers, and public health departments.

In conclusion, this study shows that there is a significant difference between the number of individuals who are appropriate for referral to cancer genetic services and those who actually receive services. This study has identified potential variables that are associated with increased odds of a patient receiving genetic testing. This information can be used to begin developing a
plan for programming addressing public health genetics issues in the state of
Kentucky in the future. The CDC has released information and resources for
states on program implementation that can help improve the health of state
citizens by disease prevention and early detection. This study demonstrates the
impact that implementing programs to increase referrals of appropriate
individuals for cancer genetic services can have on cancer prevention and early
detection in Kentucky.
REFERENCES


CHAPTER 4

IMPLICATIONS FOR PUBLIC HEALTH

A. INTRODUCTION

The need for state policies and programs in public health genetics and genomics is expanding beyond the traditional role of providing newborn screening and the associated follow-up of abnormal screen results. There is significant evidence that genetic testing for predisposition diseases across the lifespan can prevent serious illness and even premature death in individuals who are found to have a genetic mutation that puts them at high risk for disease. In the field of cancer genetics, genetic testing for Hereditary Breast and Ovarian Cancer syndrome (HBOC) and Lynch syndrome (LS) has been shown to provide beneficial information for affected individuals who can then take steps to reduce the risk for cancer associated with one of these syndromes. Despite this evidence, the majority of individuals with these two conditions remain unaware of their risk because they have not been referred for genetic counseling and/or testing.
In order to bring attention to the importance of utilizing evidence-based testing for hereditary cancer syndromes and other inherited conditions, the CDC has released information ranking genetic tests and family history applications for genetic diseases based on the level of available evidence. The CDC has also developed resources to help state and local health departments implement policy and programs for addressing those diseases with the highest ranking, or Tier 1 Genomic Applications. Several pioneer states have been working for over a decade to improve awareness of and access to services for inherited cancer, cardiac, and other syndromes. These states, however, have been the exception, and the majority of states have not taken steps to address this expanded focus of public health genetics.

The aim of this dissertation was to conduct the first studies in Kentucky to determine the need for public health genetics programs for hereditary cancer syndromes. In order to conduct these assessments, data sources first needed to be identified. At this time, there is no state or national database that provides the information needed to identify all individuals who might be appropriate for referral for cancer genetic services or to determine who has received genetic testing and what the outcome of that testing was. It is also likely that few data sources exist in local environments, but these may be increasing due to the use of electronic medical records. As a result, this needs assessment was conducted using two pre-existing data sources: Kentucky Cancer Registry
data and Kentucky Medicaid Claims data. The studies in this dissertation were planned and completed in a manner that the data could be readily used to show the need for public health genomics programs and could be easily reproduced in other states that are also embarking on a needs assessment in this emerging specialty area of public health. The concluding chapter of this dissertation will briefly summarize the results of the two studies presented in Chapters 2 and 3. Based on those results, conclusions are drawn, and the implications of these studies both in Kentucky and in other states are discussed. Finally, recommendations for future action and research are outlined. The two studies contained in this dissertation represent the first effort to assess the need for public health action in Kentucky to address HBOC and LS.

B. SUMMARY OF RESULTS

Paper 1, “An Assessment of Kentucky Cancer Registry Data for Appropriate Referral to Genetic Services for Hereditary Breast and Ovarian Cancer syndrome and Lynch syndrome, 2009-2012,” utilized Kentucky Cancer Registry data to determine the number of individuals diagnosed with cancer between 2009 and 2012 who would meet select nationally established clinical criteria for referral to genetic counseling services. The study also assessed whether the current genetic counselors employed in Kentucky would be able to manage the increase in referrals that would likely result from the implementation of programs to increase patient identification. The results of Paper 1 show that there are
a significant number of individuals diagnosed with breast, ovarian, fallopian tube, endometrial and colorectal cancers each year in Kentucky who are appropriate for referral for genetic services for HBOC or LS. Between 2009 and 2012, 15,477 breast, ovarian, fallopian tube, endometrial and colorectal cancers (55.1% of all diagnosed cases of these cancers during the same time period) were determined to be appropriate for referral to genetic services. The cases that were identified as appropriate for referral had an overrepresentation of diagnoses at more advanced stages (Stage 3 or 4 33.21%) and of diagnoses under the age of 50 (31.08%), largely due to young age at diagnosis being an indicator for referral.

An analysis of appropriate cases for referral by county in 2012 showed that every county had residents who were diagnosed with one of the cancers included in this study and were appropriate for referral. The highest number of cases occurred in Jefferson County (n=729, 18.38% of cases identified in Kentucky), Fayette County (n=255, 6.43% of cases identified in Kentucky) and Kenton County (n=108, 2.72% of cases identified in Kentucky). These three counties also house all of the full-time on-site genetic counseling services in Kentucky. Genetic counselors at these institutions provide outreach and/or telemedicine services in 9 additional counties; however, 90% of Kentucky counties do not have genetic counseling services available in the county. Area development districts (ADDs) were also assessed for appropriate cases and genetic
counseling services. The study found that 75% of individuals who were identified as appropriate for referral to genetic services in 2012 would have been able to access these services in their ADD. Six of the 15 ADDs lack locally available genetic counseling services. This data was presented as count data in order to illustrate the need for genetic counseling services across the state and to provide local leaders with a tangible number of people who would utilize these services.

An assessment of genetic counselors in Kentucky shows that there are currently 10.5 genetic counselors providing cancer genetic counseling services in the state. This study estimates that at minimum 10 genetic counselors will be needed just to provide services to individuals newly diagnosed with cancer in Kentucky each year and their relatives. Additional genetic counselors will be needed to provide services to those individuals previously diagnosed with cancer who did not receive genetic counseling, individuals who have not been diagnosed with cancer but are appropriate for referral, individuals at risk for hereditary cancer syndromes other than HBOC and LS, and individuals diagnosed with cancer who have a family history of cancer suggestive of HBOC or LS. Should a state-wide program be implemented to improve identification of patients appropriate for referral to genetic services, Kentucky does not have the genetic professional workforce to manage the increase in referrals.

Paper 2, "Utilizing Medicaid Claims Data to Assess the Use of Genetic Testing for Hereditary Breast and Ovarian Cancer Syndrome in
Kentucky and Characteristics that Influence Genetic Testing Completion,” is a secondary data analysis of Kentucky Medicaid Claims data between 2009 and 2012 for individuals who had a claim with an associated diagnosis code for breast cancer (174.*), male breast cancer (175.*), ovarian cancer (183.0) or fallopian tube cancer (183.2). This data analysis determined that during the time span of this study, 3144 individuals had a claim associated with one of the cancers of interest in this study and met the outlined criteria for referral to genetic services. This included 1849 women diagnosed with breast cancer under age 50, 74 males diagnosed with breast cancer, and 1221 women diagnosed with ovarian or fallopian tube cancer. Of these individuals, 241 (7.7%) had a claim for genetic testing.

Several variables were found to be associated with the outcome variable genetic testing (yes/no). Logistic regression showed that for every 5 year increase in patient age (earliest age at the time of claim included in the data set), the odds of an individual having genetic testing decreased by 13.2% (p<0.0001). Cancer type also significantly affected whether an individual had a claim for genetic testing with women diagnosed with breast cancer having 9.137 times the odds of having testing than women diagnosed with ovarian or fallopian tube cancer (p<0.0001). No males diagnosed with breast cancer identified in this data set had a claim for genetic testing, despite 25% or more of male breast cancers being due to HBOC. Having one or more claims from a
gyneecologist (p=0.0083) or oncologist (p<0.0001) during the study period also increased a person’s odds of having a genetic testing claim.

This study found that several variables previously discussed in the literature as having an effect on referral to and/or uptake of genetic testing were not statistically significantly associated with having a genetic testing claim. These included race, distance from a genetic counseling clinic, and living in an Appalachian designated county.

C. CONCLUSIONS

When considered together, the two studies included in this dissertation provide preliminary information regarding the need for and use of genetic testing for hereditary cancer syndromes in Kentucky. Paper 1 shows that there are a significant number of individuals diagnosed with cancer each year who should be referred for genetic counseling and testing services in Kentucky, and Paper 2 provides evidence that the utilization of genetic testing services is low. This information should be used to begin discussions with state and local public health leaders about the importance of further investigating the role of public health genetics in Kentucky. Genetics providers should also be engaged and encouraged to share best practices among clinics and with public health leaders. Genetic providers can also likely provide valuable information about the barriers in Kentucky to obtaining patient referrals and providing services that can then be taken into account during future public health genetics program development. Given the results of this
dissertation, developing policies and programs to increase awareness and knowledge of genetic counseling for hereditary cancer syndromes should also be strongly considered. Programs designed to more uniformly provide referrals to at-risk individuals should also be considered. It would also be important to involve the genetic counseling community in helping to develop strategies for expanding the genetic counseling workforce, as these studies suggest that if programs were implemented to increase referral to and use of genetic counseling services, it is likely that the genetic counseling workforce in Kentucky would need to increase.

The results of these studies also begin to show the type of impact that an increase in referral to genetic counseling services can have on cancer prevention in Kentucky. Two of the cancers for which individuals with HBOC are at increased risk, breast and ovarian cancers, are the second and fifth causes of cancer deaths in women. It is estimated that HBOC is responsible for approximately 5% of female breast cancer (9.5% of breast cancers diagnosed under age 50) and up to 18% of ovarian cancers\textsuperscript{5,6,8}. It is estimated that LS causes 2-4% of colon cancers\textsuperscript{12}. If individuals with these hereditary cancer syndromes were routinely identified before cancer developed, there are screening and prevention methods that can significantly reduce the risks for these cancers. Based on the data obtained from the Kentucky Cancer Registry, 192 cases of breast cancer (5% of 3846 diagnoses), 54 ovarian and fallopian tube cancers (18% of 303) and 50 colon cancers (2% of 2470) could have been
prevented in 2012 alone had individuals with HBOC and LS been uniformly identified on a consistent basis prior to cancer development or diagnosed at earlier stages through increased screening. Of course, not all patients identified through these programs would choose to pursue genetic testing, but all individuals should be informed about the availability of testing.

D. IMPLICATIONS

The results of this dissertation have implications for public health practice in Kentucky and other states. Although the information contained in this dissertation is specific to Kentucky, it is likely that similar situations exist in other states that have not previously done significant work with genetic conditions that have tier 1 genomic applications. Each state will have unique circumstances and will need to conduct an independent needs assessment, but it is likely that the methods used in this dissertation can be replicated in other states with similar sources of data.

In Kentucky, these results have a number of implications for the public health, healthcare, and genetic services workforces. Currently, public health genetics in Kentucky focuses solely on newborn screening and short term follow-up of infants with positive screening results. The results of this dissertation have revealed a significant gap in public health services in Kentucky that would have a significant impact on cancer prevention efforts. When considering public health genetics and cancer, the state of Kentucky currently fulfills none of the 10 Essential Public
Health Services, but this research provides preliminary information to monitor health status, investigate health problems, and inform, educate and empower people about the health issue of hereditary cancer. Unlike other screening and prevention programs for cancer, identifying individuals at risk for hereditary cancer syndromes allows for targeted interventions in individuals with the highest risks of developing cancers. While traditional cancer prevention programs remain important, we cannot continue to ignore the unique needs of individuals with hereditary cancer.

While resources would certainly need to be allocated to growing public health genetics in Kentucky and educating the existing public health workforce about the importance of genetics in the care of patients with common disease such as cancer, these efforts have the potential for significant benefits.

Although cancer genetic services have been offered in Kentucky since the introduction of BRCA1 and BRCA2 testing, these services have often been fragmented. Kentucky currently does not have a state genetics professional organization, regular meetings for genetics professionals, or a consistent method for genetic professionals to share ideas and best practices. If we are to move genetic counseling for hereditary cancer syndromes from a one provider, one patient model to a public health based model, the genetic counseling community in Kentucky will need to address these issues. An expansion of public health genetics in Kentucky
will be most successful if a unified effort is made by the genetic counseling community to promote the importance of such programs.

E. RECOMMENDATIONS

The results from this dissertation provide a significant contribution to the literature regarding genetic counseling and testing in Kentucky, specifically for the Tier 1 Genomic Applications for HBOC and LS. Based on these results, it is recommended that the state health departments, local health departments, genetic providers and healthcare institutions in Kentucky begin to consider the growing impact of genetics on cancer screening, prevention and treatment. The first step in this process is education. Public health workers, healthcare providers and the public need to be educated about genetics and the importance of genetic risk assessment and testing in cancer prevention. Furthermore, a focus on increasing awareness of genetic services in Kentucky is imperative. Although genetic counseling services are only provided full-time on site in three cities (Louisville, Lexington, and Covington) there are a number of outreach clinics and telemedicine clinics available to residents who live outside these cities. However, it would be difficult for providers to refer to these services if they are unaware of their availability. Currently, Kentucky does not have a listing of genetic counselors providing services in the state or any other state-wide resources regarding genetic testing and hereditary cancer syndromes.
In order to assure services to those who are at risk for hereditary cancer syndromes, new and innovative programs will need to be considered as the model for genetic services transitions from a one provider, one patient model to population based methods. One type of program that has been implemented in other states and is included in the CDC’s Tier 1 Genomic Applications Toolkit is bidirectional cancer registry reporting. Bidirectional cancer registry reporting involves applying evidence-based guidelines for the identification of individuals at-risk for hereditary cancer syndromes to the submitted case data to identify those individuals diagnosed with cancer in the state who should have a referral to genetic counseling services. This information is then reported back to the healthcare institutions, physicians, and/or patients directly along with information about hereditary cancer and accessing genetic counseling services. Given that state cancer registries receive information on all cases of cancer diagnosed in a state, this type of program helps to promote uniform referral of appropriate patients. This would help to overcome some of the disparities associated with genetic counseling identified in this dissertation. Specifically, this type of program would help to reach individuals who live in Appalachian counties, see physicians who are not aware of genetic counseling services or referral criteria, or are not diagnosed at a very young age with cancer. Recently, the CDC and the Genetic Alliance have worked to create additional resources for states interested in implementing bidirectional cancer registry reporting.
programs, including an educational video about bidirectional cancer registry reporting for providers, written materials that can be used to report back cancer registry data to institutions, and educational information for providers and patients including a full length slide set on HBOC and LS$^{34}$.

Although this dissertation is the first to assess the need in Kentucky for cancer genetic counseling services, additional research needs to be done in order to further determine the specific needs of Kentucky residents that should be considered as public health genetics and genomics programs are planned and implemented. Additional studies should focus on:

1. Determining provider identified barriers to referring patients for genetic counseling for hereditary cancer syndromes.

2. Exploring methods to document cancer family history and barriers to the accurate documentation of this information. A future study on this topic could look at the family history question currently included in data reported to the Kentucky Cancer Registry. Key informant interviews could then be carried out with cancer registrars and/or providers at healthcare organizations to determine barriers to accurately documenting this information. The development and inclusion of additional family history questions on the Kentucky Cancer Registry abstracting forms to more accurately document family history for identification of appropriate patients for genetic services should also be explored.
3. Assessment of current programs in Kentucky being conducted by genetics professionals, healthcare systems, state public health departments, and local public health departments that include information on genetics and genomics related to Tier 1 Genomic Applications or could have this information easily assimilated into the existing program. By understanding what is currently being done in Kentucky, gaps can be identified and addressed in the development and implementation of future programs. Having documentation of current efforts in public health genomics will also help to prevent duplication of efforts and resources.

4. Review health insurance plans in Kentucky to determine whether these plans have guidelines that follow the national, evidence-based guidelines for referral to cancer genetic services.

5. Implementation of a pilot project of bidirectional cancer registry reporting. The Kentucky Cancer Registry is a valuable resource to the state of Kentucky and has the potential to play an important role in the advancement of public health genetics and genomics in the state.

These studies and others will be needed in order to more fully understand how to implement programs that will best address the needs of Kentucky residents. However, conducting these studies and pilot projects will require funding and time, both of which are in short supply. Currently, there is sparse funding for public health genetics and genomics
outside of newborn screening, although some resources do exist. Funding sources include the CDC Office of Public Health Genomics, Healthy People 2020 grants, and other grant resources. The preliminary information contributed by this dissertation combined with the results of future studies could be utilized to help secure grant funding for Kentucky in the future.

A second barrier to implementing programs in public health genetics in the state of Kentucky is the sparse genetic counseling workforce. Just as there is little funding available for public health genetics and genomics, it can be difficult to justify the addition of genetic counselors in a healthcare system because these departments often do not produce significant revenue. This is partially due to the way that genetic counseling services can be billed, which can be especially difficult if the state does not license genetic counselors, as is the case in Kentucky. Recently, there has been an effort to pass a licensure bill at the state level to establish licensure for genetic counselors, and these efforts are ongoing. Public health practitioners and healthcare systems should support these efforts moving forward as this is an important step in expanding the genetic counseling workforce and preparing Kentucky for the increasing need for genetic services.
REFERENCES


## APPENDIX 1

Cancer Genetic Counseling Clinics in Kentucky April 2015

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<tr>
<th>Genetic Counseling Clinic Main Site</th>
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EDUCATION
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- Cornell Tradition Fellow: Fellowship awarded to outstanding undergraduates who take part in all aspects of campus life including academics, work, and volunteer activities

WORK EXPERIENCE
University of Pittsburgh Genetic Counseling Program, Assistant Program Director, May 2015-Present
- Participate in the continued development of the Genetic Counseling Program
- Develop and teach genetic counseling courses
- Provide guidance to student thesis projects

- Provide expertise on content and contribute to the development of two videos on implementation of bidirectional reporting systems and the importance of early screening for Tier 1 conditions
- Develop, in conjunction with project team, final scripts for project videos
- Consult in terms of expertise on project entitled, “Key Approaches to Cascade Screening in the States”

Region 4 Long Term Follow-Up Workgroup Facilitator, Independent Subcontract with Michigan Public Health Institute, September 2014-Present
- Facilitate monthly teleconference workgroup meetings for the Region 4 Long Term Follow-up Workgroup
- Collaborate with workgroup lead to analyze workgroup needs and coordinate workgroup projects
- Provide reports on workgroup progress

Graduate Assistant, University of Kentucky College of Public Health, September 2013-May 2015
- Develop lectures for graduate level global public health course
- Review and select supplemental class materials for global public health course
- Textbook editing with a focus on tables and figures
- Teaching assistant for graduate level public health course Plagues & Politics

Research Assistant, University of Kentucky, Kentucky Regional Extension Center, September 2013-May 2015
- Prepare and submit IRB applications
- Design and conduct research on program implementation and outcomes
Manager, Genetic Counseling Services, Norton Cancer Institute, April 2007-September 2013
- Perform all duties outlined for genetic counselor position below
- Provide leadership for and management of the Genetic Counseling Services staff members
- Create goals for the continued development of the Genetic Counseling Services department
- Collaborate with physicians and other health care providers on patient care plans
- Develop innovative programs for the delivery of genetic counseling and testing services
- Act as a liaison between Genetic Counseling Services, Norton Centers for Prevention and Wellness, and Norton Hospital
- Provide clinical supervision to rotating genetic counseling students from University of Cincinnati
- Member of the Norton Cancer Institute ACOS cancer committee

Genetic Counselor, Genetic Counseling Services, Norton Cancer Institute, May 2005-April 2007
- Provide comprehensive cancer genetic counseling to patients
- Perform cancer risk assessments based on family history
- Coordinate genetic testing for appropriate individuals
- Construct patient visual aids, informational brochures, and form letters for new clinic
- Create and present educational programs about genetic counseling and testing for health care providers and the community

Drosophila Laboratory: University of North Carolina at Greensboro, January 2004-May 2005
- Supervisor: Dennis LaJeunesse, PhD
- Laboratory assistant
- Conducted supervised research on a variety of projects

Cytogenetics Laboratory: University of North Carolina at Chapel Hill, June-December 2003
- Supervisor: Randy Bishop
- Digitized chromosome analysis test results for cancer, prenatal, pediatric, and adult patients
- Extensive and efficient use of karyotyping computer software

OTHER RELEVANT EXPERIENCE
Michigan Department of Community Health, Genomics and Genetic Disorders Section, June 2014-September 2014
- Supervisor: Janice Bach, MS, CGC
- Developed a needs assessment plan for implementing new cholesterol screening guidelines for children in Michigan
- Attended meetings pertaining to various public health genetics and genomics topics
- Assisted in the development of questions for focus groups on sickle cell disease services in Michigan

Bullitt County Health Department: Shepherdsville, KY, March 2014-June 2014
- Supervisor: Andrea Renfrow, RN, BSN
- Created databases, analyzed data, and produced reports for multiple Health Department projects and events
- Participated in document review for Public Health Accreditation
- Facilitated group participation during a Community Dialogue

The Genetic Alliance: Washington, DC, August 2002-December 2002
- Supervisor: Sarah Wood, MS
- Genetics Education and Research Helpline intern
- Communicated with helpline users via telephone and email about a variety of rare genetic conditions
- Developed expertise in accessing online resources for genetic information
- Researched genetic conditions and constructed information sheets
- Assisted with the establish of a permanent intern program for the organization
**VOLUNTEER WORK**

- Louisville FORCE Outreach Coordinator
  - June 2009-May 2015
- Ride to Conquer Cancer Crew Member
- Gilda’s Club of Louisville Associate Board Member
  - August 2009-December 2011
- Gilda’s Club of Louisville Volunteer
  - March 2009-July 2011

**WORKSHOPS**

- 19th Summer Institute in Statistical Genetics
  - July 14-23, 2014
- Summer Workshop on Social Network Analysis
  - June 3-7, 2013

**ABSTRACTS AND PUBLICATIONS**


- Brian A, Lewis A, and Nielsen M. *Understanding the Causes of FAP in Families with no Identifiable Mutation in Kentucky*. Accepted abstract and platform presentation at the 2010 NSGC Annual Education Conference.

**SELECTED PRESENTATIONS**

- Reproductive Health in the United States
  - February 11, 2014
- Social Network Analysis
  - August 8, 2013
- Genetic Literacy
  - June 13, 2013
- Best of San Antonio: Genetics Review
  - February 20, 2013
- Genetic Counseling and Public Health
  - October 4, 2012
- Genetic Counseling as a Career
  - February 1, 2012
- Cancer Genetic Testing Overview: World Affairs Council
  - October 21, 2011
- Knowing Your Family Health History
  - October 19, 2011
- Rare Cancers and Their Contributions to Genetic Risk
  - July 14, 2011

**CERTIFICATIONS**

- American Board of Genetic Counseling, Certified Genetic Counselor
  - September 1, 2007

**PROFESSIONAL MEMBERSHIPS**

- National Society of Genetic Counselors, Full Member
  - 2005-Present
- National Society of Genetic Counselors, Familial Cancer Risk Counseling SIG
  - 2005-Present
- National Society of Genetic Counselors, Public Health SIG
  - 2013-Present
- American Society of Human Genetics
  - 2011-2013
- Collaborative Group of the Americas on Hereditary Colon Cancer
  - 2010-2012