Application of Genomics in Nursing Practice

Elizabeth Cameron Hassen
Clemson University, hassen02@charter.net

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APPLICATION OF GENOMICS IN NURSING PRACTICE

A Dissertation
Presented to
the Graduate School of
Clemson University

In Partial Fulfillment
of the Requirements for the Degree
Doctor of Philosophy
Healthcare Genetics

by
Elizabeth Cameron Hassen
December 20___

Accepted by:
Dr. Margaret Wetsel, Committee Chair
Dr. Linda Ward
Dr. Matt Boyer
Dr. Stephanie Davis
ABSTRACT

This dissertation begins with the introduction of genetics, genomics, and the Healthcare Genetics (HCG) model. The five concepts of the HCG model, genetics/genomics, education, environment, clinical testing and therapeutics, and ethical/legal/social implications (ELSI) are defined. These concepts are threaded throughout the manuscripts and dissertation chapters.

Chapter II defines molecular testing and differences between single-gene and multi-gene testing. The Kaplan Meier Curve and its use in research, to illustrate survival over time, is discussed. The chapter provides specific examples of both predictive and prognostic genomic testing used in breast, lung, colon, and prostate cancers.

Chapter III examines the application of the Theory of Planned Behavior (TPB) in genomic nursing practice. The TPB constructs—attitude, subjective norms, and perceived behavioral control—are described along with genomic research examples. The chapter concludes with three exemplars that illustrate the importance of genomic-competent care in nursing practice.

Chapter IV presents a mixed-methods study that explored nurses’ use of genomics in practice and identified barriers to genomic-competent care. The quantitative and qualitative results found that gaps exist between genomic education and practice. The most commonly cited barriers were a lack of knowledge, support, and costs.

Chapter V begins with a summary of the previous four chapters. Limitations are described related to the content of Chapters I through III and the research study presented in Chapter IV. Chapter V concludes with recommendations for future research based on this dissertation.
I would like to dedicate my dissertation work to my family and friends. My husband, David, for his love and support throughout this journey. To my children, my daughter, Cameron, and my son, Brandon, who have been patient with me, supported me, and loved me while mom has been in school.

Also dedicated to my lifelong best friend and fellow science lover Dr. Amanda Gates Wright, and my Bunco Girls who prayed, praised, and provided unwavering love.
ACKNOWLEDGMENTS

I first would like to thank my mentor, Dr. Julie Eggert, who shares my love of oncology, for her support, knowledge, time, and guidance throughout my doctoral program journey.

Thanks to my dissertation committee members, Dr. Margaret ‘Ann’ Wetsel, Dr. Linda Ward, Dr. Matt Boyer, and Dr. Stephanie Davis, along with retired members Dr. Julie Eggert and Dr. Mary Beth Steck for their expertise, knowledge, and guidance throughout my research and dissertation work. I would like to acknowledge Dr. Kathleen Calzone for her mentorship and guidance as my Jonas Scholar mentor. I would like to express my gratitude to Spartanburg Regional Healthcare System and AnMed Health for allowing me to conduct my dissertation research at their facilities.

I give thanks to my husband, children, family, and friends for all their encouraging words and support! A special thanks to my parents, Dennis and Evelyn Cameron for all the encouragement and various means of support you have provided, and my in-laws, Fred and Barbara Hassen.

I would like to thank my friends in the doctoral program who have made this journey more bearable by listening and encouraging. Specifically, I would like to acknowledge Tracy Lowe, who has been a constant friend and support throughout this program. Our research projects and presentation trips will be forever memories. Last, thanks to the Clemson University School of Nursing faculty and staff for their support.
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CHAPTER I
INTRODUCTION

Genomics is the study of genes collectively, including their interactions together and with the environment (National Human Genome Research Institute (NHGRI), 2020). Genomic research has gained momentum over the past two decades. Genomic knowledge, gained from the Human Genome Project (NHGRI, 2020), increased the utilization of technology, expanded the employment of large data bases and bioinformatics, and accelerated research development (Aiello, 2017; Shendure, Findlay, & Snyder, 2019). As the largest group of health care professionals, it is imperative that nursing professionals take responsibility to educate themselves, become competent, and apply genomics in the care of patients and their families (Jenkins, 2019).

Watson and Crick (1953) first described DNA as a double helix in 1953 and developed a model that is still in use (Pray, 2008). Neonatal testing and prenatal counseling have been a part of genomic nursing practice since the 1960s (DeLuca et al., 2013). In 1997, the American Nurses Association recognized genetics as a nursing specialty (International Society of Nurses in Genetics, 2007). The Scope and Standards of Clinical Genetics Nursing was first published in 1998 by the International Society of Nurses in Genetics (ISONG) and the American Nurses Association (ANA) (ISONG and ANA, 1998). This landmark document was followed by Scope and Standards of Practice, Genetics/Genomics Nursing, 2nd edition, in 2016 (ISONG and ANA, 2016). In addition, the Oncology Nurses Society (ONS) published scopes and standards of practice guidelines in genomics for nurses (Lubejko and Wilson, 2019).
As essential members of the healthcare team, nurse and advanced practice nurses must be prepared to provide genomic competent care to patients and families, and to guide the implementation of care that promotes optimal patient outcomes (Rogers et al., 2017). In addition to the documents cited, three other seminal documents advanced genetics and genomics in nursing education. The American Nurses Association (ANA) published the Essentials of Genetic and Genomic Nursing: Competencies, Curricula Guidelines, and Outcome Indicators (2nd ed.) in 2009 and was endorsed by 47 nursing organizations. Genomics is also addressed in the American Association of Colleges of Nursing (AACN) Essentials of Baccalaureate Education for Professional Nursing Practice (2008) and the Essentials for Master’s in Nursing (2011) for nursing education.

The Essentials of Baccalaureate Education for Professional Nursing Practice (AACN, 2008) addresses genomics in Essential I, V, VII, and IX. These essentials define the knowledge needed for nursing practice, e.g. basic genetic/genomic concepts, screening and prevention, genetic diseases and predisposition, pharmacogenomics, family history and pedigree, and genetic testing and diagnostic trends (2008). Studies have explored the genomic knowledge of both faculty and undergraduate students (Donnelly et al., 2017; Munroe & Loerzel, 2016; Read & Ward, 2016). Read and Ward (2016) compared faculty and student knowledge and found them to be similar. Donnelly et al. (2017) found that most of the nursing faculty, who participated in their study, lacked genomic knowledge and confidence in teaching genetic/genomic content. Munroe and Loerzel (2016) reported that, although students in their study had an increase in genomic knowledge after a semester of nursing classes, nursing students revealed that they were
not confident to incorporate genomics into nursing practice. Genomic knowledge and competencies in baccalaureate nursing education provide a foundation for genomic-competent nursing practice and serve as the basis for continuing nursing education and application in nursing practice.

The Master’s Essentials (AACN, 2011) addresses genomics in Essentials I and VIII and may be applied in Essentials IV, VI, VII and IX. The Master’s Essentials document describe competencies, that build upon the baccalaureate nursing foundation, and prepare advanced practice nurses for increased responsibilities in embedding genomics into direct care activities. For example advanced practice nurse should incorporate genetic/genomic evidence in care, translate research and participate in collaborative teams to improve health outcomes, influence health care policy and finance, provide patient centered care, and integrate health promotion and prevention in patient education and nursing interventions. As described in the Master’s Essentials, genomics can be applied to leadership and quality improvement through mentorship, integration in organizations, and care delivery to improve patient outcomes. Donnelly et al. (2017) found that the majority of the doctorally-prepared faculty in their study reported that Master’s Essentials competencies were not being met in their graduate program.

“As the voice of academic nursing, the American Association of Colleges of Nursing (AACN) serves as a catalyst for excellence and innovation in nursing education, research, and practice” (AACN, 2019, p. 3). In 2020, AACN published a DRAFT The Essentials: Core Competencies for Professional Nursing Education (AACN, 2020). In this document, domains, competencies and sub-competencies are identified for Entry-
level Professional Nursing Education and Advanced-level Nursing Education. “In the new model, competency-based education provides the structure for nursing across degree programs” (AACN, 2020, p. 16). As the domains, competencies and sub-competencies are broadly framed, genetics/genomics is referenced only once in Domain 2: Person-Centered Care, Competency 2.2 Communicate effectively with individuals. In Advanced-level Nursing Education, sub-competency 2.2j states, “apply personalized information, including genetic/genomics, to health care (AACN, 2020, p. 24).

The Essentials of Genetic and Genomic Nursing (ANA, 2009) describes professional responsibilities and outcomes for genetic and genomic competencies and education, including expectations for recognizing one’s own belief, values, and attitudes; taking a three generation family history, constructing a pedigree and identifying risk factors; advocating for services and resources for patients; promoting informed decision making; recognizing ethical issues with the use of information and technology; and for understanding relationship of genomics in health promotion and prevention, screening, diagnosis, and treatment, including pharmacogenomics. Collectively, these publications have defined and guided genomic nursing education and genomic nursing competencies.

While these documents have been available for over ten years, nurses continue to report a lack of knowledge and competency in the application of genetics and genomics in nursing practice (Calzone et al., 2012; Calzone et al., 2013; Coleman et al., 2014; Daack-Hirsch, Dieter, & Quinn Griffin, 2011; Thompson & Brooks, 2011). Calzone et al. (2018) led an implementation project in Magnet hospitals using leadership dyads to increase genomic education and awareness. An important finding from this study was
that long-term interventions are needed for the successful integration of genomics in nursing practice (Calzone et al., 2018).

The framework for this dissertation is the Healthcare Genetics (HCG) Model of Care (Figure 1.1). The model was developed collaboratively by Healthcare Genetic Ph.D. students and faculty during an HCG course and illustrates the interdisciplinary nature of genomics. At the center of the model is Healthcare Genetics, which this investigator expanded to include Genomics. Linkages extend to the constructs of genetics/genomics, education, clinical testing and therapeutics, environment, and ethical, legal, and social implications (ELSI). Green and Guyer (2011) discussed a vision for the future of genomic medicine which included several of the HCG model constructs, e.g. the essence of genomics, education and training, and genomics and society, which included ethical, societal, and policy issues.

Genetics is defined as the study of individual genes (National Cancer Institute, 2020). Genomics is a broader term, defined as the study of all genes and the interaction among them and the environment (National Human Genome Research Institute, 2020). Individual genes and their expression influence phenotype at a molecular or cellular level (Green & Gurry, 2011). A genetic change in deoxyribonucleic acid (DNA) could impact the transcribed ribonucleic acid (RNA) leading to a translational protein error (Green & Gurry, 2011). Understanding the mechanisms by which genes and gene variants influence health will assist nurses and advanced practice nurses to provide genomic competent care and education for patients and their families.
Genetic and genomic education is important for all healthcare providers, beginning with their professional education and continuing throughout their careers. A lack of genomic knowledge and care has been identified in all healthcare providers (Calzone, et al., 2013; Korf, et al., 2014; Selkirk, et al., 2013). The Institute of Medicine held a round table discussion in 2016 to discuss barriers to the incorporation of new genomic technology in clinical practice and identify strategies to increase healthcare professionals’ genomic education (Dougherty, Wicklund, & Taber, 2016).
Clinical testing may involve examining genetic changes at multiple levels, e.g. chromosomal analysis with karyotyping, genetic testing for gene mutations, and protein analysis. It may also indicate an increased risk for hereditary diseases or conditions and can be utilized to guide treatment and for pharmacogenetics. With the expansion of genomic testing as an aspect of clinical testing, the need for nurses to understand the different types of tests is essential in order to educate and answer questions for patients and their families (Aiello, 2017).

The environment and modifiable factors such as diet, exercise, and environmental pollutants can impact an individual’s risk for disease(s) (World Health Organization, 2017). The interaction of one’s environment and their genome can guide the assessment of individual risk (2017). Nurses’ ability to take an accurate family history and recognize risks can offer opportunities to educate patients and their families. Also, as members of the interprofessional healthcare teams, nurses can recognize “red flags” for genetic testing and participate in interdisciplinary team discussions regarding screenings for various diseases and conditions.

Ethics plays an important role in the nursing profession and in genomics. The Human Genome Project (HGP) promoted the establishment of a working group to anticipate and examine the ethical, legal, and social implications that would arise with research and discoveries through sequencing the human genome (NHGRI, 2012). This foresight led to the consideration of potential societal implications of genomic healthcare. One key policy that arose to offer protections around genomic testing was the Genetic Information Nondiscrimination Act (GINA). Enacted in 2008, GINA was the first
federal policy that prohibited health insurance eligibility and employment discrimination based on genomic testing results (Steck & Hassen, 2019).

The ANA Code of Ethics (2015) includes genomics and the application of genomics in nursing practice. ELSI is important for nurses to consider the implications of genomics in clinical practice and research. For example, genomic testing can be beneficial in guiding health prevention and promotion recommendations and treatment discussions. Those benefits must be balanced by potential risks of learning genomic information that may affect patients and their families in a number of ways.

Although the HCG model shows the relationships between the constructs as bi-directional, all constructs are linked in the model through the Healthcare Genetics/Genomics core construct. As the application of genomics continues to expand in healthcare, the HCG model constructs can guide the incorporation of genetics/genomics in nursing program entry level education and continuing education of nurses and other healthcare professionals to facilitate the use of genomics in patient care across the healthcare continuum.

In addition to Chapter I, this dissertation comprises four additional chapters that highlight the application and utilization of genomics in nursing practice.

Chapter II presents an overview of tumor profiling and how genomic testing is used in the field of oncology. Molecular testing results can be both prognostic and/or predictive and is used to guide decisions about cancer treatment. An overview of genomic tests and their utilization in breast, lung, colon, and prostate cancer is presented.
The chapter addresses the importance of genomic knowledge and awareness of molecular testing and biomarkers used to guide personalized medicine.

Chapter III presents an adaptation of Ajzen’s Theory of Planned Behavior (TPB) model (1991, 2002) and three exemplars applying genomics in nursing practice. The first exemplar discusses the importance of a complete family health history as a diagnostic tool to guide decisions about genomic testing and treatment for patients and at-risk family members. The second exemplar examines the use of genomic testing in cancer and the impacts on treatment discussions and decisions. The third exemplar highlights the influences of financial toxicity, costs and financial impacts on healthcare. Nurses can provide education, resources, and referrals to mitigate financial stressors to patients and their families and support other members of the interdisciplinary healthcare team in these efforts. The chapter closes with a discussion of the importance of having genomic-competent nurses caring for patients and their families.

Chapter IV presents original research examining the use of genomics in nursing practice. A mixed-methods study was conducted using Ajzen’s TPB (1991, 2002) as a framework. The constructs of the model—attitude, subjective norms, and perceived behavioral control—were examined quantitively and qualitatively related to the use of genomics in nursing practice (behavior). This chapter concludes with a discussion of the study findings and recommendations for future research.

Chapter V concludes the dissertation with a summary of the findings in Chapters II through IV and conclusions drawn from the findings. This chapter also highlights limitations of the information presented in each chapter. Chapter V closes with
recommendations for embedding genomics in nursing education programs, continuing
education, and clinical practice to promote the application of genomic-competent care for
patients and their families.

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CHAPTER II
TUMOR PROFILING

Introduction

*Tumor profiling* is a molecular analysis to identify alterations in DNA, RNA, and proteins (Adenoid Cystic Carcinoma Research Foundation, n.d.). Also referred to as *molecular profiling*, various techniques are used to analyze the tumor to help guide treatments and personalized cancer care. As Chu (2011) stated, “In theory, this approach should result in enhanced clinical efficacy, improved safety profile, and lower overall pharmacoeconomic costs” (p. 69). These analyses are already being used in the diagnostic and treatment guidelines for multiple cancers including breast, lung, and colon cancers and lymphomas and leukemias. This chapter offers information that will assist clinical trial nurses (CTNs) working in oncology-specific research with a focus on solid tumors to understand tumor profiling and how these genetic tests can be interpreted for application to clinical trials.

Tumor Profiling

Tumor profiling uses molecular analysis to determine characteristics of tumors, which assists with prognostic assessment, treatment planning decisions, and the advancement of personalized medicine. Techniques for profiling include DNA microarrays, RNA sequencing, and next-generation DNA sequencing. Currently, DNA microarrays and RNA sequencing are most commonly used in tumor profiling, but as cost
continues to decrease for next-generation sequencing of DNA, its use will increase (Walther & Sklar, 2011).

Tumor profiling is being used today to guide treatment plans, such as determining the use or type of chemotherapy and the use of specific targeted therapies for better prognosis and outcomes (Chu, 2011; Walther & Sklar, 2011). There has been a shift to molecular tumor profiling or analysis from testing for single alterations because of the increasing number of molecular-targeted drugs (Walther & Sklar, 2011). Molecular analysis allows the tumors to be tested for an array of alterations and mutations, including base substitutions referred to as single nucleotide polymorphisms, and insertions and deletions in DNA. These genetic changes in DNA are discussed in Chapter 31 of the book. These various alterations can activate oncogenes, leading to alterations in the signal transduction pathways (Walther & Sklar, 2011). The alterations and mutations identified through tumor profiling can guide treatment decisions to determine an individual’s likelihood of response to specific targeted therapies (Walther & Sklar, 2011).

When reading information about molecular profiling, one may see the terms biomarker, single-gene marker, or multigene markers. Biomarker is defined by the National Cancer Institute (NCI, n.d.-a) as “a biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition.”

Single-gene markers usually refer to a single-gene, protein, or other molecule that can be used to predict clinical outcomes (Galanina, Bossuyt, & Harris, 2011). These
markers include receptors such as the estrogen receptor (ER), progesterone receptor (PR), or binding sites for key signaling proteins such as the epidermal growth factor receptor (EGFR) (Chu, 2011; Galanina et al., 2011).

*Multigene biomarkers* use one analysis to assess multiple genes found in a tumor (Galanina et al., 2011). Examples of multigene biomarkers assays include Oncotype DX® and MammaPrint®. A list of currently used tumor markers can be found on the NCI fact sheet on tumor markers (NCI, 2011).

Biomarkers can be used as prognostic or predictive markers. *Prognostic* markers are used to determine the risk or likelihood of the disease recurring (NCI, n.d.-c). *Predictive* markers are used to determine if a patient will benefit from a specific treatment (NCI, n.d.-b). CTNs need to understand the source of the biomarker in the development of the tumor type and how the test is used (i.e., prognostically or predictively) to facilitate the correct interpretation.

**Kaplan-Meier Survival Curve**

Many researchers use Kaplan-Meier estimate curves to illustrate the benefit of a certain drug or treatment as it relates to patient survival, requiring CTNs to understand the definition, collect the necessary data for the calculation, and be able to communicate this information with other personnel working with the clinical trial (Oncology Nursing Society, 2010). A Kaplan-Meier curve plots the probability of an event occurring at a specified time; it is also referred to as a *product limit estimate* (Goel, Khanna, & Kishore, 2010). This estimate is commonly used in clinical trials to illustrate survival time after treatment. Specifically, it evaluates the number of living individuals who have survived
after an intervention, such as a chemotherapy drug, over a period of time (Goel et al., 2010). To calculate this estimate, the total number of subjects living at the start of the intervention, minus the number of subjects who have died, is divided by the total of subjects living at the start, at a given point in time (see Figure 2.1 below) (Goel et al., 2010).

In a Kaplan-Meier survival curve, the $x$-axis represents time, and the $y$-axis represents the estimated probability of survival within a defined population (Vanderbilt University Department of Biostatistics, 2011). In general, a high start is seen to the left side of the graph with a decrease as the curve moves to the right of the graph (Vanderbilt University Department of Biostatistics, 2011). This can be explained by noting that as time elapses, the number of people decreases; they either died or became lost to follow-up during the trial. The Kaplan-Meier survival curve is an estimate of survival at a point in time, not the actual number of survivors at that point in time (Goel et al., 2010).

CTNs may be required to gather survival data for two groups of subjects, such as in comparison of standard treatment with a new treatment, so that the Kaplan-Meier curves can be compared. A survival plot would be created for each group, and it would be important to monitor any gaps between these two curves. A vertical gap indicates that one intervention, such as treatment, resulted in more subjects surviving at a specific time.

$$S_t = \frac{\text{Number of subjects living at the start}}{\text{Number of subjects living at the start}} \frac{\text{Number of subjects living at the start}}{\text{Number of subjects living at the start}} = \frac{\text{Number of subjects living at the start}}{\text{Number of subjects living at the start}}$$

Figure 2.1. Survival Probability.
point compared to the other treatment group (Goel et al., 2010). A horizontal gap indicates a longer time of survival before one treatment group experienced a certain fraction of deaths (Goel et al., 2010).

Biomarkers in Specific Cancers

Breast Cancer

Breast cancer researchers use biomarkers to identify subsets of patients (grouping patients according to positive or negative receptors) with use as both predictive and prognostic markers. Currently, the presence or absence of ER, PR, and HER2 receptors is routinely used as a predictive marker to determine patient-specific treatment of breast cancer (Galanina et al., 2011). Furthermore, multigene biomarkers from the breast tumor are used as prognostic markers, predicting risk of recurrence. These prognostic markers, including Oncotype Dx, MammaPrint, Breast Cancer Index, and PAM50 (Galanina et al., 2011), can help practitioners determine treatment types to use based on the patients’ personal recurrence risk. This approach offers each patient personalized medicine.

The Oncotype DX Breast Cancer Assay is a 21-gene assay that uses reverse transcription polymerase chain reaction technology on paraffin-embedded tumor tissue to calculate a recurrence score that correlates with the likelihood of breast cancer recurrence within 10 years of initial diagnosis (Genomic Health, n.d.-b; Paik et al., 2004). The National Surgical Adjuvant Breast and Bowel Project (NSABP) B-14 trial validated the correlation of the recurrence score as “quantifying the likelihood of distant recurrence in tamoxifen-treated patients with node-negative, estrogen-receptor-positive breast cancer” (Paik et al., 2004, p. 2817). Subsequently, in the NSABP B-20 trial, researchers assessed
the chemotherapy benefit by testing the interaction between chemotherapy treatment and the recurrence score (Paik et al., 2006). The population used to validate the Oncotype DX assay was patients with early-stage breast cancer, defined as stage I or II, lymph node negative, ER positive (Paik et al., 2004).

An Oncotype DX Breast Cancer Assay report contains a recurrence score, a number between 0 and 100 that correlates to a specific likelihood of breast cancer recurrence within 10 years of initial diagnosis (Paik et al., 2004). The recurrence score is calculated from 16 cancer-related genes and five reference genes (reference genes are those that normalize the expression of cancer-related genes) (Paik et al., 2004; Zhang, Ding, & Sandford, 2005). The score places patients into one of three categories: low risk, defined as a score of less than 18; intermediate risk, defined as a score of 18-30; and high risk, defined as a score of 31 or higher (Paik et al., 2004). Using this score, a practitioner can determine if a type of treatment will provide a longer disease-free survival time. For example, the NSABP B-20 study found that tamoxifen plus chemotherapy provided a significant benefit in the high-risk group (Paik et al., 2006). The low- and intermediate-risk groups did not show a significant statistical benefit with the addition of chemotherapy to the treatment with tamoxifen (Paik et al., 2004). Ongoing studies are evaluating the intermediate-risk group (Paik et al., 2006). The National Comprehensive Cancer Network® (NCCN®) and the American Society of Clinical Oncology guidelines incorporate the use of Oncotype DX for women with ER-positive, node-negative disease and tumors larger than 0.5cm (Harris et al., 2007; NCCN, 2015a).
Genomic Health implemented further studies, including Eastern Cooperative Oncology Group 5194, which contributed to the development of a validated 12-gene algorithm to predict recurrence risk in patients with ductal carcinoma in situ (DCIS) (Genomic Health, n.d.-a; Solin et al., 2013). This report provides a DCIS score plus two additional scores: a percentage for any local event recurrence and an invasive local event recurrence score to be used to guide treatment plans, such as local excision without radiation (Genomic Health, n.d.-a; Solin et al., 2013).

MammaPrint is another prognostic multigene assay. It targets 70 genes associated with breast cancer and uses microarray technology to determine a recurrence score for early-stage breast cancer (van’t Veer et al., 2002). The study focused on women with early-stage breast cancer, defined as invasive stage I or II (T1 or T2), smaller than 5 cm, and including both lymph node-positive and lymph node-negative disease (van de Vijver et al., 2002). MammaPrint stratified the results into two prognostic groups, good or poor, based on a correlation coefficient predicting recurrence during the first five years after therapy (van de Vijver et al., 2002). Other studies evaluated the predictive value of MammaPrint, concluding that chemotherapy plus endocrine therapy had a significant clinical benefit in the high risk, poor-prognosis groups. The addition of chemotherapy was not shown to be beneficial to the good-prognosis group (Knauer et al., 2010).

Mammostrat is a third prognostic test for stage I and II, node-negative, ER-positive breast cancer. Mammostrat, is a five-antibody immunohistochemistry panel targeting expression levels of the tumor proteins SLC7A5, HTF9C, P53, NDRG1, and CEACAM5 (Bartlett et al., 2010; Clarient Diagnostics Services, GE Healthcare, n.d.).
An algorithm calculates a risk index score to classify patients into one of three categories based on the percentage of cancer recurrence in 10 years. The categories include low, moderate, and high risk for relapse. Women at low risk would probably not receive additional benefit from chemotherapy, but those at high risk would have long-term benefit from chemotherapy plus hormonal therapy. Validation studies have not incorporated the status of other hormone receptors, but more evidence is supported for the ER-positive ranking (Bartlett et al., 2010).

**Lung Cancer**

Strong evidence exists for EGFR, the 5’ endonuclease of the nucleotide excision repair complex (ERCC1), the *KRAS* oncogene, and the *ALK* fusion oncogene as prognostic and predictive markers (NCCN, 2015b). Additional biomarkers identified for predictive or prognostic value in non-small cell lung cancer (NSCLC) include the ribonucleotide reductase enzyme (RRM1) and thymidylate synthase (Andrews, Yeh, Pao, & Horn, 2011).

EGFR is a transmembrane receptor that is known to have predictive treatment benefit from EGFR tyrosine kinase inhibitor therapy with the presence of an exon 19 deletion or exon 21 L858R mutation (Miller et al., 2008; Sequist et al., 2008). *EGFR* mutation and copy number were positively correlated with a higher response rate and progression-free survival (Miller et al., 2008). Sequist et al. (2008) showed favorable clinical outcome for patients with *EGFR* mutation treated with first-line gefitinib, an *EGFR* inhibitor.
The *KRAS* oncogene has shown to be prognostic of survival. Studies have demonstrated that a *KRAS* mutation has an unfavorable prognostic value with shorter survival regardless of treatment (Mitsudomi et al., 1991; Slebos et al., 1990; Tsao et al., 2007). The *ALK* gene has been shown in studies to have predictive value of response to crizotinib, an *ALK* and *MET* tyrosine kinase inhibitor (NCCN, 2015b).

Testing for the expression of ERCC1 can provide both prognostic and predictive information. For prognostic value, a high ERCC1 expression is associated with improved outcomes in early-stage NSCLC (Olaussen et al., 2006). For predictive value, many studies have researched its ability to predict response to platinum-based therapies. Research results have shown that low expression of ERCC1 has improved overall survival with platinum-based treatment, especially in advanced disease (Andrews et al., 2011; Olaussen et al., 2006; Simon, Sharma, Cantor, Smith, & Bepler, 2005).

Another identified prognostic factor is the enzyme RRM1. Similar to ERCC1, studies have revealed that a high expression of RRM1 is associated with an increased survival in patients with early-stage NSCLC (Zheng et al., 2007). Zheng et al (2007) divided patients into four subgroups based on the expression of the RRM1 and ERCC1 proteins: high expression of both proteins (high/high), low expression of both proteins (low/low), high RRM1 expression and low ERCC1 expression, and low RRM1 expression and high ERCC1 expression. The study concluded that high expression of both RRM1 and ERCC1 had a statistically significant increase in disease-free and overall survival (Zheng et al., 2007). In addition, several studies focused on the predictive role of RRM1, wherein patients with a high RRM1 expression are not sensitive to
gemcitabine-based chemotherapy, and patients with low RRM1 expression have increased time to survival when the chemotherapy agent cisplatin is added to gemcitabine (Andrews et al., 2011). Andrews et al (2011) suggested that a screening panel including more than one biomarker may be more reliable for prognostic purposes based on the ERCC1 and RRM1 data.

Colon Cancer

Much research is ongoing in the study of biomarkers for additional predictive values, or further explanations of response to therapy, in people with colon cancer. Currently, the KRAS oncogene is a biomarker with known predictive value for response to anti-EGFR monoclonal antibodies (Dienstmann, Vilar, & Tabernero, 2011). A study by Amado et al. (2008) demonstrated that KRAS mutations have a negative (inverse) predictive value, meaning that patients with KRAS tumor mutations had better outcomes after treatment with chemotherapy alone and no monoclonal antibody therapy. However, in another study, Bokemeyer et al. (2010) concluded that KRAS wild-type (typical gene without mutation) tumors have increased response rates to chemotherapy with the addition of a targeted agent. The conclusion from multiple clinical trials, including retrospective analyses, is that KRAS mutations can be used as a predictive marker for treatment with anti-EGFR monoclonal antibodies (Dienstmann et al., 2011). Additional predictive markers for anti-EGFR agents include BRAF, NRAS, and PIK3CA status. The loss of protein expression by PTEN, a tumor suppressor gene, continues to be investigated for predicting a lack of benefit to treatment with monoclonal antibodies and
a negative correlation with overall survival (Er, Chen, Bujanda, & Herreros-Villanueva, 2014).

Similar to breast cancer, colon cancer has genomic profiling options to predict recurrence risk. These include Oncotype DX, ColoPrint, and ColDx. The Oncotype DX Colon Cancer Assay (Genomic Health, n.d.-c) is a 12-gene panel consisting of seven (7) cancer genes and five (5) reference genes (Gray et al., 2011).

Another profiling approach discussed the relationship of tumor gene expression and risk of cancer recurrence in four individualized cohorts to evaluate surgery alone versus surgery plus adjuvant 5-fluorouracil (5-FU) plus leucovorin in both stage II and stage III disease (O’Connell et al., 2010). These researchers used the quantitative reverse transcription polymerase chain reaction technique to identify 48 genes associated with recurrence risk and 66 genes associated with benefit of 5-FU/leucovorin (O’Connell et al., 2010). From this, seven of the recurrence genes and six of the treatment-benefit genes were identified and are the foundation of the algorithm used to categorize patients with stage II and III colon cancer into three categories: low, intermediate, and high risk of recurrence (O’Connell et al., 2010). The development of this assay was validated and confirmed for stage II colon cancer in the QUASAR (Quick and Simple and Reliable) and the Cancer and Leukemia Group B 9581 studies. Use of the gene expression levels of the cancer genes allows for the calculation of a recurrence score. A report is generated with a colon cancer recurrence score that ranges from 0-100: a score less than 30 has a recurrence risk of 15% or less; a score of 30 or greater indicates a recurrence risk greater than 15%; and a recurrence score of 41 or greater indicates a recurrence risk greater than
18% that overlaps with T4 patients (Genomic Health, n.d.-c). The report also includes information on mismatch repair (MMR) status.

MMR is a conserved process during DNA replication that corrects mismatches of bases (Kunkel & Erie, 2005). A deficiency in MMR identifies a small subset of stage II colon cancer tumors with significantly lower recurrence risk compared to tumors with expression (Genomic Health, n.d.-c). A study by Gray et al. (2011) concluded that the 12-gene assay was able to validate the recurrence score for stage II colon cancer tumors treated with surgery alone but was not validated as a predictive marker for treatment with adjuvant 5-FU or folinic acid chemotherapy.

ColoPrint (Agendia, n.d.) is an assay that quantifies the expression of 18 genes and is a prognostic marker that classifies patients into two categories: low versus high recurrence risk (Salazar et al., 2011). In the development of the ColoPrint assay, 188 tumor samples consisting of stage I, II, and III colon cancers were categorized into A, B, and C groups based on mutational status of BRAF (Salazar et al., 2011). Then, using the B group, an 18-gene optimal assay was developed and validated using a sample of 206 subjects. In this study, researchers assessed the mutations for BRAF, KRAS, and P13KCA in addition to running the 18-gene assay. Based on the ColoPrint analysis, patients were categorized as having either low or high risk of recurrence based on five-year survival. The study concluded that ColoPrint improves prognostic accuracy and was able to identify patients with stage II disease that could be managed without chemotherapy (Salazar et al., 2011).
ColDx (Almac Group Ltd., n.d.) is a DNA microarray multigene assay that uses 634 probes to stratify patients as having either high or low risk recurrence (Kennedy et al., 2011). Kennedy et al. (2011) performed validation on a sample of 144 patients with stage II colon adenocarcinoma, categorizing them into the two groups based on recurrence risk at five years. The study also demonstrated that the insulin-like growth factor, tumor growth factor-beta, and the high mobility group B protein (HMGB1) signaling pathways were the most significant in the gene signature (Kennedy et al., 2011); each pathway was reported to promote tumor growth, invasion, and prevention of apoptosis, or programmed cell death (Nosho et al., 2004, Tsushima et al., 1996, Völpe et al., 2006).

Prostate Cancer

Cooperberg et al. (2013) discussed the use of the Oncotype DX Prostate Cancer Assay to identify risk of metastasis in men recently diagnosed with early-stage prostate cancer. The Oncotype DX test reveals the activity of 17 genes and uses an algorithm to produce an individualized Genomic Prostate Score to indicate the likelihood of tumor spread to other organs or the bone (Cooperberg et al., 2013). This test is a prognostic marker that can be used to guide treatment decisions by patients (NCCN, 2015c).

Summary

This chapter summarized some of the biomarkers and gene panels used to predict treatment and prognosis in different solid cancers. Currently, tests are being developed at an amazing rate, each with more genes and better predictability. CTNs need to be aware
of new literature as molecular testing availability increases for each specific tumor type. Because tumor profiling offers both predictive and prognostic information, CTNs must be knowledgeable as to which mutations are being used to profile different solid tumors and if the implications are different in the various tumor types. For CTNs, it enhances an individualized approach to health care to provide very personalized medicine to patients enrolled in clinical trials in order to offer new hope for alternative approaches to diagnosis or new treatment options for their metastatic, resistant, or recurring cancer (Chu, 2011).

The basics of genetics and molecular analysis on tumor tissue, along with pharmacogenomics and pharmacokinetics, are discussed in Chapter 31.

**Key Points**

- A variety of techniques are used for the molecular analysis of gene and protein alterations associated with profiling malignancies.

- Tumor profiling is used to personalize treatment plans to determine the use or type of chemotherapy or the use of specific targeted therapies for better prognosis and outcomes.

- The Kaplan-Meier curve is used in clinical trials to illustrate the benefit of a drug or treatment as it relates to patient survival.

- A variety of genes serve as biomarkers for specific cancer types, especially breast, lung, colon, and prostate, and are used to determine individualized treatment and prognosis.

- Genetic testing is being developed that can evaluate the presence of multiple genes with one assay.

- Understanding the significance of tumor profiling in oncology clinical trials is crucial to the role of CTNs in interpreting the correct treatment plan and educating patients and families.
References


CHAPTER III

APPLYING THE THEORY OF PLANNED BEHAVIOR IN GENETIC-GENOMIC NURSING PRACTICE

Elizabeth Hassen, Ph.D.(c), MSN, RN, OCN

Linda D. Ward, Ph.D., CNE, FNP-C,
(Clemson University School of Nursing, College of Behavioral, Social and Health Sciences, Clemson, SC)

Margaret A. Wetsel Ph.D., R.N.
(Clemson University School of Nursing, College of Behavioral, Social and Health Sciences, Clemson, SC)

Abstract

Genetic and genomic research impacts screening, diagnosis, and treatment of multiple diseases and conditions. Nurses must be equipped with genomic knowledge, skills, and resources as a foundation for patient/family education, and to help patients and families by providing competent, quality genomic patient care. Ajzen’s Theory of Planned Behavior (TPB) is useful in applying genomics in nursing practice. This article presents the TPB and describes how the constructs of attitude, subjective norm, and self-perceived behavior may impact nurses’ intentions and actual behaviors in the delivery of genomic-competent nursing care. Family history, genomic testing, and financial toxicity exemplars are presented to illustrate the application of genomic knowledge in nursing practice.

Keywords: genetics, genomics, theory of planned behavior, nursing, family history, genomic testing, financial toxicity.
Theory of Planned Behavior in Genetic-Genomic Nursing Practice

As genetic and genomic research and technology have expanded, testing is more readily available, new gene-based treatments are more commonly being used, and genomic information is increasingly applied in health and healthcare (Calzone, Kirk, Tonkin, et al., 2018; Stark et al., 2019). Genetics is the study of individual genes, while genomics is broader and encompasses the study of all genes together, their interactions with each other and the effects of environmental factors. Common health conditions and chronic diseases, such as cancer, heart disease, and diabetes are genomic disorders as they occur due to alterations in multiple genes along with environmental influences (Feero, Guttmacher, & Collins, 2010). This article will use the broader, more holistic term genomics to include both genetic (single gene) and genomic (complex) disorders and interventions.

Genomics plays a role in nearly all diseases and health conditions and increasingly influences health and care across the care continuum (Calzone, Kirk, Tonkin, et al., 2018; Leach et al., 2016). As the number and types of genetic and genomic tests expand, more patients have an option to complete genomic testing. Test results may guide personalized health promotion and disease prevention activities, or additional screening and/or treatment. To provide genomic-competent care to patients and their families, nurses need knowledge of genomic diseases and conditions and their symptoms and treatments, as well as relevant practice policies and resources. This knowledge guides the provision of nursing care across the continuum of assessment, diagnosis, mutual goal setting, planning, implementation, and evaluation. Genomic
knowledge and competency are also essential to educate and advocate for patients and their families (Fu et al., 2019; Williams & Cashion, 2015). Nurses have a professional duty to develop genomic competency in their initial and continuing professional education and translate that competency to action in the care and education of patients and families, and in mentoring colleagues.

Genomic competencies specific to nursing have been articulated and broadly endorsed by the American Association of Colleges of Nursing [AACN] (2008) and American Nurses Association [ANA] (2009). However, practicing nurses continue to report low or poor levels of knowledge and competency in these areas (Aiello, 2017; Anderson et al., 2015; Calzone, Jenkins, Culp et al., 2013). Nurses require knowledge about new genomic tests and technologies, and an understanding about which patients may benefit, as well as evidence-based educational information and resources for patients and their families. Effective use of genomics in nursing practice requires a behavior change, which can be challenging. Applying Ajzen’s Theory of Planned Behavior (TPB) can help nurses to identify challenges and develop strategies to deliver genomic-competent care. This article provides an overview of Ajzen’s TPB and illustrates the theory’s application in genomic nursing practice using three practice-based exemplars.

Theory of Planned Behavior (TPB) and Genomic Nursing

Ajzen’s (1991, 2002) TPB is an explanation of the phenomenon of a behavioral intention or action and is illustrated in Figure 3.1. Ajzen & Fishbein’s initial work (1970, 1980) was described as the Theory of Reasoned Action (TRA) and explored the influence of attitudes and subjective norms on behavioral intention (the intent of performing an act)
and the act or behavior occurring. In 1991, Ajzen expanded TRA to the TPB and included the construct of perceived behavioral control. Perceived behavioral control is described as an individual’s access to resources and opportunities (non-motivational factors), which contributes to intention and behavior.

The TPB is comprised of three constructs: attitude, subjective norm, and perceived behavior control (1991, 2002). Together, these constructs influence an individual’s intention to perform some behavior. This theory can be utilized to inform genomic care in nursing practice (Leach et al., 2016). For example, a nurse may know how to elicit a three-generation family history and believe it to be an important aspect of nursing care (attitude), and she/he may work in a setting that supports family history being embedded into assessment and care (subjective norm). However, if the electronic health record (EHR) has no option for documenting a complete family history with
information about the extended family (perceived behavioral control), the nurse may only document the patient’s personal history and omit information about grandparents, parents and siblings. Without having a three-generation pedigree readily available, the healthcare team may not identify genomic risk factors and therefore miss opportunities to implement recommended screening guidelines or make appropriate referrals. Figure 3.1 illustrates how each TPB construct influences a nurses’ intention to act in applying genomics to the care of patients and their families.

Attitude is defined as, “to the degree to which a person has a favorable or unfavorable evaluation or appraisal of the behavior in question” (Azjen, 1991, p.188). Attitude can be described as affective or evaluative (Ajzen, 1991; Ajzen, 2002). Affective attitude is whether the behavior incites positive or negative feelings in an individual. Evaluative attitude is whether the behavior is viewed as beneficial or harmful to the individual (Ajzen, 1991; Madden, Ellen, & Ajzen, 1992). A person’s affective feelings and the perceived benefit of an action can influence both their attitude and their intention to perform the behavior.

In two studies, almost 70% of nurses felt a need to become more knowledgeable in genomics, demonstrating a positive affective attitude for genomics. They also perceived genomics to be very important to nursing practice (Calzone, Jenkins, Culp et al., 2013; Calzone et al., 2012). Evidence suggests genomic knowledge can positively influence evaluative attitude and promote nurses’ use of genomics in practice (Chen et al., 2018; O’Driscoll et al., 2018; Tanguay et al., 2020). Chen et al. (2018) found that after nurses and other healthcare providers attended a family health history genomics
workshop, they exhibited increased knowledge and a more favorable attitude, which led to an increase use of genomics in their practice as reported in a three-month follow up survey.

Subjective norm is defined as “. . . perceived social pressure to perform or not to perform the behavior” (Azjen, 1991, p. 188). Subjective norms reflect attitudes and behaviors of those who exhibit influence on a person’s behavior. For example, if family members, peers, or the social network support the behavior and/or perform the behavior themselves, then an individual is more likely to perform the behavior.

Because nursing care is delivered in teams, nurses work together, mentor each other, and collaborate to provide the best care for patients and their families. Therefore, attitudes and behaviors of a nurse on a unit or in a department or institution can influence the attitudes and behaviors of other nurses. In addition, institutional and unit-specific nursing competencies, policies, and procedures establish expectations and guide nursing practice. Embedding genomic-competent nurses with leadership skills influences the implementation of genomics in practice (Andrews et al., 2014; Leach et al., 2016). In a multi-site study, genomic training of leadership dyads positively influenced genomic awareness and intention among nursing colleagues and led to resource development for integration of genomics in nursing care (Calzone, Jenkins, Culp, et al., 2018).

Perceived behavioral control is defined as, “. . . the perception of the ease or difficulty of performing the behavior of interest” (Ajzen, 1991, p. 183). Perception includes both internal and external factors of influence (Godin & Kok, 1996). Internal factors of influence include a person’s confidence, capability, and ability to overcome
obstacles and challenges that impact one’s perceived behavioral control. External factors of influence include cost, access to resources, and transportation (Ajzen, 1991).

In the TPB model, perceived behavioral control also has a direct impact on behavior/action. For example, in a study of risk reduction in African Americans with a family history of Type 2 diabetes, researchers examined the influences on behavior change. While diabetes knowledge and family history awareness were the foci of this study, the researchers found that perceived individual control over making lifestyle changes and choices, had the greatest impact on behavior change (Seaborn et al., 2016).

Individually and together, attitudes, subjective norms, and perceived behavioral control affect a person’s intentions to implement a behavior or take an action, as well as whether the behavior is actually performed (Ajzen, 2002). Nurses’ limited genomic knowledge, understanding of the competencies, and lack of confidence can impact their intention, resulting in the inability to use genomics in nursing practice. TPB can guide the implementation of genomic-competent nursing care to improve patient outcomes.

**TPB Applications in Genomic Nursing**

Enhancing nurses’ attitudes, subjective norms, and perceived behavioral control can increase their behaviors in applying genomics to nursing practice. Three exemplars are presented to illustrate the impact of nurses’ genomic knowledge and skills on the care of patients and their families. The first illustrates how a detailed family history (pedigree) can alert the need for referral. The second focuses on patient and family education about genomic testing to guide treatment. The final exemplar describes how
Family History

Nurses at all levels of preparation have a responsibility to assess family history across the healthcare continuum in every setting and specialty (Calzone et al., 2010). Genomic nursing competencies outline specific information to gather when eliciting a family history, including age of disease onset and cause of death (ANA, 2009). Taking a family history is a non-invasive and economical method to obtain detailed information that may identify patients at risk for various diseases and conditions (Ford, Rooks, & Montgomery, 2016; Mahon, 2016).

Exemplar and Discussion: Family History

Mike was diagnosed by his urologist with prostate cancer two years ago at the age of 60. The nurse in the urology clinic, Susan, collected a focused family history. She asked Mike about his medical history and any history of prostate cancer in the family. Unaware of potential genomic implications for Mike and his family, she did not ask about a history of other cancers in family members. Given a negative family history of prostate cancer and Mike’s age of 60 at diagnosis, he was not referred for hereditary (germline) genetic testing.

Now, two years later, Mike’s prostate cancer has been found to have progressed and a referral to an oncologist is made. At the first visit, the oncology nurse, Linda, assesses the patient and completes a more detailed family history. Linda asks Mike if
anyone in his family, including his grandparents, parents, aunts and uncles, siblings, or children, have any history of cancer, other diseases, or health conditions. This detailed family history reveals both breast and pancreatic cancer in the pedigree as illustrated in Figure 3.2. When Linda documents Mike’s family history in the EHR, she also asks about each family member’s age at the time of their cancer diagnosis, and the age and cause of death for any family member who is deceased.

Linda discusses the pedigree and family risks with the oncologist. Examination of the pedigree reveals that Mike’s mother Mary had breast cancer and her brother George had pancreatic cancer, both of which have been associated with mutations in \textit{BRCA} genes. This significant family history is documented in the oncologist’s note and Mike is referred to a genetic counselor, who recommends germline testing. A deleterious germline mutation is detected in \textit{BRCA2}. The identification of the \textit{BRCA} mutation has several implications for Mike and his family. Based on these results, the oncologist can offer Mike targeted treatment or a clinical trial for his prostate cancer. In addition, nurses and/or the genetic counselor can provide education for Mike and his family regarding testing for the children and implementing recommended guidelines for cancer prevention and early screening for all family members. In this scenario, Linda’s actions positively impacted the care management for Mike and his extended family.

A detailed family history is essential to identify all family members who might benefit from early prevention, screening, and testing to guide clinical management. Genetic red flags provide guidance in analyzing a pedigree for possible referral to a genetic counselor or specialist. Red flags include early onset of disease (such as <50
years old), multiple affected generations, and ethnic predispositions (Schaaf, 2016). Guidelines for prevention and screening recommendations for patients identified at high risk have been published by several professional organizations (National Comprehensive Cancer Network (NCCN), 2019; Mital et al., 2016). Without taking a detailed family history including age of diagnosis for diseases and conditions, nurses may miss opportunities to recognize at-risk patients who need referrals. They may fail to educate
these patients on risk reduction strategies and early screenings and/or make appropriate recommendations to the multidisciplinary team.

Applying TPB, genomic knowledge can positively influence affective attitudes, evaluative attitudes and perceived behavioral control, leading nurses to apply genomics in their practice and improve patient outcomes (Chen et al., 2018; O’Driscoll et al., 2018; Tanguay et al., 2020). Nurses need competencies in assessing family history, constructing a three-generation pedigree (including history of diseases and conditions, age of onset, with cause and age of death), identifying red flags, and sharing information with the multi-disciplinary team (American Nurses Association, 2009). Based on this information, the healthcare provider can discuss options and refer patients for prevention, screening, and genomic testing if indicated. By sharing knowledge with patients, families, and colleagues, genomic-competent nurses will facilitate the integration of genomic applications in nursing practice.

Genomic Testing

Nurses, depending on their area of practice, should be familiar with different types of genetic-genomic testing. Genetic testing now extends beyond single gene testing and often involves multiple genes when testing for either germline or somatic mutations. Nurses should be knowledgeable about both types of mutations. Germline mutations are changes in genes that are passed from one generation to another through the DNA in the gametes and are present in the DNA of every cell (NCI, 2020). When germline mutations are suspected, a referral to a genetic counselor is indicated for in-depth testing. Somatic mutations are mutations that occur in specific cells after conception and are not
inherited or passed down to children (NCI, 2020). A variety of tests are available to identify somatic mutations, particularly in cancer cells. Next-generation sequencing (NGS) is technology that allows DNA sequencing of the genomes of particular tissues (Yohe & Thyagarajan, 2017), e.g., sequencing tumor DNA or sequencing fragments of tumor DNA that are found in blood (a liquid biopsy) (Alix-Panabieres, 2020).

Beginning in the 1980s, a type of genetic testing known as companion diagnostic testing was introduced to determine whether a therapeutic treatment is likely to benefit a patient, based on the patient’s genomic profile. The test and the linked therapy are “companions” (Agarwal, Ressler, & Snyder, 2015; Stockley et al., 2016). Examples of companion diagnostics include testing for mutations in genes such as *EGFR* in non-small cell lung cancer, *BRAF* in melanoma, and *KRAS* in colon cancer. When a patient with non-small cell lung cancer is tested and a particular mutation, e.g., *EGFR* L858R, is found, identification of the mutation guides the oncologist to select a treatment targeted to that mutation, such as erlotinib (Tarceva®), osimertinib (Tagrisso®), or gefitinib (Iressa®). Nurses’ knowledge of genomic testing and treatments allows them to answer questions and provide resources for patients and families.

**Exemplar and Discussion: Genomic Testing**

Karen, a 58-year-old woman, had a screening colonoscopy during which a polyp was discovered, removed, and sent to pathology for testing. The pathology report revealed she had colon cancer. Karen was scheduled for a colon resection to remove the area of identified cancer and surrounding lymph nodes. When Karen followed up with her surgeon, Dr. Cook, she learned the pathology showed local invasion of cancer cells.
through the mucosa and two positive lymph nodes. Dr. Cook told Karen she had stage III colon cancer and referred her to an oncologist to discuss further treatment with chemotherapy. To determine the best treatment regimen, Karen’s oncologist explained that her tumor tissue was being tested for a harmful mutation within the KRAS gene in a companion diagnostic test. If a KRAS mutation was identified in the tumor cells, standard chemotherapy would be started; if no mutation was found, a monoclonal antibody would be added to the chemotherapy treatment regimen (NCCN, 2020b).

As no KRAS mutation was identified, Karen began a standard of care treatment regimen, FOLFOX (leucovorin calcium, fluroucaril, and oxaliplatin) with the addition of a monoclonal antibody. Now, six months after Karen completed the initial treatment regimen, a follow-up CT scan is ordered which reveals evidence of a lesion in the liver. A biopsy is performed, and the pathology report indicates Karen now has stage IV metastatic colon cancer. Her oncologist orders next-generation sequencing of the liver lesion tissue to identify mutations specific to her cancer metastases, as these findings can guide treatment decisions and indicate appropriate clinical trials based on mutations found. Karen’s NGS results show mutations in the ATM, TP53, and PALB2 genes in her metastatic tumor cells. Accordingly, the oncologist proceeds with second line standard of care treatment per clinical guidelines. Information in the genomic report can also be used to guide future discussion about options for off-label treatments and clinical trial options.

The KRAS companion diagnostic test is a somatic single-gene test performed on tumor tissue to identify a mutation in a specific single gene (KRAS), to guide selection of treatment options. NGS is a somatic multi-gene DNA analysis which provides
information about many genes and is often completed in the presence of metastatic
disease or when cancer progresses despite treatment. By identifying mutations in
primary or metastatic tumor tissue, NGS allows selection of therapeutic treatments
targeted to particular gene mutations and may lead to identification of clinical trials
available for patients with a particular mutation profile.

The use of companion diagnostic testing guides personalized cancer treatment and
leads to better outcomes and longer survival (Stockley et al., 2016). In recent years,
genome science has identified a number of proteins, hormone receptors, and other
biomarkers that are associated with carcinogenesis and indicate which therapies are most
likely to be effective. Karen’s case provides an example in which a companion
diagnostic test for a KRAS mutation indicate whether a particular treatment (in this case
monoclonal antibody therapy) should be added to a patient’s chemotherapy regimen.
Another example is testing for the HER2 protein in breast cancer. If the HER2 protein is
overexpressed on the surface of tumor cells, then a targeted therapy such as trastuzumab
(Herceptin®) is included in the treatment regimen. This approach has shown drastic
reduction in the size of tumors (NCCN, 2020a). The KRAS mutation and HER2 protein
are examples of identifiable targets that allow targeted therapies to be included in a
patient’s treatment regimen which can improve their response to treatment and survival.

Using TPB, as illustrated in the exemplar, genomic testing knowledge and
resources influence attitudes, subjective norms, and perceived behavioral control.
Knowledge of genomic testing and its use guides treatment discussions and decisions. As
part of the interdisciplinary treatment team, nurses answer patient and family questions; educate them about treatment options; and provide support during and after treatment.

Financial Toxicity

Financial Toxicity is defined as patient concern related to the cost of medical care (NCI, 2020). Financial toxicity affects both non-insured and insured patients. Concerns about health costs for non-insured patients can deter persons from seeking health care. In addition, treatment costs can lead to debt and bankruptcy. Even patients with health care insurance may experience burdensome health costs from high premiums, deductibles, copayments, and non-covered treatments. Financial toxicity is especially likely to affect patients being treated for cancer, which is among the costliest health conditions in the United States, with many treatments costing more than $10,000 per month (NCI, 2020).

Genomic advances such as companion diagnostics and multi-gene testing can lead to targeted therapies that are effective; however, both testing and the treatments are very expensive, even for people with insurance coverage. Recent research identifies that the high cost of quality cancer care limits access to recommended management and is associated with reduced therapy compliance, diminished quality of life, and increased mortality (Carrera, Kantarjian, & Blinder, 2018; De Souza et al., 2017; Yousuf Zafar, 2016). To provide holistic care that recognizes multiple determinants of health, nurses need to incorporate patients’ social factors and knowledge of available health services in order to identify available resources (Office of Disease Prevention and Health Promotion, 2020).
Exemplar and Discussion: Financial Toxicity

Sue, who has been living with breast cancer for 8 years, recently learned that the cancer has spread to her liver despite her current treatment. At Sue’s initial diagnosis, breast biomarker testing was performed on the original biopsy tissue. Breast biomarkers, estrogen receptor (ER), progesterone receptor (PR), and HER2 protein expression are routinely completed at initial diagnosis to guide decisions about clinical treatment, which may include surgery, chemotherapy, and/or radiation. Now that Sue has stage IV metastatic cancer, the oncologist orders somatic multi-gene sequencing (NGS) of metastatic tumor tissue from a recent liver biopsy to identify any additional treatment options or clinical trials for which Sue would be eligible.

NGS is usually performed when a patient is diagnosed with metastatic, stage IV cancer or with progression to stage IV disease despite treatment. Testing of metastases is useful due to cancer’s genomic instability. Genomic instability refers to acceleration of the rate of errors that occur as cancer cells divide, resulting in new mutations that accumulate in subsequent generations of cancer cells (Tubbs & Nussenzweig, 2017). Metastatic cells therefore have additional mutations that were not present in cells of the primary tumor. Genomic instability occurs due to the loss of DNA repair mechanisms that protect normal cells (Tubbs & Nussenzweig, 2017). Most NGS is ordered with disease progression since there is an increased chance to find a mutation due to the genomic instability and cancer progression.

Sue returns to clinic today for a follow-up visit to receive her NGS results. Sequencing shows a PIK3CA mutation in the metastatic cells. Alpelisib (PIQRAY®) has
been approved by the Federal Drug Administration (FDA) for PIK3CA mutated, hormone positive (ER and PR), HER2 protein negative breast cancer. Based on Sue’s known ER and PR positive, HER2 negative biomarkers from her earlier testing, along with the identification of the PIK3CA mutation in metastatic cells, the oncologist will discuss treatment with PIQRAY, which costs an estimated $19,000 per treatment each month. Patients typically remain on this treatment until their cancer progresses or side effects make treatment intolerable. Although PIQRAY and other targeted therapies are FDA approved, many have high co-payments.

When Sue is seen for her follow-up appointment, the nurse, John, asks her about any symptoms she is experiencing. Sue tells John that she has had increasing pain and fatigue, but no nausea, vomiting, or diarrhea. When John asks Sue how her pain and fatigue are impacting her activities of daily living, Sue begins to cry and says that she has not been able to work for 3 weeks. The loss of her income has significantly impacted her family and she is concerned about losing her job and what it could mean for her family, income, and insurance coverage.

After Sue and the oncologist discuss the recommended treatment with PIQRAY, John seeks approval for the targeted therapy from Sue’s insurance company and co-payment assistance from the pharmacy. He involves the multi-disciplinary team, including a nurse navigator and social worker, to support Karen. John’s recognition of the multiple determinants of health, including costs and the impacts of side effects of cancer and cancer treatment on daily activities for patients and their families, prompts him to assess Sue’s resource needs; identify and provide information about available
resources; and make appropriate referrals. These nursing behaviors are part of providing holistic care and are associated with improved patient outcomes.

Financial toxicity impacts medication adherence, health outcomes, and quality of life (Neugut et al., 2011; Dusetzina et al., 2014; Yousuf Zafar, 2016). Transportation needs, medication costs, genomic testing costs, and unnecessary follow-up visits can impact costs of care. Lack of resources have been noted as a barrier to care in multiple studies (Curtis et al., 2019; Sperber et al., 2016). Having financial aid forms, medication assistance programs, and resources available for patients who are undergoing genomic testing and treatment helps nurses to address and ease patients’ financial concerns. Involving nurse navigators, social workers, and the entire healthcare team in assessing needs, coordinating care, and providing care offers support to patients and their families during treatment into survivorship. Utilization of nurse navigators and a multidisciplinary healthcare team approach can offer opportunities for open discussions about stressors experienced by patients and their families, leading to support, improved care coordination, and resource utilization (Fessele, 2017). The Oncology Nursing Society (2017) offers a variety of resources for nurses, including an Oncology Nurse Navigator Toolkit with a module on, “Helping Patients Navigate Financial Issues”.

The TPB constructs of attitude, subjective norms, and perceived behavioral control have direct influence on behaviors nurses perform. Nurses’ awareness of the benefits of reducing stress (positive attitudes) for patients and their families by providing resources, with a supportive multi-disciplinary team that collaborates to provide holistic care, can increase nurses’ intention and use of genomics (behavior). Connecting patients
and their families with nurse navigators, social workers, financial assistance programs, and other resources are important aspects of applying genomics in nursing practice.

Conclusions

The utilization of genomics in healthcare has increased exponentially in the post-genome era. Research has demonstrated the positive impact of genomic applications in health promotion, prevention, screening, testing, detection, and treatment of various diseases and conditions. Nurses have a responsibility to educate themselves and their patients about genomics and apply their knowledge and skills in their care of patients and families.

Ajzen’s TPB guides understanding of how intentions and behaviors are influenced by attitudes (affective and evaluative), subjective norms, and perceived behavioral control. The exemplars demonstrated the impact of the TPB constructs on the application of genomics (behavior). Understanding the influences of these constructs on nurses’ intentions and actual behavior can inform strategies to promote genomic-competent care.

As members of the healthcare team, nurses make critical contributions to patient outcomes by completing patient risk assessments; providing support; facilitating referrals, testing and resources; and participating in discussions about evidence-based treatment decisions. The advancement of genomics in nursing requires nursing knowledge and awareness of recommended guidelines, cultivation of genomic nursing leaders, institutional support, and evidence-based resources for patients and their families. In this way, nurses at all levels will be empowered to incorporate genomics into their nursing practice.
References


CHAPTER IV

ASSESSMENT OF GENOMIC USE IN CLINICAL NURSING PRACTICE

Abstract

Aim: To describe nurses’ attitudes, perceptions, and experiences with the application of genomics in nursing practice and what barriers are identified to its use.

Background: Genomics impacts patient and families across the health care continuum. Research reveals a gap between genomics in nursing education and practice. While nursing students, faculty, and nurses’ genomic knowledge and confidence are consistently reported as ‘low’, less is known about how genomics is used by nurses in hospitals.

Design: Cross-sectional study.

Methods: A mixed-methods study was conducted with registered nurses at two hospitals. A 28-question survey, based on the Theory of Planned Behavior (TPB), was distributed electronically to nurses at two hospitals (n=151, quantitative component). The survey results were used to develop focus group questions for an in-depth exploration of barriers to applying genomics in nursing practice (n=7, qualitative component).

Results: The survey revealed that most participants lacked genomic knowledge and felt unprepared to take a family history with a genetic focus, identify “red flags” for inherited disorders, and use genomics with genetic testing, medications, patient teaching, and referrals. Six themes emerging from focus group discussions on the application of
genomics in nursing practice were: knowledge, family history, genetic counseling, genomic testing, support and barriers.

**Conclusions:** Nurses need genomic knowledge and resources to answer patient and family questions, provide patient education, and deliver genomic-competent care. Based on these findings, implementation research using the TPB is needed for nurses to promote the use of genomic-competent care.

**Relevance to Clinical Practice:** Nurses need genomic knowledge gained through nursing entry level and continuing education program, and institutional support for the application of genomics in nursing practice.

**Keywords:** genomics, nursing practice, Theory of Planned Behavior

**Introduction**

Genomics impacts screening recommendations, diagnosis, and treatment of patients, requiring nurses to have an increased knowledge in genomics for patient care (Calzone et al., 2012). Research findings reveal a gap between genomic knowledge and the application of genomics in nursing practice (Aiello, 2017, Anderson et al., 2015, Calzone, et al., 2013; Calzone et al., 2012). The American Nurses Association ([ANA], 2009) published the *Essentials of Genetic and Genomic Nursing: Nursing Competencies, Curricula Guidelines, and Outcome Indicators*. These competencies guide nursing faculty in developing curricula that embed critical genomic concepts to prepare nurses for genomic-competent care. Although the Essentials were first published in 2006, investigations reveal a gap between nursing education and genomic literacy (Daack-Hirsch, Dieter, & Griffin, 2011; Kirk et al., 2011; Calzone et al., 2013; Read & Ward,
Ajzen’s Theory of Planned Behavior (TPB, 1991, 2002) was used as the framework for this study. The purpose of this mixed methods study was to explore the attitudes, subjective norms, and perceived behavioral control that impact nurses’ intentions and use of genomics in nursing practice.

Background

Daack-Hirsch et al. (2011) assessed the genetic literacy of faculty and students and concluded that faculty needed to be aware of their own knowledge in order to prepare nursing students with genetic knowledge. In their benchmark survey of 1000 nurses, Calzone et al. (2013) found that only 15% had a genomics course in their nursing education program. Kirk et al. (2011) examined nursing curricula and identified five barriers to the integration of genomics, including educators’ lack of knowledge, lack of awareness at the government level, limitations of resources, lack of the ‘patient voice’, and lack of evidence regarding outcomes.

The Secretary’s Advisory Committee on Genetics, Health, and Society ([SACGHS], 2011) examined education and training issues for point-of-care health professions, including nurses, public health providers, and consumers and patients. The commission found a lack of genetic literacy in faculty, a limited incorporation of genetics in already “crowded” curricula, and the presentation of genetics content that did not lead to long-term knowledge retention were barriers to translating new genetic knowledge into practice (US Department of Health and Human Services [USDHHS], 2011). Read and Ward (2016) surveyed nursing faculty about genetic/genomic knowledge and compared these results to a previous survey of students. Most faculty respondents rated their
genomic knowledge as “fair” or “poor,” which was consistent with their mean score of 48% on the Genomic Nursing Concept Inventory (GNCI), a scale used to measure the understanding of genetic/genomic concepts most critical to nursing practice (Ward et al., 2014). Faculty performance on the GNCI was slightly higher than students, who achieved a mean score of 42% correct. Read and Ward (2016) recommended that faculty need to be proactive in seeking out genomic education as student competency is dependent on faculty knowledge, understanding, and competency in genomics.

In addition, SACGHS also noted that genomic competencies were not reflected in the standards for licensure (USDHHS, 2011). The National Council of State Boards of Nursing (NCSBN) is the regulatory body for the licensure examination which all nursing program graduates are required to pass in order to be licensed and practice as registered nurses. The current test plan has the term genetics/genomics listed only once and it is in relation to health history and risk assessment (NCSBN, 2018). The lack of substantive inclusion of genomics in the National Council Licensure Examination (NCLEX) test plan illustrates the gap between genomic nursing education and practice.

A lack of genomic knowledge has also been found in practicing nurses. Calzone et al. (2013) found that over half of the 619 nurses in their study reported their knowledge of genomics as “poor” to “fair” and had never heard of the ANA Essentials (2009). When examining the of integration of genomics in practice, they also found that 60% of the participants lacked family history assessment skills. A baccalaureate nursing education was correlated with the likelihood of “often” or “always” collecting a family history (Calzone et al., 2013). In a study of nurses, Rogers et al. (2017) measured
genomic knowledge after a 12-month education initiative at a Magnet hospital. Their results revealed that repeated education and exposure was needed to prepare nurses for the application of genomics in practice. Calzone et al. (2013) recommend that an immediate challenge for nursing is to prepare a genomically competent workforce. Rogers et al. (2017) reiterated the importance of genomic as nurses have an essential role in providing genomic-competent care.

While studies provide guidance on genomic application in nursing, including the use of case studies, research on the use of genomics in nursing practice from the nurses’ perspective is lacking. This study was guided by two research questions. The quantitative question is: What are the attitudes, perceptions and experiences of registered nurses at two upstate South Carolina hospitals regarding the application of genomics in their practice? The qualitative question is: What are the attitudes, perceptions and experiences of registered nurses at two Upstate South Carolina hospitals regarding the barriers to application of genomics in their practice?

Methods

Setting

The study was conducted at two upstate South Carolina hospitals, one with 461-beds and the other 540-beds. Clemson University and each hospital’s Institutional Review Board (IRB) approved all procedures.
Design

A mixed methods design was used for this descriptive study. Quantitative data was collected using a Qualtrics® survey questionnaire. Qualitative data was obtained through focus group interviews.

Theoretical Framework

Ajzen’s (1991) Theory of Planned Behavior (TPB) was used as the framework for this study. TPB constructs are attitude, subjective norm, and perceived behavioral control, all of which influence behavioral intention. Attitude is defined as, “to the degree to which a person has a favorable or unfavorable evaluation or appraisal of the behavior in question” (1991, p. 188). Subjective norm is defined as “. . . perceived social pressure to perform or not to perform the behavior” (1991, p. 188). Perceived behavioral control is defined as, “. . . the perception of the ease or difficulty of performing the behavior of interest” (1991, p. 183). Individually and collectively, attitudes, subjective norms, and perceived behavioral control affect a person’s intentions to implement a behavior or take an action, as well as whether the behavior is performed (Ajzen, 2002). Leach et al. discussed theories associated with the implementation of genomics in nursing practice and identified Ajzen’s Theory of Planned Behavior (TPB) as the “core underpinning theory” (2016, p. 311). TPB constructs can be used to understand the application of genomics in nursing practice, identify barriers in its use, and make recommendations about strategies to promote the application of genomics in nursing practice.
Quantitative Methods

The quantitative research question is: What are the attitudes, perceptions and experiences of registered nurses at two upstate South Carolina hospitals regarding the application of genomics in their practice?

Sample

A convenience sample of registered nurses (RNs), who provide direct care to patients were invited to participate in the study through an email invitation, by hospital administration, with a link to the consent form and survey. Inclusion criteria were associate or baccalaureate degree in nursing, not currently enrolled in school, working in a clinical setting, licensed as a registered nurse in South Carolina, and not a travel nurse.

Instrumentation

Respondents were required to select ‘I consent’ to continue to a 27-question Qualtrics survey. The survey was designed by the investigator, based on the constructs of TPB, to investigate the application of genomics in nursing practice. The first seven questions elicited demographic information about the respondents, including nursing experience and genomic nursing education. Using Ajzen’s (2002) TPB questionnaire development considerations, 15 questions were developed which described nurse’s attitudes regarding genomics; their experience using specific genomic concepts based on established genomic competencies; and nursing administration and colleague support of genomics at the healthcare institution or on the nursing unit. Responses to these questions were measured using Likert scales with counterbalanced adjective pairs as
endpoints (positive and negative). Four questions asked about the use of specific genomic competencies in nursing practice (Yes or No responses). The final two questions allowed open-ended narrative responses to explore respondents’ views on the barriers and challenges which impacted the use of genomics in their nursing practice and about their experience with genomics. The survey questions were independently reviewed by genetic and research members of the investigator’s Ph.D. dissertation committee to validate that questions addressed the TPB constructs.

Analysis

Descriptive statistics, including means, modes and percentages, were calculated for the responses on the 28-item survey. Results were analyzed individually for each item and collectively for each TPB construct.

Qualitative Methods

Research Question: What are the attitudes, perceptions and experiences of registered nurses at two upstate South Carolina hospitals regarding the barriers to application of genomics in their practice?

Sample

A convenience sample of nurses who participated in the quantitative survey were recruited for a focus group held at each of the Upstate South Carolina hospitals.
Procedures

Nurses, who responded to the quantitative survey, were invited to participate in the focus group by emailing the investigator after completion of the survey. A one-hour focus group was held at each Upstate of South Carolina hospital to conduct an in-depth exploration of the application of genomics in nursing practice. Participants received and signed a consent form prior to the start of each focus group. Participants were informed about the study purpose and that the session was being recorded with a digital audio recorder and a video camera as a backup (sound only). Prior to the start of each focus group, a brief statement about the research and a definition of genomics was read. At each focus group, refreshments were available, and each participant’s name was placed in a drawing for a year’s membership in a nursing organization of the participant’s choosing, held at the end of each focus group session.

In each focus group, the investigator and focus group moderator read the same 10 open-ended questions. These questions were developed by the investigator based on the quantitative survey results (TPB attitudes, subjective norms, and perceived behavioral control) and on the nurses’ intention to apply genomics in nursing practice. For example, over 50% of nurses reported “little” to “no” comfort in taking a family history on the survey. This information guided the development of the following focus group question, “Describe how you take a family history on your patient? Which family members do you include in the history?” Family history, attitude towards genomics, genomic education, genomic tools in the electronic health record, and barriers to use were explored in each focus group. After each session, responses were transcribed verbatim by the investigator.
The identification of emergent themes and patterns of meaning were completed using content analysis and using NVivo, a qualitative data analysis software.

Analysis

The investigator read through each transcript twice to familiarize herself with the data prior to coding. During the third reading, the investigator highlighted repeated terms in each transcript and made a list of the terms which were used to identify emergent themes. Next, the transcribed files were uploaded into NVivo for analysis. Nodes were entered to code the transcribed data, and emergent themes and patterns were identified. The transcripts, data, emergent themes and patterns of meaning were reviewed for rigor and accuracy by a qualitative methodologist, who did not have a background in genomics or nursing.

Findings

Quantitative Findings

Participant Demographics

One hundred and fifty-one registered nurses, employed at two upstate South Carolina hospitals, completed the survey. The typical respondent was female (93%), white (93%) and held a baccalaureate degree in nursing (77%). Nurses who participated in the study were more likely to have a baccalaureate degree than other nurses in South Carolina ([50%), (South Carolina Office for Healthcare Workforce, 2018) or nationally ([41.7%], NBSBN, 2017). National data is based on RNs who reported a BSN as the degree that qualified them for their first US nursing license. Thirty-four percent of the
respondents reported they had learned about genomics in nursing school, but only 8% had a genetics/genomics course in their nursing program. The participant’s nursing experience ranged from 1 to 56 years (mean=14 years, mode=5 years). Table 4.1 presents the nursing specialties in which study participants were working.

Survey Results

The survey examined TPB’s constructs (attitude, subjective norms, and perceived control behavior) applied to genomics using 5-point Likert scales. Attitude was measured by two questions. For affective attitude (if the use of genomics elicited positive or negative feelings) 43% of the respondents rated their attitude as a 4 or 5 (positive) and 50% reported neutral attitude (3). When asked about evaluative attitude (if the behavior is beneficial or harmful to the individual), 44% responded that genomic information was beneficial for patients, 19% responded that it was overwhelming, and 37% had no opinion.

Subjective norms (a reflection of those who influence nurse’s attitudes and behavior) was measured by questions on the institution, nursing management, and peers. Most participants reported “little” to “no” support for using genomics by the nurse manager or leader and the institution as shown in Table 4.2. The majority (92.67%) rated their peers as using genomics “little” or “none at all.” Genomic concepts were not included in unit competencies for the majority (91%) of these nurses.

To investigate perceived behavior control (the perception of how easy or difficult it is to perform the behavior), questions were asked about experience with genomic concepts based on the competencies endorsed by the American Association of Colleges
Table 4.1. Specialty Type.

<table>
<thead>
<tr>
<th>Nursing Specialty</th>
<th># of Nurses</th>
<th>% of Nurses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical-Surgical</td>
<td>30</td>
<td>21.19%</td>
</tr>
<tr>
<td>Oncology</td>
<td>9</td>
<td>5.96%</td>
</tr>
<tr>
<td>OB</td>
<td>12</td>
<td>7.95%</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>6</td>
<td>3.97%</td>
</tr>
<tr>
<td>Cardiac</td>
<td>34</td>
<td>22.52%</td>
</tr>
<tr>
<td>Other</td>
<td>58</td>
<td>38.41%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>151</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

Table 4.2. Subjective Norm Responses.

<table>
<thead>
<tr>
<th>Questions:</th>
<th>A Great Deal</th>
<th>A Lot</th>
<th>Moderate Amount</th>
<th>A Little</th>
<th>None at all</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does your manager/leadership support the use of genomics in your practice?</td>
<td>2.67%</td>
<td>6.67%</td>
<td>20%</td>
<td>26.67%</td>
<td>44%</td>
</tr>
<tr>
<td>Does your clinical organization demonstrate support towards genomics?</td>
<td>1.33%</td>
<td>8%</td>
<td>26%</td>
<td>27.33%</td>
<td>37.33%</td>
</tr>
<tr>
<td>Do your peers utilize genomic practices or competencies in their clinical practice?</td>
<td>1.32%</td>
<td>0%</td>
<td>5.96%</td>
<td>32.45%</td>
<td>60.26%</td>
</tr>
<tr>
<td>Does your hospital or unit competencies include genomic concepts?</td>
<td>0.67%</td>
<td>0.67%</td>
<td>7.33%</td>
<td>14.67%</td>
<td>76.67%</td>
</tr>
</tbody>
</table>

of Nursing ([AACN], 2008) and American Nurses Association ([ANA], 2009). These included: family history, identification of ‘red flags’, pharmacogenomics, and genetic testing. As presented in Table 4.3, these nurses reported “little” to “none at all” comfort or experience applying genomic concepts in nursing practice, e.g., obtaining a family history 54%, identifying “red flags” 63%, using genetics for appropriately identifying medications for patients (pharmacogenomics) (91%), knowledge and experience with genetic testing (96%) and identifying referrals (94%). Survey revealed that 77.48%
Table 4.3. Responses on Experience with Genomic Concepts.

<table>
<thead>
<tr>
<th>Questions:</th>
<th>A Great Deal</th>
<th>A Lot</th>
<th>Moderate Amount</th>
<th>A Little</th>
<th>None at all</th>
</tr>
</thead>
<tbody>
<tr>
<td>How would you rate your comfort level with obtaining a family history of a disease/disorder?</td>
<td>9.27%</td>
<td>14.57%</td>
<td>22.52%</td>
<td>27.81%</td>
<td>25.83%</td>
</tr>
<tr>
<td>Do you have any experience with identifying ‘red flags’ of inherited family diseases/disorders?</td>
<td>0.0%</td>
<td>9.27%</td>
<td>27.81%</td>
<td>41.72%</td>
<td>21.19%</td>
</tr>
<tr>
<td>Do you have any experience using genetics for appropriately identifying medications for your patient (pharmacogenomics)?</td>
<td>0.0%</td>
<td>2.65%</td>
<td>5.96%</td>
<td>19.21%</td>
<td>72.19%</td>
</tr>
<tr>
<td>I have ___ knowledge and experience with genetic testing in the clinical setting?</td>
<td>0.0%</td>
<td>1.32%</td>
<td>2.65%</td>
<td>33.11%</td>
<td>62.91%</td>
</tr>
<tr>
<td>I have _____ experience identifying when patient should be referred for genetic testing?</td>
<td>0.66%</td>
<td>1.32%</td>
<td>4.64%</td>
<td>37.09%</td>
<td>56.59%</td>
</tr>
</tbody>
</table>

of nurses do not take a three-generation family history as recommended by the ANA *Essentials of Genetic and Genomic Nursing* (2009).

The final asked participants whether they used genomics in nursing practice and if they utilized resources (behavior). The overwhelming majority (80%) responded they did not currently use genomic concepts or services (genetic counselors or testing) in their nursing-practice. Of the 12% who used genomics, the use was related to genetic testing, referrals for genetic counseling, oncology research, anesthesia, breast cancer, Type 2 diabetes, and cardiac care. Only 12% of those surveyed utilized genomic tools or resources either on their unit or online, e.g., breast cancer gene testing, research studies, and National Comprehensive Cancer Network (NCCN) Guidelines. Documentation tools used included the following: family history (EPIC®), admission history, and referral for
other genetic testing. Of these participants, 21% had spoken to a healthcare provider about a high-risk patient regarding genetics.

The quantitative survey concluded with two open-ended questions: one which asked barriers and challenges these nurses experienced utilizing genomics in practice, and the other perceptions or experiences with genomics. The most common responses to barriers and challenges were little knowledge/lack of education about genomics (39%), not seeing genomics as applicable to their practice (19%), not enough time/time consuming (11%), and cost of testing (6%). Other perceptions nurses shared about genomics included a desire to learn more about genomics and available resources. The nurses described additional genomic experiences such as having personal genetic testing, working with genetic counselors in oncology, and seeing the impact of genomics on cancer patient treatment.

**Qualitative Findings**

**Participant Demographics**

Sixteen nurses responded to the invitation to participate in the focus groups. Due to challenges in scheduling a time for the focus groups related to the participants working different shifts, only seven nurses (Hospital 1=4, Hospital 2=3) participated in a focus group. Five nurses worked on inpatient units (oncology, labor and delivery, neurology, and recovery) and two nurses worked in a hospital-based outpatient clinic (oncology support).
Themes

Six themes emerged related to participants’ use of genomics in nursing practice: knowledge, family history, genetic counseling, genomic testing, support and barriers.

Knowledge

Knowledge was a broad theme that included three sub-themes, “understanding,” “educate,” and “competency.” The following quotations of participants captured feelings about the value of genomic knowledge, “You want to speak with confidence and that’s something that’s hard to speak confidently about because…it requires such a knowledge base” and “. . . involving those people who specialize. . . in that knowledge field [genomics] is imperative.” The participants discussed their lack of genomic knowledge and education which they believed impacted their use of genomics in practice and their ability to educate patients and families.

Participants were interested in additional genomics education. The importance of genomics was discussed, by the focus group, related to increasing their knowledge for their own understanding and so that they would be better prepared to educate patients. One participant stated, “Understand your subject better [and] you’re able to educate people.” Participants also discussed their desire to have training on genomic topics and about referral resources for testing. One participant shared that when she looked for genomic educational opportunities, she did not see any announcements or notifications for genomic continuing education. Another participant shared that she had started the Oncology Nursing Society (ONS) genomics course because it was available at no cost. However, she was unable to finish the course due to the amount of information presented
during the time-period that access was allowed. Finally, there was lack of awareness about the genomic competencies published by the ANA (2009) and AACN (2008, 2011).

Family History

To explore family history, participants were asked if they took family histories, how many generations they inquired about, and how they documented family histories. The responses ranged from taking at least a two-generation pedigree, including age and cause of death of those deceased, to only asking about a patient’s history. An experienced, acute care participant shared, “So back then, we would kind of ask about family history but now we don’t really. We ask about a patient’s history, but family history is done in the offices and is put in there. If anesthesia sees the patient, they will ask a little bit more in depth family history.” An oncology nurse participant stated, “I usually think about two generations and ages at diagnosis and which specific diagnosis [the person] had or passed away from.” One participant related the lack of depth in asking about the family history to the electronic health record, “Our EPIC. . . I’m not sure it goes that deep into family history.”

Genetic Counseling

Asking participants about their experiences with genetic referrals, they discussed genetic counseling. One participant stated that the time slots for genetic counseling were filled at their institution, thus illustrating the need. Another participant shared that she called patients to explain the purpose of genetic counseling and testing. This participant stated, “Any of the physicians can refer for genetic counseling. I can only speak to that.
But our priority is given to patients that need the appointment for a treatment decision.”

The participants in the focus groups shared that genetic counselors were involved in the oncology multidisciplinary conferences at both hospitals.

Participants felt that genetic counselors should be involved when the patient is undergoing genetic testing because these counselors understand the ethical issues and treatment implications. One participant stated, “Involvement of the genetic counselor involves more than just delivering a test result.” Another expanded on this by saying, “. . . [when] consenting someone for a test… they [genetic counselors] involve things like ethics and . . . the implications of knowing or not knowing [the genetic testing results], that probably don’t take place in a physician visit discussing genetics and genomics.”

Although the participants felt the services provided by genetic counselors are important, they shared that some physicians ordered genetic tests themselves and did not involve genetic counselors.

**Genetic Testing**

Qualitative data revealed that genetic testing is being done by providers from a variety of disciplines. Genetic testing was ordered for oncology patients, in labor and delivery for fetal demise, in pediatrics, and for adults with symptoms of rare diseases. One participant noted that testing is now more available, “I think for us in cancer care. . . we have just started doing genetic testing here at the campus. . . I think it’s opened up more doors for our community to be able to participate in testing. . .” Labor and delivery nurses shared a different perspective, “So, genetic studies are not done very often. Medicaid won’t pay for them which is a large population that we have and the doctor’s
let them know [that test results are] . . . going to take like three months to come back and most likely it will not give you any answers.”

Several participants indicated that most of their knowledge was from either personal experience or a friend’s experience with genetic testing, not from their baccalaureate nursing program. One participant, who underwent genetic testing herself for a rare disease, stated, “. . . it took eight years. . . . the Mayo Clinic decided to do genetic testing and they found that we had this neurological disorder and that’s [genetic testing] the only thing that diagnosed us [participant and sister].” Another participant discussed a friend and coworker’s experience of having her daughter tested due to development delays. Both participants’ personal experience or friends’ experiences led these nurses to seek out more genomic information and continuing education.

Support

Discussions of organizational support in the focus groups suggested that promotion of genomic integration existed but there was a lack of knowledge about what specific support was needed. “They’re [hospital leadership] all supportive. I think they’re all inquisitive about what it entails.” One participant felt that physicians were supportive but was unsure of how her nurse manager felt about genomics. This nurse stated, “I mean our physicians work with us about it [genetics] and our surgical techs. . . I have never and I’ve never seen anyone even talk to our boss [about genetics], so I don’t know.” One participant illustrated organizational support for genomics by saying that policies were in place to prevent discrimination in hiring those with genetic conditions.
The lack of conversations about genomics, support for genomics, and mentorship from nurse managers warrants further exploration.

**Barriers**

Knowledge, support, and costs were identified multiple times in both focus groups as barriers to the utilization of genomics in nursing practice. Participants felt they needed knowledge to explain genomics, answer questions, and speak with confidence to patients and families about genomics. One participant stated, “Barriers to being able to properly educate patients…nurses [don’t] . . . fully understand the process . . . we aren’t actually doing anything except filling out a form.” All focus group participants expressed the need for more continuing education as well as grant support for education and research. One nurse stated, “[It’s] just lack of education. Maybe we could have some mandatory education through our clinical unit educator to help us understand.” Another said, “I would like more continuing education opportunities.”

Cost was viewed as a barrier to genomic testing because of the expense of testing (in addition to already high health care costs), the potential lack of coverage for testing by insurance companies, and the possibility of testing results providing no answers regarding the cause of a condition. “Cost, because it’s probably going to be one of the first things they [patients] ask,” illustrated these nurses’ concerns about the costs of testing, insurance coverage for testing, and the ability to answer questions about testing for their patients. One participant shared, “First of all, they have to understand what’s going on . . .” She went on to explain that she felt it is hard for patients to understand they may have to pay for an expensive test which may not provide any answers.
Discussion

Results of this study support previous research findings indicating gaps between genomic education and the application of genomics in nursing practice still exist. While over 75% of participants had a baccalaureate degree in nursing, only 34% reported learning about genomics and only 8% had a genomics course in their nursing program. Data illustrates a lack of genomic content in nursing curricula and the importance of genomic continuing education and attending genomic themed conferences/sessions.

Themes identified in the qualitative component of this study reaffirmed knowledge and application deficits identified in the quantitative survey. Participants felt that genomic knowledge is needed and important; but that barriers exist in providing genomic-competent care to their patients. The quantitative survey’s findings of “Little to no comfort” in obtaining a family history was confirmed in the focus group discussions. In the focus groups, most participants expressed that they only asked about the patient’s history. This may explain the lack of experience in identifying “red flags” in patients for genetic testing among the participants.

The focus groups also illustrated that while nursing administration and nurse managers may support genomics, there was a lack of understanding about what that support should entail. Few participants shared the inclusion of genomic education in their current position, mirroring the survey findings that 90% of participants felt that there was little to no emphasis on genomic competencies in their hospital or on their unit. These findings were also reflected in the lack of knowledge and support for genomics barriers identified in the focus groups.
Gaps continue to exist for both knowledge and use of genomics in nursing practice. Calzone et al. (2013) found that participants in her study were unaware of the *Essentials of Genetic and Genomic Nursing: Nursing Competencies, Curricula Guidelines, and Outcome Indicators* (ANA, 2009). The results of this study were consistent with Calzone et al. (2013) findings and was illustrated by the following focus group statement, “I’m not aware of which bodies [that] verify competency …of people providing services.” Finally, a lack of confidence in taking a family history was also found in both components of this study. These findings align with the results of other studies on nurses in practice, underscoring the need for and importance of continuing education in genomics for nurses.

**Strengths and Limitations**

A strength of this investigation on genomic knowledge and application in nursing practice was having a mixed method approach. One hundred and fifty-one nurses, working on a variety of specialty units, responded to the Qualtrics survey examining attitudes, subjective norms, perceived behavioral control, and barriers in using genomics in nursing practice. The quantitative results guided the development of focus group questions to further explore these challenges. The qualitative findings added to the depth of understanding about the attitudes, subjective norms, and perceived behavioral controls of using genomics in nursing practice. Both sets of findings were consistent with the results of previous studies on nurses’ knowledge and use of genomics in practice. Study limitations included utilization of a convenience sample for both the quantitative and
qualitative components of this investigation and that few nurses were able to participate in the qualitative component due to scheduling.

Implications for Practice

The findings of this study revealed that nurses need genomic knowledge and resources to answer patient and family questions, provide patient education, and deliver genomic-competent care. Competency-based continuing education in genomics is key to closing the education-practice gap. The participants in this study viewed support from their peers, front-line nurse managers, and institutions as essential to increasing an awareness and implementation of genomics in hospitals. Based on these findings, the next steps are the following: initiate genomic education implementation studies, using the TPB; develop an infrastructure to integrate and support the utilization of genomic competencies in nursing practice; provide genomic resources for patients and families; and promote delivery of genomic-competent care by nurses.

References


CHAPTER V

SUMMARY, LIMITATIONS, AND RECOMMENDATIONS

Since completion of the Human Genome Project in 2003, genomic research has generated increased knowledge, advanced the use of technology, led to the creation of huge data bases and new bioinformatics applications, and expanded genomic applications in healthcare (Aiello, 2017; Shendure, Findlay, & Snyder, 2019). Genomics impacts patients and families across the healthcare continuum, including prevention, screening, diagnosis, and treatment (Calzone et al., 2018). Across this continuum of care, nurses are called to provide patient-centered care across a wide variety of settings, e.g., community, hospitals, clinics, offices, and long-term care. As the largest group of health care professionals, nursing professionals must take responsibility to educate themselves about genomics, achieve professional competencies, and apply genomics in patient care (Jenkins, 2019). As genomic applications in healthcare continue to expand, nurses will need to acquire new genomic knowledge and skills to provide genomic-competent care.

The Doctor of Philosophy degree program in Health Care Genetics in Clemson University’s School of Nursing was designed as an interdisciplinary program to prepare graduates to generate knowledge and develop theories focusing on genomics and health; translate genomic knowledge from a variety of disciplines; formulate genomic-focused health promotion, disease prevention and treatment strategies; and lead the development and application of ethical guidelines and health policy in genomics (Clemson University, School of Nursing, 2020). The HCG care model presented in Chapter I illustrated an interdisciplinary approach to healthcare genetics and genomics. The central/core
concept, healthcare genetics/genomics, has linkages to genetics/genomics, education, clinical testing and therapeutics, environment, and ethical, legal, and social implications concepts. Guided by the HCG model, this dissertation explored the HCG model concepts through scholarly works in Chapters II and III and a research study describing the application of genomics in nursing practice in Chapter IV.

Chapter II

Tumor Profiling and Genomic Testing

Chapter II, Tumor Profiling, described and explored molecular profiling in oncology. This chapter contributed to the development of genetics/genomics, education, and clinical testing and therapeutics concepts in the HCG model. The chapter defined single-gene biomarkers and multigene tests and their use as both prognostic and predictive indicators. The chapter also presented use of the Kaplan-Meier survival curve to evaluate the impact of interventions, such as oncologic treatments, on survival.

Chapter II also described how molecular testing is utilized in the field of oncology to guide patient discussions on treatment recommendations. Breast cancer biomarkers (ER, PR, HER2) are used in diagnostic evaluations and to guide treatment recommendations. Three breast cancer assays (Oncotype DX, MammaPrint, Mammostrat), used in evaluating recurrence risk, offer information to help guide discussions and decisions about breast cancer treatment plans. In lung cancer, for example, a genetic mutation in EGFR has an identified targeted therapy associated with increased survival. Genetic tests to identify aberrations in the ALK and KRAS genes and
measure expression of enzymes ERCC1 and RRM1 have also shown prognostic value in lung cancer.

Colon cancer also has recognized biomarkers with treatment implications. For example, KRAS mutations impact treatment recommendations for the addition of monoclonal antibodies. As with breast cancer, several assays are utilized to predict recurrence risk. Finally, a genomic test for prostate cancer can be used to guide treatment decisions, e.g. surveillance versus radiation. In each of these examples, molecular testing guides discussions and decisions about treatment options.

Limitations

With rapid growths in research and technology, the types and utilization of biomarker and genomic testing has expanded. Since the publication of the Chapter II manuscript in 2015, the number of genetic mutations used to guide treatment recommendations and decisions, has increased significantly, as has access to expanded multi-gene genomic tests. For example, the manuscript described mutations in two genes, EGFR and ALK, for lung cancer. In the 2020 National Comprehensive Cancer Network (NCCN) guidelines, testing for seven different biomarkers, each associated with an FDA approved therapy, is now recommended for advanced and metastatic lung cancer.

Recommendations

Although Chapter II offered recommendations for clinical trial nurses, nurses in all practice settings need genomic knowledge. Research on the utilization of genomic
knowledge, testing, and the role of the nurse in testing across the care continuum is important. Providing support for nurses to expand their knowledge of genomic profiling beyond cancer to include other health conditions is key to enhancing the involvement of nurses, as interdisciplinary team members, in discussions and decision-making with patients and their families about diagnostic testing and treatment options.

Chapter III
Theory Application in Genomic Nursing Practice

Chapter III illustrates the importance and incorporation of the HCG model concepts in genomic-competent nursing care, e.g., education, clinical testing and therapeutics. The chapter introduces Ajzen’s Theory of Planned Behavior (TBP), the constructs of attitude, subjective norms, and perceived behavioral control, and its application to genomics in nursing practice (Ajzen, 1991, 2002). Three exemplars illustrate the use of genomic-competent nursing care for oncology patients and their families. The first exemplar, family history, applies genomic competencies in eliciting, analyzing, and applying family history in clinical testing and treatment as part of genomic-competent nursing care. The second exemplar, genomic testing, describes typical approaches in testing for germline or somatic mutations in multiple genes, and the clinical application of test results. The final exemplar, financial toxicity, explores the impacts of social factors, e.g., testing and treatment costs and related access issues.
Limitations

Nurses’ lack of genomic knowledge and skills impacts the utilization of genomics in clinical practice. While these exemplars provided unique nursing applications, all three were drawn from the field of oncology. Exemplars illustrating the use of genomics in other nursing specialties would be beneficial.

Recommendations

Ajzen’s TPB constructs of attitude, subjective norms, and perceived behavioral control guided the development of these oncology exemplars. These constructs could be used to develop exemplars for other nursing specialties, e.g., maternal-child health, pediatrics, and behavioral health. Ajzen’s constructs should be used in the development of practice-transforming strategies addressing attitudes, subjective norms, and perceived behavioral control. Developing strategies based on these constructs will promote the implementation of genomic-competent care.

Chapter IV

Assessment of Genomics in Nursing Practice

Research reveals a gap between genomics in nursing education and nursing practice (Aiello, 2017, Anderson et al., 2015, Calzone, et al., 2013; Calzone et al., 2012). Chapter Four describes a mixed methods study of the application of genomics in nursing practice. Ajzen’s TPB (1991, 2002) was used to guide this study. In the quantitative component, a convenience sample of 151 registered nurses (RNs) at two Upstate South Carolina hospitals completed a 27-item Qualtrics survey based on the TPB constructs.
(attitude, subjective norms, and perceived behavioral control). The quantitative survey results guided the development of 10 open-ended focus group questions (qualitative component). A focus group was held at each hospital to explore barriers to nurses applying genomics in the care patients and their families.

The survey identified a lack of genomic education and knowledge that was confirmed by focus group participants. Nurses in the focus groups discussed a need for additional genomic education in order to answer patient and family questions; educate patients and families about genetic testing and conditions and provide resources; and provide genomic-competent care. Both the quantitative and qualitative arms of the study revealed that nurses felt unprepared to take a three-generation family history. The survey also found a lack of support by nurse leaders and healthcare organizations for genomic education and application. Focus group discussions revealed that nursing leaders and administrators value genomics but lacked an understanding of how to support nurses’ integration of genomics into practice. Insufficient knowledge, lack of administrative support, and costs emerged as barriers to application of genomics in practice.

Limitations

Several study limitations were identified. First, the study participants were a convenience sample of nurses from two upstate South Carolina hospitals. This sample may not reflect the attitudes, subjective norms and behaviors of nurses from different healthcare institutions and across specialties. While 16 nurses responded with an interest to participate in a focus group, only seven nurses were able to attend due to challenges in
scheduling a meeting time, based on their work schedules. Finally, both focus groups were scheduled for one hour which may have limited discussion.

Recommendations

With continued gaps in genomic knowledge and its application, research is needed to identify best practices to promote the dissemination of genomic knowledge and skills in nursing education programs and continuing education for nurses. Using TPB constructs (attitude, subjective norms, and perceived behavioral control), is key to understanding the relationship between increased intention and actual use of genomics in nursing practice. Finally, implementation research is needed to develop effective strategies that overcome barriers and bridge the education to practice gap.

Conclusions

In conclusion, a healthcare genetics/genomics model is useful in understanding the relationships between genetics/genomics, education, clinical testing and therapeutics, environmental influences, and ethical/legal/social implications. Genomic education about tumor profiling is essential for nursing involved in clinical trials and oncology. Clinical exemplars illustrated the importance of genomic competencies in nursing. Finally, a lack of genomic knowledge was found among practicing nurses, demonstrating the importance of genomic education in nursing programs and in continuing education to increase the use of genomic knowledge by nurses in practice.
References


APPENDICES
Appendix A

Research Proposal
Dissertation Proposal Narrative

Elizabeth Hassen

ASSESSING THE FACILITATORS, BARRIERS, AND CHALLENGES OF APPLYING GENOMICS IN NURSING CLINICAL PRACTICE

PRINCIPLE INVESTIGATOR: Elizabeth Hassen

TO BE CONDUCTED AT: Spartanburg Regional, AnMed Health, Bon Secours St. Francis

Background & Significance:

Over the last decade there has been an exponential increase in genetic and genomic knowledge, technologies, and research impacting the use of genomics across the healthcare continuum and healthcare disciplines (ANA, 2009; Calzone, Jenkins, Nicol, Skirton, Feero, & Green, 2013b). Currently, three important documents have been published to advance genetics and genomics in nursing education with the goal to incorporate into nursing clinical practice in the care of patients. The American Association of Colleges of Nursing (AACN) published the Essentials of Baccalaureate Education for Professional Nursing Practice (2008) and Essentials for Masters in Nursing (2011) for nursing education. The American Nurses Association (ANA) published the Essentials of genetic and genomic nursing: competencies, curricula guidelines, and outcome indicators, 2nd ed (2009). These publications by the AACN (2008) and the ANA (2009) have defined and guided genomic competency, including conducting family health history, recognizing genetic risks, and recognizing relationships of genetics and genomics to the health continuum. The competencies impact patient care in areas of prevention, screening, diagnosis, and treatment of disease. Although Essential competencies apply to the education of nurses with the implication for nurses to use in the clinical setting, studies indicate the majority of nurses report their knowledge and competency of genetics and genomics as low (Calzone, Jenkins, Culp, Bonham, & Badzek, 2013a; Calzone et al., 2013b; Thompson & Brooks, 2011).

Other areas of significance include nursing education and the nursing workforce. Various nursing organizations support competency integration into all entry levels of nursing education programs. Kirk, Calzone, Arimori, and Tonkin (2011) recognized barriers in their study on integration of genetics-genomics into nursing education: deficits among educators, decreased awareness at the government level, limitations of resources, lack of ‘patient voice’, and lack of evidence on outcomes. The International Society of Nurses in Genetics (ISONG) and the American Nurses Association provide fundamental support for the integration of genetics into health-care delivery. This is evidenced by their support of research and the genomic competencies.

The nursing workforce was comprised of nearly 45% of nurses that were 50 or older in 2008 and the average age reported in 2010 was 47 years old (Robert Wood
Considering the Human Genome Project was completed 2003, unless continuing education has been completed, many nurses lack genetic knowledge. A workforce survey reports only 36% of nurses have a baccalaureate in nursing (BSN) and less than 5% have a masters or doctorate (Buden, Zhong, Moulton, & Cimiotti, 2013). This survey reveals the majority of nurses have an associate degree. The growth of genetic and genomic research and discoveries is impacting the care and treatment of patients in all aspects of the healthcare system. Genomics will continue to have application in healthcare through personalized medicine.

**Problem Statement:**
Genomics is impacting screening recommendations, diagnosis, and treatment of patients impacting nursing care. The problem is there remains a gap in knowledge and application of genomics in nursing clinical practice (Calzone, Jenkins, Culp, Bonham, & Badzek, 2013a; Calzone et al., 2013b; Thompson & Brooks, 2011). Kirk, Calzone, Arimori, and Tonkin (2011) performed a small-scale international survey using open-ended questions to explore facilitators and barriers of genetic-genomic progress in the respondent’s country. They found genetics-genomic competences were not fully integrated into nursing education from the participating countries and were not reflected in the standards for registration or licensure (Kirk et al., 2011). Kirk et al. (2011) also noted challenges at both the national and international levels to produce a genetic-genomic competent nursing workforce. Other past researchers have also reported the lack of genomic knowledge and competency in nursing clinical practice (Calzone et al., 2013a; Calzone et al., 2013b; Rogers, Lizer, Doughty, Hayden, & Klein, 2017). The literature discusses application for genomics and presents case studies on how to apply genomics but no actually study exist that looks directly at translation of genomics from the nurses’ perspective. Thompson and Brooks (2011) evaluated the implementation of the Essentials using a survey, but about half of the respondents were nursing faculty. Finally, Leach, Tonkin, Lancastle, and Kirk (2016) reported behavior change theories for implementation of genomics into nursing practice, and presented a framework to inform change, which includes the Theory of Planned Behavior (TPB) as the “core underpinning theory” (p. 311). The authors also called for future research to look at the influence of both environmental and social factors on the application of genomics in nursing clinical practice (Leach et al., 2016).

**Purpose of Study:**
The purpose of this two-phase research study is to investigate the attitudes, social norms, and perceived behavioral control that affect the intentions and use of genomics in nursing clinical practice.

**Research Questions:**
1. What are the perceptions and experiences of licensed registered nurses working in inpatient settings at upstate South Carolina community hospitals with application of genomics?
2. What are the perceptions and experiences of licensed registered nurses working in inpatient settings at upstate South Carolina community hospitals with barriers to application of genomics?

**Contribution to healthcare genetics and nursing research:**

The proposed study may contribute to the current research for clinical nurses’ perspectives on the barriers, facilitators, and challenges of applying genomics in nursing clinical practice. Findings could guide implementation strategies and policy for genomics in nursing practice.

**Theoretical framework:** Ajzen’s Theory of Planned Behavior

![TPB theoretical framework. (Ajzen, 1991)](image)

**Specific Aims:**

**Specific Aim 1:** Examine the attitudes that nurses have towards the use of genomics in their nursing clinical practice.

**Specific Aim 2:** Examine the social norms including the encouragement, support, and the feelings of their professional social network and colleagues toward the use of genomics in nursing clinical practice.

**Specific Aim 3:** Identify the behavioral control, the facilitator and barriers, which exist in applying genomics in nursing clinical practice.

**Specific Aim 4:** Identify the behavioral intentions for the use of genomic concepts in nursing clinical practice.

**PROCEDURE**

**Population and Sample:**

The target population will consist of sample will consist of licensed registered nurses currently working in the clinical setting. The sample for phase one will consist of a minimum of 50 nurses completing the Qualtrics survey. A purposeful sample of 10 and no more than 20 licensed registered nurses in South Carolina currently working in the
inpatient clinical setting for the focus groups in phase two. Recruitment of nurses will be from three local large community hospitals.

Eligibility requirements:
- ADN or BSN degree
- Not currently enrolled in school
- Work in an inpatient clinical setting
- Licensure in SC
- Not a travel nurse

Methodology:
Phase I, a Qualtrics survey (n=50) is to investigate the application of genomics based on the constructs of the Theory of Planned Behavior (TPB) and the AACN’s Essentials. The results from Qualtrics descriptive statistics and t-test results will be utilized to guide the specific types of questions used in the second phase of the research.
Phase II, focus group methodology (n=10-15) further explores the positive and negatives of the TPB constructs. Data collection will involve three focus groups held in three different locations across the upstate of South Carolina to gather verbal data to ask about the attitudes, social norms, and perceived behavioral control towards the intention of applying genomics in nursing clinical practice. Data analysis will employ NVivo, a qualitative data analysis software, for content analysis of the verbal data for emergent themes.

Demographic questions
1. Race/Ethnicity
2. Gender
3. Nursing degree level – ADN or BSN
4. Years of clinical experience
5. Specialty: Med-Surg, Cardiac, OB, Oncology
6. Did you have a genomics class
7. Did you learn about genomics in nursing school

Focus Group questions
Phenomenological open-ended questions for the focus groups will be guided by the constructs of the Theory of Planned Behavior. Questions will consist of:
- Attitude
  - How would you describe your attitude towards using genomics? What experiences do you have with these competencies?
    - Use of family history
    - Identifying familial trends
    - Pharmacogenomics
    - Genetic testing
    - Referrals for genetic testing
  - What are your perceptions and experiences with the use of genomics in clinical practice?
• What is your view on whether it is beneficial or harmful?

-Subjective norms
  • What are your perceptions and experiences with manager/leadership support for use of genomics?
  • Discuss your perceptions and experiences with organizational support demonstrated towards genomics?
  • What are your perceptions and experiences with genomic practices or competencies you or your peers use in practice?

-Perceived behavioral control
  • What are your perceptions and experiences with genomic tools or resources available?
  • What are your perceptions and experiences with documentation tools available for genomics?
  • What are your perceptions and experiences with tools used for referrals for genomics?
  • What are your perceptions and experiences with barriers and challenges that prevent you from utilizing genomics in practice?

**Timeline for the Project:**
Upon approval by Spartanburg Medical Center IRB and Clemson University IRB, data collection will begin. Phase I survey will be distributed and open for 2 weeks. Analysis will begin as soon as the survey is closed. Phase II focus group questions will be revised. Focus groups planned to be held in June 2018 over a 2-week period. Analysis of qualitative data using Nvivo will begin as soon as focus groups are completed. Research will be submitted for publication, and presentation of research will be made at Clemson University. Research will also be presented at health systems in which research was done as requested, including Spartanburg Regional Nursing Research Council. Abstract has been submitted to present data at International Society of Nurses in Genetics (ISONG) in October 2018 based on research proposal.

**Human Subjects Research:**
Clemson University IRB and the HSSC e-IRB approval will be obtained. The primary investigator has completed the required Collaborative IRB Training Initiative (CITI) courses. There are no racial or ethnic limitations for the sample participants.

**Risk to Subjects**
There are minimal risks to the participating subjects involved in the research. Informed consent for participation will include the purpose of study and any potential risks and benefits of participation. Subjects will be informed that all information obtained in the Qualtrics survey will remain anonymous and will not have any identifying information. The responses will be secured in a file that only the principle investigator
can access. Permission will be obtained by participants of focus groups to be video and audio recorded for transcription purposes and will be signed prior to the start of each focus group. In addition, confidentiality and privacy will be ensured.

**Limitations:**
While three local community clinical sites are utilized, they are all located in one region of South Carolina.

**Potential Benefit of the Research:**
This research will inform and support future implementation of genomics into nursing clinical practice.

**References:**


Appendix B

IRB Approval Form
NOTICE OF FINAL APPROVAL

TO: Elizabeth Hassen, MSN
Principal Investigator

FROM: Ronald Januchowski, DO
Chairperson IRB Committee A - Spartanburg Regional Healthcare System

DATE: May 15, 2018

RE: eIRB ID #: Pro00078129
Protocol Title: Assessing Genomics in Nursing Clinical Practice:
ASSESSING THE FACILITATORS, BARRIERS, AND CHALLENGES OF APPLYING GENOMICS IN NURSING CLINICAL PRACTICE

STUDY STATUS: Approved for accrual

REVIEW TYPE: Expedited

APPROVAL DATE: 5/14/2018
EXPIRATION DATE: 5/13/2019

APPROVAL INCLUDES: • Assessing Genomics in Nursing Clinical Practice Protocol
• eIRB Study Application
• Preliminary Research Survey
• Focus Group Questions
• Phase I Qualtrics Survey
• Phase II Focus Group Consent

ALL SRHS APPROVED INVESTIGATORS MUST COMPLY WITH THE FOLLOWING:

• Federal regulations require that all research be reviewed at least annually. It is the Principal Investigator’s responsibility to obtain review and continued approval before the expiration date. You may NOT continue any research activity beyond the expiration date without IRB approval.
• The research must be conducted according to the proposal/protocol that was approved by the IRB.
• Changes to the procedures, recruitment materials, or consent document must be approved by the IRB prior to implementation.
• If applicable, each subject should receive a copy of the approved dated consent document
• It is the responsibility of the principal investigator to report promptly to the IRB:
  o Unanticipated problems and/or unexpected risks to subjects
  o Adverse events affecting the rights or welfare of any human subject participating in the project
• Research records, including signed consent documents, must be retained for at least three years after the termination of the last IRB approval.

PWA0000822 / JDRG00000990 Spartanburg Regional Health Services District, Inc.
#HRB0001369 – SRHS IRB Committee A
Page 1 of 2
• No subjects may be involved in any study procedure prior to the IRB approval date, or after the expiration date. For continuing research, an update of the study is required prior to the expiration date. The PI is responsible for initiating the Continuing Review process. At the time a study is terminated (closed), a final report should be submitted to the IRB.
Appendix C

Consent Phase I

Information about Being in a Research Study
Clemson University

Assessment of Genomics in Clinical Nursing Practice

Description of the Study and Your Part in It

Elizabeth C Hassen, Ph.D.(c), RN, OCN is a Ph.D. student at Clemson University conducting this study with the guidance of Rosanne Pruitt, dissertation chair. The purpose of this two-phase research study is to investigate the barriers and use of genomics in nursing clinical practice.

Your participation will involve taking a 27 question Likert-type scale questionnaire, six demographic questions and an additional 21 questions to gather data about the use of genomics in your clinical nursing practice. It will take you about 20 minutes to complete the survey. At the conclusion of the survey, it will provide further instructions should you want to participate in a follow up focus group. The focus group will take about an hour of your time to discuss your experiences with using genomics in your clinical nursing practice.

Risks and Discomforts

There is minimal risk or discomfort to you as a result of participation in this research study. Sometimes when answering questions about an unfamiliar subject, it is possible for one to experience anxiety or discomfort, especially when questions are respective to your employment. Elizabeth Hassen has been a nurse for 16 years and can address concerns at the time of the focus group.

Possible Benefits

There are no direct benefits from participation in this study. However, this research can help us to understand the barriers and experiences of using genomics in clinical nursing practice which will allow us to bring education and implementation strategies back to nurses to increase genomics application in clinical nursing practice.

Incentives

For those participating in the focus groups, one participant will be selected at random to receive a membership to a nursing organization of their choice for a year.
Protection of Privacy and Confidentiality

The surveys will be completed in Qualtrics without identifiable information. For those participating in focus groups, video and audio recording will be done during the group discussion for translation and transcription of data for analysis. Participants’ identity will be coded to protect their privacy. Some comments, de-identified, could be included as quotations to emphasize certain points of the data. Storage of video and audio recordings and will be included in the folder of data and consent forms stored in a cabinet in a locked office. These will be appropriately destroyed after five years.

The results of this study may be published in scientific journals, professional publications, or educational presentations; however, no individual participant information will be identified.

Choosing to Be in the Study

You do not have to be in this study. You may choose to take part in Phase I, the Qualtrics survey, and not to take part in Phase II, focus groups. You may choose to stop taking part in the research study at any time. Your participation in the research and follow-up focus groups will not be affected in any way if you decide not to be in the study or to stop taking part in the study.

Contact Information

If you have any questions or concerns about this study or if any problems arise, please contact Elizabeth Hassen at Clemson University at 864-764-4797.

If you have any questions or concerns about your rights in this research study, please contact the Clemson University Office of Research Compliance (ORC) at 864-656-0636 or irb@clemson.edu. If you are outside of the Upstate South Carolina area, please use the ORC’s toll-free number, 866-297-3071. The Clemson IRB is a group of people who independently review research. The Clemson IRB will not be able to answer some study-specific questions. However, you may contact the Clemson IRB if the research staff cannot be reached or if you wish to speak with someone other than the research staff.

Consent

By participating in the study, you indicate that you have read the information written above, are at least 18 years of age, been allowed to ask any questions, and are voluntarily choosing to take part in this research. You do not give up any legal rights by taking part in this research study.
Appendix D

Survey Questions

Preliminary Research Survey

Demographic questions:
1. Race/Ethnicity
   __ Caucasian    __ African American  __ Hispanic  __ Other
2. Gender
   __ Male       __ Female
3. Nursing degree level
   __ ADN        __ BSN
4. Years of clinical experience _____________
5. Specialty:
   __ Med-Surg    __ Cardiac     __ OB    __ Oncology __ Peds __ Other
6. Did you have a stand-alone genomics class in nursing school?  
   __ Yes   __ No

Research Questions:
7. Have you learned about genomics in nursing school or another setting?  
   __ Nursing school       __ Another setting       __ Neither

   Text box: What type of setting?

8. How would you rate your attitude towards using genomics in the clinical setting?  
   Positive 5 – 4 – 3 – 2 – 1 Negative

   What experiences do you have with the following genetic American Association of 
   Colleges of Nurses (AACN) Essential competencies?
9. How would you rate your comfort level with obtaining a family history of a 
   disease/disorder?
   A Great Deal – Much – Somewhat – Little – Never

10. How many generations do you seek information on when taking a family history?
    
    1 – 2 – 3 – 4 – 5

11. Do you take a 3-degrees (generations) of family history?  
    __Yes - No

12. Do you have any experience with identifying ‘red flags’ of inherited family 
    diseases/disorders?
    A Great Deal – Much – Somewhat – Little – Never
13. Do you have any experience using genetics for appropriately identifying medications for your patient (pharmacogenomics)?

   A Great Deal – Much – Somewhat – Little – Never

14. I have ______________ knowledge and experience with genetic testing in the clinical setting?

   A Great Deal – Much – Somewhat – Little – Never
   (Text box: Please describe)

15. Do patients ask you for information about genetic testing?

   A Great Deal – Much – Somewhat – Little – Never

16. I have ______________ experience identifying when patient should be referred for genetic testing?

   A Great Deal – Much – Somewhat – Little – Never

17. How would you rate your perceptions and experiences with the use of genomics in clinical practice?

   Positive 5 – 4 – 3 – 2 – 1 Negative
   (Text box: Please describe an example either positive or negative)

18. Do you feel the genomic information provided to patients is beneficial to patients or overwhelming?

   Beneficial – Overwhelming – No opinion

19. Does your manager/leadership support the use of genomics in your practice?

   A Great Deal – Much – Somewhat – Little – Never

20. Does your clinical organization demonstrate support towards genomics?

   A Great Deal – Much – Somewhat – Little – Never

21. Does your hospital or unit competencies include genomic concepts?

   A Great Deal – Much – Somewhat – Little – Never

22. Do your peers utilize genomic practices or competencies in their clinical practice?

   A Great Deal – Much – Somewhat – Little – Never
23. Do you currently use genomic concepts and/or services in your nursing clinical practice?

Yes – No

(Text box: If so, which concepts and/or services)

24. Have you utilized any genomic tools or resources that are available?

On Unit – Online – Both – Neither

(Text box: If so, which tools or resources?)

25. Have you used any documentation tools available for genomics?

Yes – No

(Text box: If so, which tools?)

26. Have you spoken to a care provider or physician regarding a high-risk patient?

Yes – No

(Text box: If so, which concepts?)

27. What are the barriers and challenges that prevent you from utilizing genomics in practice?

Text box

28. Text Box: Additional comments: Please share any other perceptions or experiences with genomics that you would like to add that has not been asked here.

If you would be willing to participate in a focus group to further explain this research, please email me at ehassen@clemson.edu. The focus group will allow discussion to expand on the above concepts to identify use and barriers of genomics in patient care. The focus group would last approximately 1 hour in length with appetizers and drinks provided.
Appendix E

Consent Phase II

Information about Being in a Research Study
Clemson University

Assessment of Genomics in Clinical Nursing Practice

Description of the Study and Your Part in It

Elizabeth C Hassen, Ph.D.(c), RN, OCN is a Ph.D. student at Clemson University conducting this study with the guidance of Rosanne Pruitt, dissertation chair. The purpose of this two-phase research study is to investigate the barriers and use of genomics in nursing clinical practice.

Your participation will involve taking a 27 question Likert-type scale questionnaire, six demographic questions and an additional 21 questions to gather data about the use of genomics in your clinical nursing practice. It will take you about 20 minutes to complete the survey. At the conclusion of the survey, it will provide further instructions should you want to participate in a follow up focus group. The focus group will take about an hour of your time to discuss your experiences with using genomics in your clinical nursing practice.

Risks and Discomforts

There is minimal risk or discomfort to you as a result of participation in this research study. Sometimes when answering questions about an unfamiliar subject, it is possible for one to experience anxiety or discomfort, especially when questions are respective to your employment. Elizabeth Hassen has been a nurse for 16 years and can address concerns prior to the focus group beginning.

Possible Benefits

There are no direct benefits from participation in this study. However, this research can help us to understand the barriers and experiences of using genomics in clinical nursing practice which will allow us to bring education and implementation strategies back to nurses to increase genomics application in clinical nursing practice.

Incentives

For those participating in the focus groups, one participant will be selected at random to receive a membership to a nursing organization of their choice for a year.
Protection of Privacy and Confidentiality

The surveys will be completed in Qualtrics without identifiable information. For those participating in focus groups, video and audio recording will be done during the group discussion for translation and transcription of data for analysis. Participants’ identity will be coded to protect their privacy. Some comments, de-identified, could be included as quotations to emphasize certain points of the data. Storage of video and audio recordings and will be included in the folder of data and consent forms stored in a cabinet in a locked office. These will be appropriately destroyed after five years.

The results of this study may be published in scientific journals, professional publications, or educational presentations; however, no individual participant information will be identified.

Choosing to Be in the Study

You do not have to be in this study. You may choose to take part in Phase I, the Qualtrics survey, and not to take part in Phase II, focus groups. You may choose to stop taking part in the research study at any time. Your participation in the research and follow-up focus groups will not be affected in any way if you decide not to be in the study or to stop taking part in the study.

Contact Information

If you have any questions or concerns about this study or if any problems arise, please contact Elizabeth Hassen at Clemson University at 864-764-4797.

If you have any questions or concerns about your rights in this research study, please contact the Clemson University Office of Research Compliance (ORC) at 864-656-0636 or irb@clemson.edu. If you are outside of the Upstate South Carolina area, please use the ORC’s toll-free number, 866-297-3071. The Clemson IRB is a group of people who independently review research. The Clemson IRB will not be able to answer some study-specific questions. However, you may contact the Clemson IRB if the research staff cannot be reached or if you wish to speak with someone other than the research staff.

Consent

By participating in the study, you indicate that you have read the information written above, are at least 18 years of age, been allowed to ask any questions, and are voluntarily choosing to take part in this research. You do not give up any legal rights by taking part in this research study.

I have read this form and have been allowed to ask any questions I might have. I agree to participate in the study. I agree to have my conversation audio taped and
photographs to be taken and used, without identifying information, in posters and journal articles.

Participant’s Printed signature: __________________________________________

Participant’s signature: __________________________________________

Date: ______________
Appendix F

Focus Group Interview Questions

Phenomenological open-ended questions for the focus groups will be guided by the constructs of the Theory of Planned Behavior and will be guided based on the preliminary survey results. Questions will consist of:

- **Attitude**
  - How would you describe your attitude towards using genomics?
  - Do you have experience with the use of these genomic competencies in clinical practice?
    - Use of family history
    - Identifying familial trends
    - Pharmacogenomics
    - Genetic testing
    - Referrals for genetic testing
  - Do you feel that genomic information is beneficial for patients?

- **Subjective norms**
  - What are your perceptions and experiences with manager/leadership support for use of genomics?
  - Discuss your perceptions and experiences with organizational support demonstrated towards genomics?
  - What are your perceptions and experiences with genomic practices or competencies you or your peers use in practice?

- **Perceived behavioral control**
  - What are your perceptions and experiences with genomic tools or resources available? Have you completed any continuing education on genomics?
  - Do you use documentation tools available for genomics? Are they within your electronic medical system?
  - What are your perceptions and experiences with tools used for referrals for genomics? Have you spoken to a physician about high risk patients?
  - What do you see as barriers and challenges that prevent you from utilizing genomics in practice? Knowledge? Lack of support? Others?