The Acquisition of Clinical Genetics Knowledge in Medical Students

by

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BS, University of Virginia, 2019

Submitted to the Graduate Faculty of the

Department of Human Genetics

Graduate School of Public Health in partial fulfillment

of the requirements for the degree of

Master of Science and Master of Public Health

University of Pittsburgh

2022

UNIVERSITY OF PITTSBURGH

GRADUATE SCHOOL OF PUBLIC HEALTH

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Non-genetic physicians report feeling uncomfortable and unprepared to order genetic testing, interpret test results, and counsel patients on genomic information (Arora et al., 2016). The purpose of this study was to learn about the acquisition of genetic knowledge in medical students. A survey was distributed to first year medical students at the University of Pittsburgh School of Medicine before and after they completed a required Human Genetics course. The survey asked the students to rank their knowledge of clinical genetic concepts, answer knowledge multiple choice and true/false questions, as well as provide information about previous experiences and exposures to genetic information.

The survey was distributed to 158 first-year medical students. Twenty-four participants responded to the pre-course survey (a response rate of 15.2%). Fourteen participants responded to the post-course survey (a response rate of 8.9%). A Wilcoxon Signed Rank Test was performed on the responses of the 12 participants who completed the pre-course and post-course survey to provide information on how the participants' perceived and actual knowledge changed from the pre-course survey to the post-course survey. The results indicated a statically significant ($p=0.003$) increase in average test scores.

Overall, the participants reported feeling more confident in their knowledge after completing the Human Genetics course. However, responses suggested that after completion of the course, participants still struggled to accurately interpret certain clinical situations and genetic test results. Participants had difficulty recognizing which family member would be most

informative to test first given a family history of cancer, which genetic test to order, how to disclose a prenatal genetic finding, and the clinical significance of a variant of uncertain significance.

The results of the study indicate a need for educational and policy changes. While one genetic course can improve the knowledge of students, it may not be sufficient to prepare students for clinical genetic scenarios, especially when students lack experience applying genetic knowledge throughout their medical education. This study is relevant to public health because non-genetic providers require a certain level of genetic knowledge to provide appropriate patient care.

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Acknowledgements

Writing a thesis can be a daunting task filled with mixed emotions of success and setbacks. The process includes long days of researching articles, analyzing data, and writing and revising. Some days I was proud of my progress, but often the project challenged my thought process. Other days were filled with worry about collecting enough data responses and meeting writing deadlines. Fortunately, I had an experienced committee and mentors who helped guide me along the process. I also had trusted classmates who provided support and stress relief.

Thank you to my committee: Dr. Mylynda B. Massart, Dr. John R Shaffer, Christine Munro, and Dr. Robin E. Grubs. Thank you for your time and assistance in helping me to grow as a professional during this past year. A special thanks to Robin, who always found time to meet with me and provided encouraging words and thoughtful critiques. Your belief in me has been very appreciated.

I would also like to thank my classmates for the dedicated writing dates that included providing emotional support, exchanging writing strategies, and consuming too much caffeine. I cannot imagine going through this process without you. Lastly, I would like to thank my family for their unconditional support and encouragement.

1.0 INTRODUCTION

1.1 Background and Specific Aims

Advances in genetic technology have made genetic testing more accessible and affordable. However, while genetic testing information aids in the diagnosis and management of patients, most nongenetic physicians are not comfortable counseling patients on genomics and genetic test results. Additionally, physicians feel unprepared to discuss genetic information with patients as well as to order genetic testing and interpret the testing results (Arora et al., 2016; Collier, 2012; Powell et al., 2012). Discussing genetic information, ordering testing, and interpreting testing results are critical components of clinical care when diagnosing and treating patients with genetic conditions. As genetic testing continues to advance, medical professionals will need to learn how to explain genetic topics, determine the risk to inherit a genetic condition, take and interpret a family history, and order appropriate genetic testing (Kaye & Korf, 2013).

Many healthcare professionals understand the clinical utility of genetic testing but find their knowledge on genetic topics limited (Powell et al., 2012). Limited genetic literacy diminishes the integration of genetic testing in primary care (Kaye & Korf, 2013). Currently, direct-to-consumer testing (DTC) offers a way for individuals to learn about their ancestry and genetic health-related information without consulting healthcare professionals. However, individuals will often consult their primary care physicians with their results, but many primary care physicians feel uncomfortable interpreting results from direct-to-consumer testing (Powell et al., 2012). When physicians lack the ability to understand and communicate genetic information, they may not know how to interpret actionable results, adjust screening recommendations, or refer a patient to a

specialist (Collier, 2012). While studies have been conducted to learn the genetic knowledge of health care professionals, undergraduate students, and the general population, there is a paucity of research that examines the acquisition of genetic knowledge in medical students. This lack in literature on the acquisition of genetic knowledge can have implications for medical school curriculum and training (Baars et al., 2005; Greb, Brennan, McParlane, Page, & Bridge, 2009; Ling, Swanson, Holtzman, & Bucak, 2008; Swanson, Case, Luecht, & Dillon, 1996).

To assess the acquisition of genetic knowledge of medical students, a survey was administered to University of Pittsburgh medical students during the fall of 2020 and 2021. The survey assessed the knowledge of clinical genetics and genetic testing using a variety of question formats, including multiple-choice knowledge questions and open-ended scenarios based on common clinic situations. The survey was designed in relation to the Human Genetics course taught by Dr. Saleem Khan. The University of Pittsburgh requires all first-year medical students to take this 14-day course, which is only offered in the fall. The first iteration of the survey was distributed in the fall of 2020, three months following the conclusion of the course, to gather preliminary data on retention of course content. For this project, in Fall 2021, the survey was distributed again to the next cohort of medical students to obtain both a pre-course response and a post-course response. The study aims to identify changes in the medical students' understanding of clinical genetics and genetic testing following completion of the Human Genetics course. Future studies plan to track medical students' acquisition of genetics knowledge as they progress through their clinical rotations to ascertain how their genetics knowledge changes during their training. We hope that the results from these studies will inform future efforts to further integrate and expand genetics knowledge in the medical school curriculum.

1.1.1 Specific Aim I

Assess the clinical genetics knowledge, including knowledge of common genetic conditions and genetic testing options, of University of Pittsburgh medical students using a previously designed, secure survey tool.

1.1.2 Specific Aim II

Evaluate the process by which medical students acquired genetic knowledge through the Human Genetics course taught during their first year. The survey was distributed to the Class of 2025 medical students prior to and following the course. Responses between these two surveys were paired using secure identifiers to detect individual changes in knowledge over time.

2.0 LITERATURE REVIEW

2.1 Genetic Knowledge

Genetic knowledge can be defined as "an individual's ability to understand and appreciate the basic principles of genetics for informed decision-making" (Morren, Rijken, Baanders, & Bensing, 2007; Schmidlen et al., 2016). Genetic knowledge and genetic literacy are often used interchangeably to signify an individual's ability to obtain, process, and understand genetic knowledge as it relates to and affects their lives (Hurle et al., 2013). Various definitions of genetic knowledge and genetic literacy often indicate that an individual demonstrates sufficient knowledge when they can make informed decisions about personal or patient care (Bowling et al., 2008). Genetic knowledge is important because the information can drive health care decision making for the individual and family members.

Patient's genetic knowledge is not always acquired through classroom learning or from health care providers; sometimes patients will use the internet and social media to learn about genetic concepts and conditions (Almomani, Al-Sawalha, Al-Keilani, & Aman, 2020). However, patients often rely on health care providers to clarify any questions as well as accurately present different management and treatment options based on genetic testing results. If health care providers lack genetic knowledge and fail to provide patients with relevant information, then patients may to be able to make informed decisions about their care. One example of a situation requiring genetic knowledge is genetic testing for breast and ovarian cancer. Individuals with a genetic susceptibility to breast and ovarian cancer need to make informed decisions about cancer

screening and risk-reducing surgical options, which requires their health care provider to have the appropriate genetic knowledge (Morren et al., 2007).

As genome and exome sequencing are becoming more available and affordable, health care providers need to identify when genetic testing is necessary and interpret the results to make decisions about care and management (Kaye & Korf, 2013). Knowledge about testing methodologies, diagnostic criteria, and treatments are continuously evolving in the genetics and genomics field. The continuous expansion of genetics knowledge requires health care providers to be lifelong learners in order to remain up-to-date and make informed medical decisions (Kaye & Korf, 2013).

2.2 Health Care Professionals' Genetic Knowledge

2.2.1 Health Care Professionals' Attitudes Toward Genetic Testing

As demand for genetic testing increases, primary care physicians and other non-genetics professionals will likely be expected to offer genetic testing to patients because medical geneticists and genetic counselors cannot meet the demand (Brothers & Knapp, 2018; Geller & Holtzman, 1995; Hofman et al., 1993). About 50% of medical genetics residency positions are not filled each year (Plunkett-Rondeau, Hyland, & Dasgupta, 2015). The shortage of genetic providers has led to the development of educational programs for non-genetic providers to help with the integration of genomic medicine in health care (Talwar, Tseng, Foster, Xu, & Chen, 2017; Thurston, Wales, Bell, Torbeck, & Brokaw, 2007). While health care providers acknowledge their responsibility to provide genetic care to patients, the type of care is unclear (Harding et al., 2019). Some health

care providers think non-genetic providers will take on similar roles of genetic providers to assist with the growing demand, while others think non-genetic providers should identify genetic conditions and refer when appropriate (Harding et al., 2019).

As genetic testing has become more affordable and available, it is expected that health care providers will integrate genetic testing into the clinical setting (Najafzadeh et al., 2012). Should they provide genetic testing, then health care providers will have to obtain consent for testing, inform patients of results, and help share the information with family members, all skills which health care providers may not have been taught or previously applied in a clinical setting (Pasquier et al., 2021). Based on self-reported lack of knowledge and lack of clinical experience, health care providers do not feel prepared to handle the growing demand of genetic testing (Selkirk, Weissman, Anderson, & Hulick, 2013).

While some health care providers recognize the clinical utility of genetic testing and express a desire to learn more about genetic testing to increase their genetic knowledge, most health care providers feel unprepared to answer patients' questions about testing, and disease susceptibility (Chow-White, Ha, & Laskin, 2017; Evenson, Hoyme, Haugen-Rogers, Larson, & Puumala, 2016; Powell et al., 2012). Even when providers feel knowledgeable about basic genetic principles like inheritance patterns, many still struggle to communicate genetic principles and genetic test results to patients (Chow-White et al., 2017). Additionally, some health care providers report feeling comfortable discussing variants of uncertain significance (VUS) with patients, but then answer questions incorrectly about management related to a VUS result when given a knowledge assessment (Macklin, Jackson, Atwal, & Hines, 2019). A majority of studies have reported that non-genetic providers feel unqualified to educate and manage patients with genetic

conditions, as well as, lack confidence in their counseling abilities (Mikat-Stevens, Larson, & Tarini, 2015).

While non-genetic providers often appreciate the clinical utility of genetic testing, they have questions about how to best incorporate testing into clinical practices. Providers have reported concern about patients understanding the limitations of negative results and experiencing a false sense of security. Also, because of their long-term relationship with providers, some patients may want providers to be directive and give advice about what to do when facing decisions related to genetic testing (Geller & Holtzman, 1995). Health care providers have expressed concerns about how to communicate incidental findings, variants of uncertain significance, and other time-consuming information that could potentially cause psychological anxiety. Health providers are also uncertain about how to discuss pre-symptomatic findings of genetic test results while limiting the potential psychosocial harms (Reiff et al., 2014).

2.2.2 Challenges Health Care Professionals Face with Genetic Testing

While genetic testing offers the opportunity to identify individuals at risk for genetic conditions and to initiate health interventions, challenges still exist with the integration of genetic testing into clinical care due to health care providers' gaps in genetic knowledge (Burke & Korngiebel, 2015; Najafzadeh et al., 2012). Health care providers report challenges with incorporating genetic testing in primary care settings due to concerns with the clinical utility of genetic testing, lack of clinical experience and genetic knowledge, limited access to genetic professionals, time, and insurance concerns (Carroll et al., 2016; Hauser, Obeng, Fei, Ramos, & Horowitz, 2018; Reiff et al., 2014).

Health care providers have struggled with understanding the usefulness of genetic testing, which then leads to the lack of implementation of genetic testing in a clinical setting (Carroll et al., 2016). Specifically, primary care physicians (PCPs) have reported not utilizing genetic testing because they have concerns about inaccurate results, ambiguous results, and the validity of testing (Mikat-Stevens et al., 2015). Health care providers' lack of understanding of genetic testing utility often stems from lack of guidelines and lack of experience applying genetic knowledge in a clinical setting (Carroll et al., 2016; Mikat-Stevens et al., 2015).

Limited genetic knowledge reported by health care providers may result from their education and/or lack of exposure to genetics in a clinical setting (Carroll et al., 2016; Haga, Kim, Myers, & Ginsburg, 2019; Hofman et al., 1993; Powell et al., 2012). For example, a qualitative study by Carroll et al. found that while almost all family physicians were aware of genetic testing options for breast and ovarian cancer, only around half knew about genetic testing for colorectal cancer (2016). Another study of primary care physicians in New York City found that while most providers had a formal genetics education, only a third of 488 providers "had ordered any genetic test, returned a genetic test result to any patient, or referred a patient for genetic counseling in the past 12 months" (Hauser et al., 2018). This study suggests that there are still challenges to integrating genetic testing into the clinical setting even when education concerns are addressed. Still, health care providers have reported wanting better resources and connections to genetic information and services in order to help compensate for their lack of genetic knowledge (Carroll et al., 2016). For example, one study found that 60% of providers felt they lacked knowledge about the genetics of common diseases and only 14% of primary care providers felt comfortable interpreting genetic test results (Hauser et al., 2018).

In an effort to learn more about genetic testing, some health care providers have expressed a desire to have a genetic professional partner who could provide advice on patient care, reliable information, and guidance on how to utilize genetic tools and resources (Carroll et al., 2016; Collier, 2012; Haga et al., 2019; Powell et al., 2012). Some healthcare providers and genetic counselors have expressed that a professional partnership could act as an additional resource to help provide trustworthy information and appropriate recommendations to health care providers in order to better serve patients (Bensend, Veach, & Niendorf, 2014; Carroll et al., 2016). Health care providers have struggled to integrate genetic testing into the clinical setting because of the limited access to genetic professionals.

Additionally, health care providers report that time is a challenge to incorporating testing. Time affects the ability for health care providers to properly consent families and provide information about complex results (Reiff et al., 2014). One study found that only 18.6% of patients received formal pre-test counseling for genetic testing for familial adenomatous polyposis (Giardiello et al., 1997). Another study found that many providers do not address the possibility of incidental findings to families during pre-test counseling because of the rarity of the event and the possibility of causing unnecessary anxiety (Reiff et al., 2014). A discussion of the chance and the potential significance of incidental findings may require additional time that health care providers do not have in a busy clinical setting.

Health care providers are also hesitant about ordering genetic testing due to insurance concerns. In one study by Hauser et al., a majority of providers expressed concern that genetic testing could lead to insurance discrimination, suggesting more health care providers need to be aware about the protections and limitation of the Genetic Information Non-discrimination Act (GINA) (2018). Providers also seem to have a mistrust towards companies that offer genetic testing

and misunderstanding of what insurance companies are willing to cover (Hauser et al., 2018). These findings indicate a need for providers to be educated about insurance coverage and protection specifically related to genetic testing. Overall, the results from multiple studies suggest that providers are not prepared for the expansion of genetic testing into the primary care setting based on numerous challenges (Carroll et al., 2016; Haga et al., 2019; Hauser et al., 2018; Powell et al., 2012; Reiff et al., 2014).

2.2.3 Barriers to Implementing Genetic Testing in a Primary Care Setting

A number of barriers exist that prevent the incorporation of genetics in a primary care setting. Other than limited genetic knowledge and confidence, health care providers experience barriers related to lack of time, lack of clearly defined roles regarding identifying and educating patients about genetic conditions, and a paucity of referral guidelines (Brothers & Knapp, 2018; Harding et al., 2019; Mikat-Stevens et al., 2015; Suther & Goodson, 2003). Four themes were identified in a literature analysis of barriers: knowledge and skills; ethical, legal, and social implications; health-care systems; and scientific evidence (Mikat-Stevens et al., 2015). Limited knowledge and skills in genetics information was addressed in the prior section.

Ethical, legal, and social implications (ELSI), a theme identified in the Mikat-Stevens et al. study, includes health care providers' concerns related to patient anxiety about unanticipated results, disclosing information about adult-onset conditions for minors, and discussing laws and protections related to confidentiality about genetic information (2015). ELSI concerns should be addressed during pretesting informed consent. A pretest consent discussion should include the clinical and personal utility of information gained from a genetic test, the impact on medical management, federal protections related to genetic discrimination, the possibility of secondary or

incidental findings, and the potential psychosocial impacts of testing (NHGRI, 2021). Health care providers would benefit from guidelines and resources that focus on what topics to address when performing pre-test and post-test counseling.

Health-care systems are also a barrier to implementing genetic testing in the primary care setting especially with lack of access to genetic services (Mikat-Stevens et al., 2015). Access issues are centered around isolation, lack of social networks, limited transportation, decreased accessibility, and lack of referrals to specialists. Non-genetic providers in certain areas note that genetic providers are inaccessible, and their locations are inconvenient for many patients (Mikat-Stevens et al., 2015). Some patients must travel multiple hours, which means taking time off work and paying for gas or possibly a hotel. Patients and families need to consider the financial cost and time of attending genetic appointments, which is then a barrier to receiving services. Overall, scheduling conflicts, out-of-pocket costs, and long wait times continue to be systematic barriers, especially for lower-income patients.

Additionally, primary care practices who serve minority, uninsured, low-income, or low English proficiency patients, are less likely to order genetic testing, which can contribute to health disparities. For example, one study found that minority-serving physicians were less likely to order genetic testing for breast cancer risk, colon cancer risk, and Huntington's disease compared to health care providers who served a smaller minority population (Shields, Burke, & Levy, 2008). Improvements need to be made at a systematic scale to decrease health disparities created by socio-economic and other factors.

Another barrier health care providers face is understanding the scientific evidence of genetic testing. Providers struggle with the concept of limited therapeutic intervention for some genetic conditions or the possibility that management may not change based on genetic testing

because non-genetic providers may not understand the clinical utility of genetic tests (Mikat-Stevens et al., 2015). Providers sometimes associate clinical utility with direct clinical benefit to the patients, but there are other aspects of genetic testing that providers may not recognize. For example, positive genetic test results can be used to identify a cause for an individual's symptoms, acquire additional supportive therapies, provide recurrence risk for future pregnancies, and identify future health concerns (Pasquier et al., 2021). Negative test results can help rule out certain genetic conditions and support the possibility of other non-genetic reasons for health concerns.

The creation of practice guidelines, risk assessment tools, and educational materials may help overcome the barriers that prevent genetic testing from being integrated into the primary care setting (Mikat-Stevens et al., 2015). There is also the possibility that providers may not know of guidelines and resources that already exist, so increasing awareness and access to the resources could improve providers' understanding.

2.3 Consequences of Patient Care due to Limited Genetic Knowledge

2.3.1 Negative Outcomes

Gaps in genetic knowledge among health care providers can lead to underutilization of genetic testing and increase the chance of negative outcomes (Clyman et al., 2007). Deficiencies in genetic knowledge and insufficient time are often cited as contributing factors for negative outcomes in patient care (Bensend et al., 2014). Negative outcomes can be categorized into three areas: ordering the incorrect genetic test, misinterpretation of the results, and inappropriate or no genetic counseling provided (Bensend et al., 2014).

Ordering the wrong genetic test can result in unnecessary cost expenses for patients and payors (e.g., insurance companies), and misinformation about possible health concerns, which can affect health management. There is evidence suggesting that about one third of genetic tests ordered by health care providers, typically oncologists and obstetricians/gynecologists, are ordered inappropriately because the provider did not follow guidelines, gave false reassurances to patients, or did not recognize differential diagnoses (Klitzman et al., 2013; Montanez, Berninger, Willis, Harding, & Lutgendorf, 2020; Shields et al., 2008).

Some health care providers also struggle with interpreting clinical testing (Marzuillo et al., 2013). A study examined how non-genetic providers understand and interpret a variant of uncertain significance (VUS) (Macklin et al., 2019). A VUS is a genetic change that does not have enough information to determine whether gene function is disrupted by the change (Macklin et al., 2019). The study asked participants to answer questions about clinical scenarios and found that a majority of health care providers did not know the definition of a VUS and made inappropriate recommendations for management and genetic testing based on a VUS result (Macklin et al., 2019). Health care providers do not always understand the likelihood to receive a VUS result. For example, there is about a 1% chance for a VUS with every gene that is on a panel and the chance of a VUS is higher for individuals who are not of European background (Macklin et al., 2019).

Another study found that surgeons made similar treatment recommendations for women with a *BRCA1/2* VUS as women with pathogenic variants in the *BRCA1/2* gene (Kurian et al., 2017). VUSs are not supposed to be used for management decisions. VUSs can be re-classified but this can take years and also classification of variants can differ between labs despite standards and guidelines from the American College of Medical Genetics and Genomics (Richards et al., 2015). Variants of uncertain significance are the second most reclassified variants. A majority of

VUS are reclassified to likely benign/benign (74.6%) compared to VUS that are reclassified to likely pathogenic/pathogenic (25.4%) (Harrison & Rehm, 2019). Another concern with VUS reclassification is patients and families sometimes assume that health care providers will follow-up as new information is discovered about different variants, but the responsibility often lies with patients to schedule follow-up appointments in order to receive up-to-date information (Reiff et al., 2014).

Health care providers also mistakenly interpreted the meaning of a negative test result 31.6% of the time based on a misunderstanding (Bensend et al., 2014). Health care providers were described as giving families inaccurate risk assessments for personal health, future pregnancies, and other family members based on incorrectly interpreting test results. For example, health care providers mistakenly thought that hereditary breast and ovarian cancer could not be paternally inherited, that an individual with negative cystic fibrosis carrier screening could not have a child with cystic fibrosis, and provided inappropriate breast screening guidelines based on a negative BRCA1/2 results, despite the family history of breast cancer (Bensend et al., 2014).

Misinterpretation of test results such as variants of uncertain significance can lead to unnecessary treatments and surgeries, avoidable anxiety, and/or false reassurance (Macklin et al., 2019). Inappropriate medical management, unnecessary prophylactic surgeries, unnecessary testing, misuse of health care dollars, ethical issues, and psychosocial distress are examples of negative outcomes from misinterpretation of genetic results (Bensend et al., 2014). Misconceptions of test results are problematic because they can cause misunderstandings about the natural history, surveillance, and treatment of a genetic condition. Additionally the risk for other family members may be over- or underestimated (Brown, Skinner, Ashley, Reed, & Dixon, 2015; Lillie et al., 2007).

Another area of testing with concern for misinterpretation is direct-to-consumer testing (DTC). DTC testing allows individuals to learn about their ancestry and health risks without consulting a physician. Individuals can learn information regarding ancestry, lifestyle/fitness, and health information (i.e. the Jewish pathogenic BRCA1/2 variants), as well as access their raw genomic data files (Kirkpatrick & Rashkin, 2016). However, direct-to-consumer genetic test results can be challenging to interpret because testing companies vary widely in testing practices, validating results, and classifying variants (Brothers & Knapp, 2018). DTC testing is largely based on single nucleotide polymorphism (SNP) genotyping rather than complete gene sequencing, which decreases clinical utility (Horton et al., 2019). The technology and limited clinical utility of DTC is not well understood, which can contribute to misinformation and false reassurances among patients and non-genetic providers.

Recent studies have estimated that 40% of genetic variants discovered by DTC raw data are false positives (Tandy-Connor et al., 2018). These types of results could lead to unnecessary evaluation and waste healthcare resources when individuals need to confirm a variant through clinical genetic testing. Additionally, while studies have suggested that the level of anxiety and distress with DTC testing is lower than previously reported, false-positive and misclassified variants can still cause negative outcomes such as unnecessary stress, medical procedures, and family member testing (Stewart, Wesselius, Schreurs, Schols, & Zeegers, 2018; Tandy-Connor et al., 2018).

Lastly, research has shown that patients do not always receive proper genetic counseling (Bensend et al., 2014). Non-genetic providers have reported that pre-test counseling is difficult due to time constraint and the challenge of talking about incidental findings and variants of uncertain significance. Studies have found that families who have comprehensive pre-test

counseling tend to have a better understanding and cope more effectively with the test results (Reiff et al., 2014).

One study surveyed and interviewed genetic counselors about the negative outcomes of patients receiving genetic services from non-genetic providers. The genetic counselors described scenarios involving "adverse psychosocial effects, inadequate genetic counseling, genetic testing and screening errors, medical mismanagement, negative shifts in attitudes toward medical providers, and unnecessary use of health care resources" (Bensend et al., 2014). Additionally, patients with limited genetic knowledge are more likely to feel confused and frustrated, which can lead to depression and isolation, which may result in patients seeking out potentially false or inaccurate information (Krakow, Ratcliff, Hesse, & Greenberg-Worisek, 2017).

2.3.2 Areas of Improvement

Health care providers commonly express the desire for more education and have identified a need for more knowledge about the modes of inheritance, environmental and genetic factors, role of genetics for multifactorial conditions, and the type of resources and information available (Guttmacher, Porteous, & McInerney, 2007; Houwink et al., 2011; Metcalfe, Hurworth, Newstead, & Robins, 2002; Qureshi, Modell, & Modell, 2004). Common themes that health care providers struggle with are connecting family histories to risk assessments, communicating and counseling patients about genetics to facilitate informed decision-making, and knowing when and how to refer patients to specialists (Harding et al., 2019; Houwink et al., 2011). Another study also found that health care providers understand the importance of collecting personal and family history of cancer, and genetic counseling, but have difficulty in interpreting family histories and providing risk assessments (Marzuillo et al., 2013).

Health care providers also report the need for information that addresses when to make a referral to genetic providers (Harding et al., 2019). Specifically, healthcare providers want to know which specialists will be the most helpful to their patients (Harding et al., 2019). One study examined the factors that affect health care providers decisions to order genetic testing. The type of genetic test was the most important factor to providers, while privacy protection laws and out-of-pocket costs of genetic testing were the least important factors (Najafzadeh et al., 2012). Understanding the factors that are important to health care providers will help tailor education materials and guidelines to better assist providers.

While health care providers should not be expected to know everything about genetic concepts and testing, providers should not order unnecessary follow-up tests or interventions. Providers should understand the benefit when ordering testing and know the limitations of testing in order to provide appropriate care to patients (Brothers & Knapp, 2018). While negative outcomes are noted to be rare, they still occur. Strategies to avoid negative outcomes include educational resources, awareness programs, standardizing testing and screening practices, and creating a system to track adverse outcomes (Bensend et al., 2014). A study by Powell et al. surveyed primary care physicians (PCPs) in North Caroline to assess their educational needs. She found that PCPs wanted to learn more about how to interpret results, the guidelines to manage risks identified by DTC results, and the different DTC tests offered to patients (Powell et al., 2012). A different study also identified that providers were mainly concerned with lack of knowledge on how to interpret the results, the different clinical utilities of testing, and the established practice guidelines (Haga et al., 2019). Standards for screening and testing options could help decrease variability among providers and reduce errors for ordering inappropriate testing. Additionally,

genetic counselors report a willingness to partner with non-genetic providers to limit negative outcomes and act as a trusted recourse (Bensend et al., 2014; Carroll et al., 2016).

2.4 Genetics Education

2.4.1 Medical School Education

There are guidelines for genetics curriculum for medical school education. The Association of Professors of Human and Medical Genetics (APHMG) developed a Core Curriculum for Medical School Genetics Education to establish competency-based education. The core curriculum includes guidelines on medical knowledge, patient care, interpersonal and communication skills, practice-based learning and improvement, professionalism, and systems based practice (Hyland et al., 2013). However, medical schools differ in philosophy and educational priorities, which leads to diversity in genetics knowledge among doctors (B. R. Korf, 2002). The education committee of the American Society of Human Genetics (ASHG) developed a set of six concept areas for genetic literacy for non-science majors at the undergraduate level consisting of the Nature of the Genetic Material, Inheritance and transmission, Gene Expression, Gene Regulation, Evolution, and Genetics and Society (Hott et al., 2002; National Academies of Sciences et al., 2016). Researchers have criticized these domains because they focus too much on Mendelian genetics, and do not focus enough on multifactorial inheritance, variable expressivity, penetrance, polygenic traits, and other complex genetic disorders (Dougherty, 2009).

The National Human Genome Research Institute assembled a working group, The Inter-Society Coordinating Committee for Physician Education in Genomics (ISCC-PEG), to narrow

the gap between evolving genomic medicine and the clinical incorporation of genetics into education. The group was created to develop and share the best practices of genomics in medicine (Bruce R. Korf et al., 2014). The ISCC-PEG's mission statement is "to improve genomic literacy of healthcare providers and enhance the effective practice of clinical genomic medicine by facilitating interactions among key stakeholders in genomics education by identifying educational needs and potential solutions, sharing best practices in educational approaches, and developing educational resources" (NHGRI, 2020).

The ISCC created practice-based competencies that fall under one of five entrustable professional activities (EPAs): Family History, Genomic Testing, Treatment Based on Genomic Results, Somatic Genomics, and Microbial Genomic Information. The competencies for each EPA are based on the six core competencies used by the Accreditation Counsel for Graduate Medical Education (ACGME) for medical residents in genomics (Bruce R. Korf et al., 2014). As listed before the six core competencies were developed by APHMG and are: medical knowledge, patient care, interpersonal and communications skills, practice-based learning and improvement, professionalism, and systems-based practice (Hyland et al., 2013).

Medical students receive genetic training, yet close to graduation they often lack sufficient genetic knowledge for daily practice (Baars et al., 2005). One survey of 450 non-genetic providers found that 62% of participants had no formal education in genomic medicine and did not know how to calculate risk predictions using genetic information (Haga et al., 2019). Another survey of 214 internists found that a majority wanted more training on when to order genetic testing, how to counsel patients, how to interpret genetic test results, and how to maintain patient genetic privacy (Klitzman et al., 2013).

While a genetic course in medical school can improve a student's genetic knowledge, one course is typically not sufficient to prepare future physicians for the different clinical situations they may face in their practice (Hofman et al., 1993). Non-genetic providers may be exposed to patients with hereditary cancer syndromes, traditional Mendelian genetic disorders, and multifactorial conditions. It has been recommended that medical students be exposed to genetic concepts throughout their education as well as in primary care settings in order to improve their genetic knowledge and reduce errors in assessing and treating patients (Hofman et al., 1993).

Studies have shown that "medical students do not retain genetics knowledge over the course of their medical career" (Powell et al., 2012). To be effective, genetic education should be introduced to individuals during their training and continued throughout their professional development, but programs have difficulty adding new courses and content to an already rigid curriculum (Talwar et al., 2017).

Non-genetic providers have requested medical schools provide up-to-date knowledge and incorporate more relevant training instead of focusing on rare conditions (Harding et al., 2019). For example, direct-to-consumer testing has recently been included in the Association of Professors of Human and Medical Genetics Core curriculum, which most medical schools use as a guide (Plunkett-Rondeau et al., 2015). A study examined the curriculum of medical schools and found that only half the programs have a standalone genetic course and 80% of programs have 40 or fewer contact hours (Greb et al., 2009; Thurston et al., 2007). For this reason, it is likely difficult for medical schools to incorporate additional curriculum such as direct-to-consumer testing. Also, a majority of professors teaching genetics are not geneticists (Plunkett-Rondeau et al., 2015). It has been suggested that medical schools integrate genetic curriculum throughout the four years

and teach students how to apply genetic knowledge in the clinical setting (Greb et al., 2009; Plunkett-Rondeau et al., 2015).

2.4.2 Post-Medical School Education

Genetic education efforts have increased due to the desire of non-genetic providers to increase their genetics knowledge, however additional interventions are needed (Crellin et al., 2019). Genetic knowledge is not always acquired through traditional learning (Almomani et al., 2020). Studies have shown that non-genetic providers tend to have greater genetic knowledge for conditions that are commonly seen in their patient population; therefore pediatricians tend to know more about cystic fibrosis while obstetrician-gynecologists tend to be more familiar with birth defects (Hofman et al., 1993). This observation indicates that clinical experiences rather than traditional classroom learning may be more beneficial in allowing non-genetic providers to acquire genetic knowledge (Almomani et al., 2020).

Non-genetic providers have offered recommendations for how best to develop educational materials. Providers want relevant education to be integrated in case-based scenarios and information on strategies to improve patient outcomes (Carroll et al., 2016; Telner, Carroll, & Talbot, 2008). Physicians from one survey identified their preferred mode of learning about genomic medicine as online continuing medical education (CME) programs, followed by professional meetings and in-person CME programs like grand rounds and case discussions (Haga et al., 2019; Telner et al., 2008).

Formal and informal education is required to keep up-to-date with current genetic knowledge, especially knowledge related to daily practice and with a focus on clinical application (Harding et al., 2019; Metcalfe et al., 2002). Collaboration between non-genetic and genetic

providers is an opportunity to enhance knowledge and provide support while optimizing patient care in an informal educational manner. Non-genetic providers and genetic counselors have expressed a desire to work together to help patients have access to genetic testing by collaborating in ordering testing and interpreting test results (Bensend et al., 2014; Carroll et al., 2016).

3.0 MANUSCRIPT

3.1 Background

3.1.1 Genetic Knowledge

While multiple definitions of genetic knowledge exist, genetic knowledge can be defined as "an individual's ability to understand and appreciate the basic principles of genetics for informed decision-making," (Morren et al., 2007; Schmidlen et al., 2016). Various definitions of genetic knowledge and genetic literacy often indicate that an individual demonstrates sufficient knowledge when they can make informed decisions about personal or patient care (Bowling et al., 2008). Genetic knowledge is important because the information can drive health care decision making for the individual and family members. If health care providers lack genetic knowledge and fail to provide patients with relevant information, then patients may not be able to make informed decisions about their care.

Over the past decade, genetic testing has advanced to make genetic testing more accessible and affordable. Due to the growing demand for genetic services, patients have turned to their health care providers to help them receive and interpret genetic test results (Brothers & Knapp, 2018). However, non-genetic physicians' genetic knowledge has not advanced at the same rate as genetic testing (Haga et al., 2019). Health care providers have reported feeling unprepared to handle the growing demand of genetic testing based on lack of knowledge with how to discuss genetic information with patients as well as to order genetic testing and interpret the testing results (Arora et al., 2016; Collier, 2012; Powell et al., 2012; Selkirk et al., 2013).

3.1.2 Barriers to Implementing Genetic Testing in the Clinical Setting

While lack of genetic knowledge is a main challenge for health care providers, it is not the only barrier to implementing genetic testing in a non-genetic clinical setting. Four themes were identified in a literature analysis of barriers: knowledge and skills (see the prior section); ethical, legal, and social implications; health-care systems; and scientific evidence (Mikat-Stevens et al., 2015).

Ethical, legal, and social implication (ELSI) barriers prevent the incorporation of genetics into the primary care setting. Additionally, these barriers relate to health care providers' concerns about patient anxiety regarding unanticipated results, disclosing information about adult-onset conditions for minors, and discussing laws and protections related to confidentiality about genetic information (Mikat-Stevens et al., 2015). ELSI concerns should be addressed during pretesting informed consent, which should include a discussion about the clinical and personal utility of information gained from a genetic test, the impact on medical management, federal protections related to genetic discrimination, the possibility of secondary or incidental findings, and the potential psychosocial impacts of testing (NHGRI, 2021).

Health-care systems are also a barrier to implementing genetic testing in the clinical setting especially with lack of access to genetic services (Mikat-Stevens et al., 2015). Access issues regarding genetic services are centered around the concentration of genetic services in urban areas, limited transportation, decreased accessibility, and lack of referrals to specialists (Mikat-Stevens et al., 2015). For example, some patients must travel multiple hours to see a genetic specialist, which means taking time off work and paying for gas or possibly a hotel. Patients and families need to consider the financial cost of attending genetic appointments, which can be a barrier to

receiving services. Overall, scheduling conflicts, out-of-pocket costs, and long wait times continue to be systematic barriers, especially for lower-income patients.

Another barrier health care providers face is understanding the scientific evidence of genetic testing. Providers struggle with the concept of limited therapeutic intervention for some genetic conditions or the possibility that management may not change based on genetic testing because non-genetic providers may not understand the clinical utility of genetic tests (Mikat-Stevens et al., 2015). Providers sometimes associate clinical utility with direct clinical benefit to the patients, but there are other aspects of genetic testing that providers may not recognize. For example, positive genetic test results can be used to identify a cause for an individual's symptoms, acquire additional supportive therapies, provide recurrence risk for future pregnancies, and identify future health concerns (Pasquier et al., 2021). Negative test results can help rule out certain genetic conditions and support the possibility of other non-genetic reasons for health concerns.

3.1.3 Negative Outcomes of Limited Genetic Knowledge

Negative outcomes associated with limited genetic knowledge can be categorized into three areas: ordering the incorrect genetic test, misinterpretation of genetic test results, and inappropriate or no genetic counseling provided (Bensend et al., 2014). These errors can result in unnecessary cost to patients and payors (e.g., insurance companies), inappropriate care, inaccurate information, and emotional harm.

Ordering the wrong genetic test can result in unnecessary cost expenses for patients as well as payors and in misinformation about possible health concerns, which can affect health management. There is evidence suggesting that about one third of genetic tests ordered by health care providers, typically oncologist and obstetricians/gynecologists, are ordered inappropriately

because the provider did not follow guidelines, gave false reassurances to patients, or did not recognize differential diagnoses (Klitzman et al., 2013; Montanez et al., 2020; Shields et al., 2008).

Some health care providers also struggle with interpreting clinical testing (Marzuillo et al., 2013). A study examined how non-genetic providers understand and interpret a variant of uncertain significance (VUS) (Macklin et al., 2019). The study asked participants to answer questions about clinical scenarios and found that a majority of health care providers did not know the definition of a VUS and made inappropriate recommendations for management and genetic testing based on a VUS result (Macklin et al., 2019). Health care providers also do not always understand the likelihood to receive a VUS result. For example, there is about a 1% chance for a VUS with every gene that is on a panel and the chance of a VUS is higher for individuals who are not of European background (Macklin et al., 2019). Therefore, some health care providers struggle with interpretating the clinical significance of a VUS, a common genetic test result.

Incorrectly interpreting test results has been another negative outcome described in the literature. In one study by Bensend et. al., health care providers also mistakenly interpreted the meaning of a negative test result 31.6% of the time based on a misunderstanding (2014). Health care providers were described as giving families inaccurate risk assessments for personal health, future pregnancies, and other family members based on incorrectly interpreting test results. For example, health care providers mistakenly thought that hereditary breast and ovarian cancer could not be paternally inherited, that an individual with negative cystic fibrosis carrier screening could not have a child with cystic fibrosis, and provided inappropriate breast screening guidelines based on a negative BRCA1/2 results, despite a family history of breast cancer (Bensend et al., 2014).

Lastly, research has shown that patients do not always receive proper genetic counseling (Bensend et al., 2014). Health care providers have reported that pre-test counseling is difficult due

to time constraints and the challenge of talking about incidental findings and variants of uncertain significance. However, studies have found that families who have comprehensive pre-test counseling tend to have a better understanding and cope more effectively with the test results (Reiff et al., 2014).

3.1.4 Medical School Curriculum

There are guidelines for genetics curriculum for medical school education. The Association of Professors of Human and Medical Genetics (APHMG) developed a Core Curriculum for Medical School Genetics Education to establish competency-based education. The core curriculum includes guidelines on medical knowledge, patient care, interpersonal and communication skills, practice-based learning and improvement, professionalism, and systems based practice (Hyland et al., 2013). However, medical schools differ in philosophy and educational priorities, which leads to diversity in genetics knowledge among physicians (B. R. Korf, 2002).

Medical students receive genetic training, yet research suggests that close to graduation they often lack sufficient genetic knowledge for daily practice (Baars et al., 2005). One survey of 450 non-genetic providers found that 62% of participants had no formal education in genomic medicine or how to calculate risk predictions using genetic information (Haga et al., 2019). Another survey of 214 internist found that a majority wanted more training on when to order genetic testing, how to counsel patients, how to interpret genetic test results, and how to maintain patient genetic privacy (Klitzman et al., 2013).

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patients with hereditary cancer syndromes, traditional Mendelian genetic disorders, and multifactorial conditions. It has been recommended that medical students be exposed to genetic concepts throughout their education as well as in primary care settings in order to improve their genetic knowledge and reduce errors in assessing and treating patients (Hofman et al., 1993).

3.1.5 Study Purpose and Aims

The goal of this study was to assess the confidence and knowledge in genetic and genomic information of first year medical students. While studies have been conducted to learn about the genetic knowledge of health care professionals, undergraduate students, and the general population, there is a paucity of research that focuses on the acquisition of genetic knowledge in medical students. Addressing this gap in knowledge can have implications for medical school curriculum and training (Baars et al., 2005; Greb et al., 2009; Ling et al., 2008; Swanson et al., 1996). More efforts are needed to increase the genetic knowledge of non-genetic professionals in order to provide adequate care to patients and reduce negative outcomes.

Specific Aim I

Assess the clinical genetics knowledge, including knowledge of common genetic conditions and genetic testing options, of University of Pittsburgh medical students using a previously designed, secure survey tool.

Specific Aim II

Evaluate the process by which medical students acquired genetic knowledge through the Human Genetics course taught during their first year. The survey was distributed to the Class of 2025 medical students prior to and following the course. Responses between these two surveys were paired using secure identifiers to detect individual changes in knowledge over time.

3.2 Methods

3.2.1 Study Population

The target population for the pre-course and post-course survey was first year medical students at the University of Pittsburgh School of Medicine (UPSOM) during the Fall of 2021. All first-year medical students were eligible because they were required to take a three-week Human Genetics course during the Fall of 2021. There are 158 students in the Class of 2025.

3.2.2 Survey Development

The survey was originally developed in the Fall of 2020 (Raker, 2021). Selected questions were modified for the survey given in the Fall of 2021 based on participant responses and feedback from Dr. Saleem Khan, the course director, and the current thesis committee (see Appendix I). Institutional Review Board (IRB) approval was obtained for the updated questions (see Appendix B). In addition, the study was approved by the University of Pittsburgh Research on Medical Students (ROMS) Committee (see Appendix C).

The study invited students to complete the survey before and after the Human Genetics course, whereas the previous study only invited students to participate after completing the course (Raker, 2021). The survey included three sections: self-assessment, knowledge assessment, and UPSOM Human Genetics course assessment and prior experience in genetics. The self-assessment asked participants to rank their knowledge and understanding for twelve statements on a variety of genetic topics using a 5-point Likert-scale. The knowledge assessment included 20 questions that were organized into three categories: inheritance, clinical genetics scenarios, and

interpretation of genetic test results. Questions in the knowledge assessment included true/false questions and multiple-choice questions with four responses. The last section of the survey included nine questions that asked participants about the difficulty of the Human Genetics course and their prior experience with genetics.

3.2.3 Recruitment and Survey Distribution

Prior to recruitment, Vincent exemption was obtained to offer a gift card incentive (see Appendix D). Participants were offered the opportunity to enter a raffle to win a $25 Amazon gift card for completing the survey. Four participants were randomly selected from both the pre-course and post-course survey participants to receive the gift card. Participants were asked at the end of the survey if they wished to be entered into the raffle. If participants said yes, they were redirected to a second survey to provide an email address. The raffle survey was used as a second survey to guarantee anonymity of participants from their answers.

The pre-course and post-course survey were distributed to the first-year medical students by the Office of Medical Education (OMED) at the University of Pittsburgh. Prior to the distribution of the survey, the OMED representative was provided with the survey distribution dates and the appropriate survey invitations. The pre-course survey opened to participants on September 10, 2021 and closed on October 10, 2021 (see Appendix E). The reminder email was sent on September 27, 2021 (see Appendix F). The post-course survey opened on November 2, 2021 and closed on December 1, 2021 (see appendix G). The reminder email was sent on November 16, 2021 (see appendix H). All survey and raffle responses were collected anonymously by the Qualtrics survey system.

3.2.4 Statistical Methods

The survey responses were analyzed with descriptive statistics to determine how often an answer choice was selected. Qualtrics and Microsoft Excel were used to generate descriptive statistics from the survey responses. The Likert scale was used to determine participants' confidence on various genetic concepts for the pre-course and post-course survey. Wilcoxon Signed Rank tests were used to compare the self-assessment and knowledge assessment for the pre-course and post-course survey. Box plots were used to visualize the confidence and knowledge scores of participants based on previous work experience in genetics. Wilcoxon rank-sum tests were used to study the association between knowledge, confidence, and prior work experience in genetics. For the study, P-values under 0.05 were considered statistically significant. Stata statistical software (Version 16) was used for all statistical analyses.

3.3 Results

3.3.1 Response Rate

The survey was distributed to 158 first-year medical students at the University of Pittsburgh. Twenty-four participants responded to the pre-course survey. The response rate was 15.2%. While 24 participants completed the self-assessment, 23 participants completed the knowledge assessment, and 19 participants completed the UPSOM Human Genetics Course assessment and prior experience in genetics section. Fourteen participants completed the post-course survey (8.9% response rate). Twelve participants completed both the pre-course and post-

course surveys. The response rate for the completion of both surveys was 7.6%. Additionally, slightly more than 50% of participants for the pre-course and post-course survey identified as female (see Table 1). Gender was included in the demographic information collected to assess the composition of the participants.

Table 1. Demographic Information I

Demographic Information	Pre-Courese Responses (N=24)	Post Course Responses (N=14)
Gender		
Male	10	6
Female	12	8
Other	1	0

3.3.2 Self-Assessment of Knowledge

Participants were asked twelve self-assessment questions during the pre-course and post-course surveys. The twelve knowledge statements were broken down into three categories: fundamental genetic concepts, genetic concepts involving clinical skills, and cancer and prenatal genetics. The self-assessment asked participants to rank their knowledge and understanding for the statements using a 5-point Likert-scale (1=strongly disagree; 5= strongly agree). The maximum score was a confidence score of 60. The average confidence score for the pre-course survey was 34.5 out of 60 (57.5% confident) (see Appendix A: Table 11). The average confidence score for the post-course survey was 46.0 out of 60 (76.7% confident) (see Appendix A: Table 12). Participants' confidence in their knowledge increased by 11.5 points after completing the Human Genetics course.

Table 2 shows the medical students confidence change from the pre-course to the post-course surveys for fundamental genetic concepts. Participants felt confident about their knowledge

and understanding of fundamental concepts of genome organization, inheritance, and population genetics before and after completing the Human Genetics course based on a majority of participants answering “Strongly” or “Somewhat” agree.

Table 2. Self-Assessment: Fundamental Genetic Concepts

Genetic Concept	Pre-Course Survey Number of Participants (N=24)	Post-Course Survey Number of Participants (N=14)
I understand the foundational concepts of genome organization.		
Strongly agree	4	8
Somewhat agree	17	4
Neither agree nor disagree	1	0
Somewhat disagree	2	0
Strongly disagree	0	2
I understand the foundational concepts of genetic inheritance.		
Strongly agree	11	9
Somewhat agree	12	2
Neither agree nor disagree	0	1
Somewhat disagree	1	0
Strongly disagree	0	2
I understand how the fundamentals of population genetics relate to modern patient populations.		
Strongly agree	1	5
Somewhat agree	14	6
Neither agree nor disagree	5	0
Somewhat disagree	3	1
Strongly disagree	1	2

The self-assessment questions for genetic concepts involving clinical skills asked students to rank their confidence in knowledge and understanding of gathering a family history, performing a risk assessment based on the family history, identifying reasons for a genetics referral, communicating genetic principles to patients with limited genetic literacy, being familiar with genetic resources, knowing about the different techniques of genetic testing, and communicating benefits, risks, and limitations of genetic testing to a patient. Table 3 shows the difference in participants’ confidence before and after the Human Genetics course for genetic concepts involving clinical skills. Most respondents answered “Strongly,” “Somewhat” disagree, or “Neither agree or disagree” for knowledge about clinical skills in the pre-course survey, while a majority of participants answered “Strongly” or “Somewhat” agree in the post-course survey in most areas. While this suggests that participants felt more confident overall about their clinical

skills after completing the course, participants were not as confident in their knowledge of different genetic testing techniques, their ability to identify indications for a genetic referral, and their ability to effectively communicate with patients who have limited genetic literacy.

Table 3. Self-Assessment: Genetic Concepts Involving Clinical Skills

Genetic Concept	Pre-Course Survey Number of Participants (N=24)	Post-Course Survey Number of Participants (N=14)
I can gather a detailed family history for a genetic indication.		
Strongly agree	1	5
Somewhat agree	4	5
Neither agree nor disagree	4	1
Somewhat disagree	8	1
Strongly disagree	7	2
I can assess genetic risk based on the information within a family history.		
Strongly agree	1	7
Somewhat agree	8	4
Neither agree nor disagree	4	0
Somewhat disagree	5	2
Strongly disagree	6	1
I am comfortable identifying indications for referral to a genetics specialist.		
Strongly agree	1	4
Somewhat agree	2	5
Neither agree nor disagree	3	3
Somewhat disagree	9	0
Strongly disagree	9	2
I can apply knowledge of genetic principles to effectively communicate with patients who have limited genetic literacy.		
Strongly agree	2	5
Somewhat agree	5	4
Neither agree nor disagree	9	2
Somewhat disagree	4	1
Strongly disagree	4	2
I am familiar with clinical genetics resources and databases.		
Strongly agree	2	2
Somewhat agree	5	8
Neither agree nor disagree	0	2
Somewhat disagree	10	0
Strongly disagree	7	2
I am knowledgeable about the principles of cytogenetics and molecular genetic techniques.		
Strongly agree	2	5
Somewhat agree	5	3
Neither agree nor disagree	4	3
Somewhat disagree	7	2
Strongly disagree	6	1
I can describe the benefits, risks, and limitations of genetic testing to a patient.		
Strongly agree	3	5
Somewhat agree	5	6
Neither agree nor disagree	3	1
Somewhat disagree	6	1
Strongly disagree	6	1

Participants' responses for the self-assessment questions for cancer and prenatal genetics (Table 4) showed a similar pattern to genetic concepts involving clinical skills. Participants were asked to rank their knowledge and understanding of how genetics relate to the development,

diagnosis, and treatment of cancer, and their awareness about diagnostic testing methods for a prenatal diagnosis. Participants' responses changed from "Strongly" or "Somewhat" disagree to "Strongly" or "Somewhat" agree after completing the course. Overall, participants self-assessment suggested an increase in confidence after completing the Human Genetics course.

Table 4. Self-Assessment: Cancer and Prenatal Genetics

Genetic Concept	Pre-Course Survey Number of Participants (N=24)	Post-Course Survey Number of Participants (N=14)
I have thorough knowledge of genetics relating to the development, diagnosis, and treatment of cancer.		
Strongly agree	3	4
Somewhat agree	3	7
Neither agree nor disagree	6	0
Somewhat disagree	8	1
Strongly disagree	4	2
I am aware of methods for prenatal diagnosis of genetic conditions.		
Strongly agree	3	6
Somewhat agree	2	5
Neither agree nor disagree	6	2
Somewhat disagree	7	0
Strongly disagree	6	1

Of the twelve participants who completed both the pre-course and post-course survey, 11 participants reported increased confidence in their genetic knowledge after completing the Human Genetics course (see Table 5). One participant reported a decrease in confidence of genetic knowledge, despite answering more knowledge questions correctly than in the pre-course survey (see Table 9). A Wilcoxon Signed Rank Test was performed using Stata to compare the mean confidence scores of the 12 participants who completed both the pre-course and the post-course surveys. There was a significant increase in mean confidence scores when comparing the pre-course survey to the post-course survey ($p=0.0327$). The Spearman's correlation was calculated to measure the association between the confidence scores of the pre-course and post-course survey. The Spearman's rho was 0.007 indicating a very weak degree of correlation between the two scores. Additionally, a Wilcoxon Signed Rank Test and Spearman's correlation were calculated again after excluding individual I. Individual I is an outlier point for both the pre-course and the

post-course survey. The Wilcoxon Signed Rank test without individual I resulted in a higher significant increase in mean confidence scores when comparing the pre-course survey to the post-course survey (p=0.001). The Spearman's rho was 0.238 indicating a weak degree of correlation between the two scores without individual I. Individual I may be a possible case of malingering bias or extreme response bias.

Table 5. Comparison of Average Confidence Scores

Comparison of Average Confidence Survey Scores		
Participants	**Pre-Course (% correct)**	**Post-Course (% correct)**
A	14 (23.33%)	22 (36.67%)
B	29 (48.33%)	52 (86.67%)
C	32 (53.33%)	53 (88.33%)
D	31 (51.67%)	48 (80.0%)
E	33 (55.0%)	52 (86.67%)
F	30 (50.0%)	50 (83.33%)
G	37 (61.67%)	47 (78.33%)
H	29 (48.33%)	53 (88.33%)
I	57 (95.0%)	12 (20.0%)
J	27 (45.0%)	30 (50.0%)
K	24 (40.0%)	58 (96.67%)
L	39 (65.0%)	60 (100%)

3.3.3 Clinical Genetics Knowledge

The knowledge assessment included 20 questions, which were divided into three categories: inheritance, clinical genetic scenarios, and interpretation of genetic test results (see Tables 6-8). Table 6 shows participants' responses to questions about inheritance. Participants improved in selecting the correct answer after completing the Human Genetic course (46.1% with a 95% confidence interval of 17.9-74.3% to 83.7% with a 95% confidence interval of 63.1-100% correct responses). While more participants correctly answered the question about calculating the

risk for an affected child, they still had difficulty calculating the risk correctly after completion of the course (39.13% correct for the pre-course survey to 64.29% correct for the post-course survey). For this question, participants were asked to determine the chance that parents are carriers for a specific condition based on family history and general population carrier frequency, and then use those number to calculate the chance to have a child with the condition (see Table 6).

Table 6. Knowledge Assessment (Inheritance): Frequency of Correct Responses*

Inheritance				
Question	**Pre-course Survey Correct n (%)**	**95% Confidence Interval**	**Post-course Survey Correct n (%)**	**95% Confidence Interval**
What is the chance that a healthy child whose sibling has an autosomal recessive genetic condition will be a carrier?	**8 (34.78%)**	**15.32-54.24%**	**12 (85.71%)**	**67.38-100%**
A woman marries her 1st cousin, once-removed. Which scenario is most likely?	**15 (65.22%)**	**45.76-84.68%**	**11 (78.57%)**	**57.08-100%**
A healthy man whose brother has an autosomal recessive genetic condition marries a woman with no family history of this condition. The carrier frequency in the general population for this condition is 1/25, i.e., 1 in 25 individuals in the general population carries one pathogenic variant for this autosomal recessive condition. What is the probability that their child would be affected by this condition?	**9 (39.13%)**	**19.18-59.08%**	**9 (64.29%)**	**39.19-89.39%**
Select the statement that best describes X-linked recessive inheritance:	**8 (34.78%)**	**15.32-54.24%**	**13 (92.86%)**	**79.37-100%**
True or False: For multifactorial conditions, when the phenotype is more common in one sex, the risk is higher for relatives of the proband of the less susceptible sex.	**10 (47.62%)**	**27.21-68.03%**	**13 (92.86%)**	**79.37-100%**
What is the chance for a male with deletion of the 22q11.2 region, otherwise known as DiGeorge syndrome, to have a child with this same condition?	**5 (22.73%)**	**5.60-39.86%**	**11 (78.57%)**	**57.08-100%**
A pregnant woman comes for genetic counseling because the father of her female fetus has Leber's hereditary optic neuropathy (LHON), a mitochondrially inherited genetic condition. What is the chance that this fetus is affected with LHON?	**18 (78.26%)**	**61.40-95.12%**	**13 (92.86%)**	**79.37-100%**

***23 students participated in the pre-course survey and 14 in the post-course survey**

Questions related to clinical scenarios are included in Table 7. While the average correct score was lower for some questions after completion of the Human Genetics course, there is no statistical evidence that students performed differently on the pre-course and post-course surveys. There is overlap between 95% confidence intervals. However, students still struggled to answer specific knowledge questions correctly after the completion of the course. Participants had difficulty answering questions about who should be tested first when there is a family history of breast cancer (30.43% correct for the pre-course survey to 14.29% correct for the post-course survey), which test to order when a child has a complex clinical presentation (34.78% to 28.57%), what screening guidelines are most appropriate for a female patient with a family history of breast and ovarian cancer and no BRCA1 or BRCA2 variants detected via direct-to-consumer testing (39.13% correct for the pre-course survey to 57.14% correct for the post-course survey), and how to interpret a variant of uncertain significance (13.04% to 28.57%).

The answer choices for the question of who to test first given a family history of breast cancer included the unaffected patient, the mother with a breast cancer diagnosis at age 45, and a first cousin with a breast cancer diagnosis at age 35. A majority of participants chose to test the patient first, rather than testing the mother who has a diagnosis of breast cancer.

Participants also struggled to identify the appropriate testing given a patient's clinical presentation in a pediatric setting. The question asked about the best test to identify a microdeletion: 28.57% of participants selected the correct answer to order a microarray. The remaining participants chose to order a karyotype, a neuromuscular disorder panel, or DTC testing.

Additionally, while more participants correctly answered the question about next steps for a patient who had direct-to-consumer (DTC) testing in the post-course survey (39.13% to 57.14%), some participants appeared to have difficulty understanding the clinical significance of results. In

the scenario, a woman with a family history of breast and ovarian cancer undergoes DTC testing and is not found to have a BRCA1/2 mutation. Based on the results, some participants would tell the patient that she is at population risk for breast cancer and should follow population screening guidelines. The participants may have selected the incorrect response thinking that DTC is clinically diagnostic, however DTC should not be used for clinical management and the patient's family history is important when considering screening recommendations.

Table 7. Knowledge Assessment (Clinical Genetics Scenarios): Frequency of Correct Responses*

Clinical Genetics Scenarios				
Question	**Correct n (%)**	**95% Confidence Interval**	**Post-course Survey Correct n (%)**	**95% Confidence Interval**
A female patient with a family history of hereditary breast and ovarian cancer shows you her results from direct-to-consumer testing. The results show that the patient does not have a mutation in the BRCA1 or BRCA2 genes. What would you recommend as next step for the patient?	**9 (39.13%)**	**19.18-59.08%**	**8 (57.14%)**	**31.22-83.06%**
A 21 year old woman reports that her mother had a BRCA1 mutation and provides you with the report confirming this information. She is unwilling to undergo genetic testing at this stage in her life, but is fearful of developing cancer. How do you counsel this patient?	**17 (73.91%)**	**55.96-91.86%**	**11 (78.57%)**	**57.08-100%**
A 30-year-old woman comes to the genetics clinic for BRCA1 and BRCA2 testing. She does not have breast cancer, but her mother was diagnosed with breast cancer at age 45, her first cousin was diagnosed with breast cancer at age 35, and her paternal aunt was diagnosed with breast cancer at age 65. To clarify the woman's risk, which of the following individuals should be tested first?	**7 (30.43%)**	**11.63-49.23%**	**2 (14.29%)**	**0-32.62%**
A woman with hereditary nonpolyposis colorectal cancer, an adult-onset condition, wants her 14 year old daughter to be tested for the known familial mutation. What do you tell this woman and her daughter?	**20 (86.96%)**	**73.20-100%**	**10 (71.43%)**	**47.77-95.09%**
A 5 year old girl presents to your clinic with dysmorphic features, developmental delay, microcephaly, and a history of seizures suggestive of a microdeletion syndrome. What is the most appropriate first genetic test to order for this child?	**8 (34.78%)**	**15.32-54.24%**	**4 (28.57%)**	**4.91-52.23%**
When is it LEAST appropriate to order a karyotype?	**14 (60.87%)**	**40.92-80.82%**	**11 (78.57%)**	**57.08-100%**
A woman is referred to your clinic at 19 weeks gestation because her amniocentesis, performed for advanced maternal age, revealed a karyotype of 47XXY (Klinefelter syndrome). The woman and her partner are tearful, and are debating whether to terminate the pregnancy. How would you discuss this result with the couple?	**19 (82.16%)**	**66.52-97.80%**	**10 (71.43%)**	**47.77-95.09%**
Non-Invasive Prenatal Testing (NIPT) has a very high detection rate for Down syndrome, therefore, diagnostic testing is not needed following a positive NIPT. Is this statement true or false?	**22 (95.65%)**	**87.32-100%**	**13 (92.86%)**	**79.37-100%**

***23 students participated in the pre-course survey and 14 in the post-course survey**

Table 8 shows participants' responses to questions about interpretation of genetic test results. Overall, participants improved on correctly answering the questions about clinical genetic

scenarios. However, participants continued to have difficulty in determining the significance of a variant of uncertain significance (VUS). In the pre-course survey, 13.04% participants selected the correct answer of testing other similarly affected family members. For the post-course survey, 28.57% participants selected the correct response (see Table 8). 71.63% of participants chose to repeat the test, test other affected family members, and test a different tissue sample. Participants appeared to have difficulty understanding the meaning of a VUS and how to determine the clinical meaning of the VUS in the context of the family history.

Table 8. Knowledge Assessment (Interpretation of Genetic Test Results): Frequency of Correct Responses*

Interpretation of Genetic Test Results				
Question	**Pre-Course Survey Correct n (%)**	**95% Confidence Interval**	**Post-course Survey Correct n (%)**	**95% Confidence Interval**
A couple whose child had a positive newborn screen for cystic fibrosis presents to your clinic for counseling. The child's sweat test returns negative and genetic testing reveals one mutation: a F508 deletion. What do these results mean for the child?	**12 (52.17%)**	**31.75-72.59%**	**11 (78.57%)**	**57.08-100%**
An infant with deletion of the 22q11.2 region, otherwise known as DiGeorge syndrome, is evaluated by medical genetics. Neither of the child's parents carry the deletion. The parents are interested in having more children and want to know their risk of having another affected child. What information would you provide when discussing recurrence risk for future pregnancies?	**15 (65.22%)**	**45.76-84.68%**	**10 (71.43%)**	**47.77-95.09%**
A genetic test report reveals a "variant of unknown significance". What does this result mean for the patient?	**17 (73.91%)**	**55.96-91.86%**	**11 (78.57%)**	**57.08-100%**
Which of the following methods can be used to determine the clinical meaning of a variant of uncertain significance?	**3 (13.04%)**	**0-26.8%**	**4 (28.57%)**	**4.91-52.23%**
If a fetus has an increased nuchal translucency and an atrioventricular septal heart defect, which of the following karyotype results is the most likely to be found on amniocentesis?	**11 (47.83%)**	**27.41-68.25%**	**13 (92.86%)**	**79.37-100%**

***23 students participated in the pre-course survey and 14 in the post-course survey**

Of the twelve participants who completed both the pre-course and post-course survey, 10 participants improved their overall knowledge assessment score and two participants had the same score (see Table 9). A Wilcoxon Signed Rank Test was performed using Stata to compare the mean knowledge scores of the 12 participants who completed both the pre-course and the post-course surveys. There was a significant increase in mean test scores when comparing the pre-course survey to the post-course survey ($p=0.002$). The Spearman's correlation was calculated to

measure the association between the scores of the pre-course and post-course survey. The Spearman's rho was 0.57 indicating a moderate degree of correlation between the two scores.

Table 9. Comparison of Average Knowledge Scores

Comparison of Average Knowledge Survey Scores		
Participants	**Pre-Course (% correct)**	**Post-Course (% correct)**
A	4 (20%)	4 (20%)
B	10 (50%)	16 (80%)
C	10 (50%)	13 (65%)
D	12 (60%)	15 (75%)
E	13 (65%)	15 (75%)
F	11 (55%)	16 (80%)
G	10 (50%)	13 (65%)
H	5 (25%)	13 (65%)
I	14 (70%)	16 (80%)
J	13 (65%)	13 (65%)
K	13 (65%)	14 (70%)
L	13 (65%)	17 (85%)

3.3.4 UPSOM Human Genetics Course Assessment and Prior Experience in Genetics

Participants were asked questions about prior experiences, and the difficulty level and areas of improvement for the Human Genetics course. Table 10 shows the answers to questions about genetic work experience and completion of a genetics course in undergraduate school. A majority of participants did not have prior work experience with genetics (greater than 60%). Figures 1 and 2 show that participants with no prior work experience with genetics had higher confidence and knowledge scores than participants with prior genetics work experience. A nonparametric t-test was performed to show the differences in self-assessment and knowledge scores between participants who had prior work experience in genetics and those who did not. There was no statistically significant difference between confidence scores for participants with prior work

experience and those who did not (p=0.5182). Additionally, there was no statistically significant difference between knowledge scores for participants with prior work experience and those who did not (p=0.0909). It is difficult to know if this is an accurate representation of the class due to the low response rate. Additionally, after completing the Human Genetics course, 10/14 (71.43%) found the course moderately challenging, while the remaining four found the class slightly challenging. Participants also requested for material to be more applicable to a clinical situation and that clinical examples correlate with lecture material.

Table 10. Demographic Information II

Demographic Information	Pre-Courese Responses (N=24)	Post Course Responses (N=14)
Prior Work Experience with Genetics		
Yes	7	4
No	11	10
Not Sure	1	0
Took Genetic Course in Undergraduate		
Yes	14	9
No	5	5
Not Sure	0	0

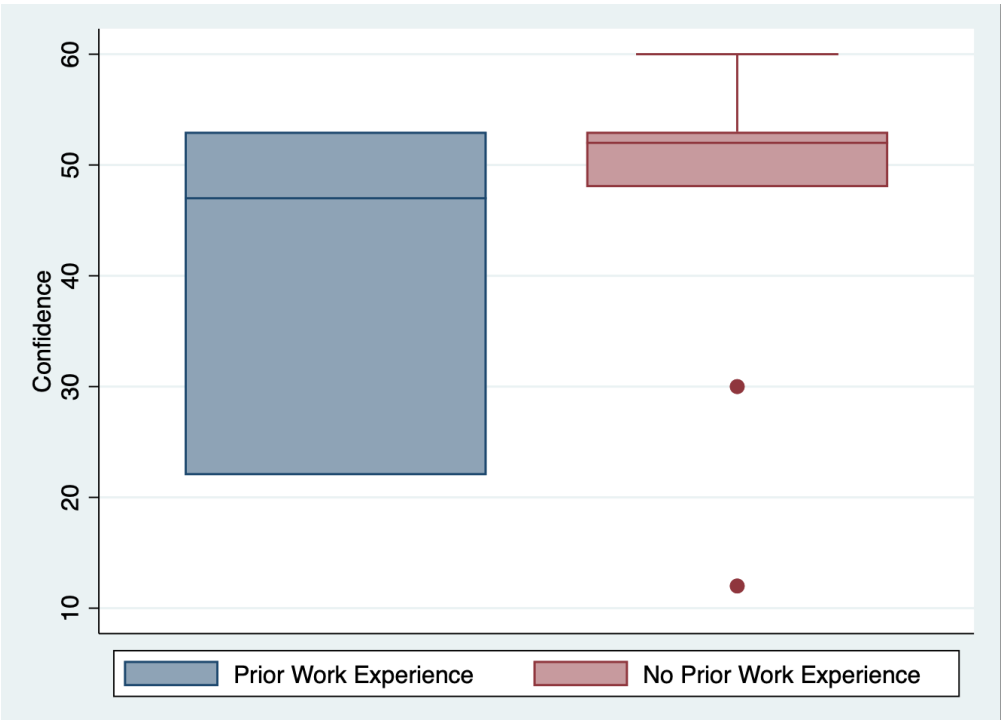

Figure 1. Confidence Scores Segregated by Prior Work Experience

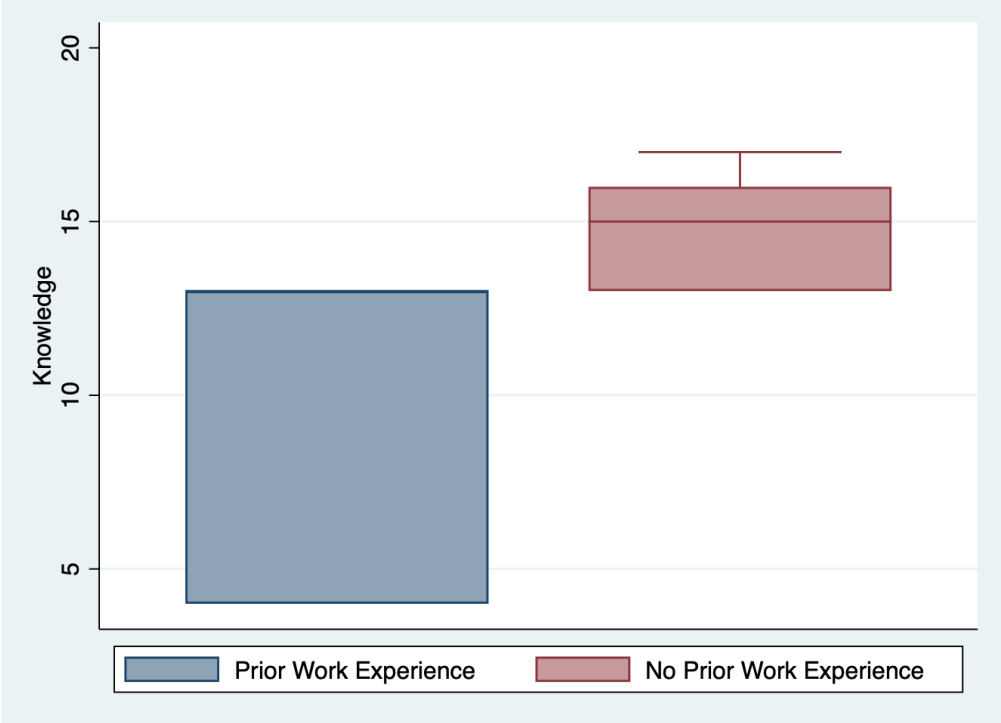

Figure 2. Knowledge Scores Segregated by Prior Work Experience

3.4 Discussion

The purpose of this study was to examine medical students' acquisition of genetics knowledge after completion of a Human Genetics course. Based on feedback and analysis of limitations from the post-course survey distributed to the Class of 2024, survey questions were edited to better match the material covered in the Human Genetics course (Raker, 2021). However, despite the rephrasing of questions, participants still struggled with knowing the best genetic test to order, interpreting direct-to-consumer genetic test results, and understanding the clinical meaning of variants of uncertain significance.

This survey also assessed confidence and knowledge of genetic concepts to help evaluate the participants' acquisition of genetic knowledge. Confidence surveys (i.e., self-assessment measures) have often been used to determine an individual's knowledge. For example, participants rate their confidence rather than answering knowledge questions. However, confidence is not always an accurate representation of a participant's knowledge, which is why a combination of confidence and knowledge questions may provide more accurate information about a participant's knowledge (Favazzo, Willford, & Watson, 2014). When analyzing the knowledge scores and confidence scores of the participants, there is a weak correlation (see Appendix A: Figure 4). One individual reported a low confidence score but had a higher knowledge score, while another individual reported a higher confidence score but had a lower knowledge score. Assessing the participants' knowledge through knowledge questions appeared to provide more accurate information about the participants' genetic knowledge and ability to apply that knowledge in clinical scenarios.

3.4.1 Confidence Scores Results

Previous surveying of the Class of 2024 showed a 7.7% difference between the confidence and knowledge scores. The Class of 2024 had an average confidence score of 79.8% (47.93 out of 60), while the average score for the Clinical Genetics Knowledge section was 72.1% (Raker, 2021). For the Class of 2025, there is also a difference between the participants' confidence in their knowledge and their actual genetic knowledge. The average confidence score for the post-course survey was 46.0 out of 60 (76.7% confident), while the average score of the knowledge assessment section for the post-course survey was 71.1%. While students reported having a higher confidence score after completing the Human Genetics course, some knowledge questions had an average correct score of less than 70%, suggesting that medical students may be overestimating their genetic knowledge.

Previous studies have shown that health care providers report confidence in their genetic knowledge but then struggle to apply the knowledge in a clinical setting and on a knowledge assessment. This suggests that some providers may not recognize their lack of knowledge (Chow-White et al., 2017; Macklin et al., 2019). However, studies have also shown that health care providers report having low confidence in their genetic knowledge and feeling unprepared to address genetic concepts in the clinical setting (Mikat-Stevens et al., 2015; Powell et al., 2012). While some participants in this survey did report low confidence in their genetic knowledge, the average confidence score was 79.7% for the post-course survey, compared to 34.5% for the pre-course survey. The increase in confidence scores indicates that a majority of participants felt more confident in their knowledge after completion of the Human Genetics course.

Participants were asked to ranked their confidence about genetic inheritance and population genetic concepts because obtaining an accurate and comprehensive family history is important for

calculating risk assessment, adjusting screening or management recommendations, and determining if a patient meets any testing criteria (Ozanne et al., 2012). 78.6% of participants were confident in their ability to assess genetic risk based on family history, understand inheritance, and understand population genetic. Participants were asked to apply this knowledge to determine a couple's risk to have a child with cystic fibrosis based on family history and general population carrier frequency. Despite 78.6% of participants being confident in their knowledge, 64.29% of participants answered the knowledge question correctly.

Limited genetic knowledge reported by non-genetic providers may result from their education and/or lack of exposure to genetics in a clinical setting (Carroll et al., 2016; Haga et al., 2019; Hofman et al., 1993; Powell et al., 2012). While a genetic course in medical school can improve a student's genetic knowledge as demonstrated in this study, one course may not be sufficient to prepare future physicians for the different clinical situations they may encounter in their practice (Hofman et al., 1993). As a result, non-genetic providers have requested medical schools provide updated knowledge and incorporate more relevant training instead of focusing on rare conditions (Harding et al., 2019). This sentiment was also mirrored in this study as participants requested for material to be more applicable to a clinical situation and that clinical examples correlate with lecture material.

Overall participants' confidence in their knowledge and understanding of genetic concepts increased after completing the Human Genetics course. While this suggests that participants felt more confident overall about their clinical skills after completing the course, participants were not as confident in their knowledge of understanding different genetic testing techniques, their ability to identify indications for a genetic referral, and their ability to effectively communicate with patients who have limited genetic literacy.

3.4.2 Knowledge Scores Results

Participants had difficulty answering certain genetic knowledge questions correctly, specifically questions related to certain clinical situations and interpreting genetic results (see Table 7 and 8). While the average correct score was lower for some questions after completion of the Human Genetics course, there is no statistical evidence that students performed differently on the pre-course and post-course surveys. However, students still struggled to answer specific knowledge questions correctly after the completion of the course. For example, participants had difficulty answering questions about who should be tested first when there is a family history of breast cancer (30.43% correct for the pre-course survey to 14.29% correct for the post-course survey), which test to order when a child has a complex clinical presentation (34.78% to 28.57%), what screening guidelines are most appropriate for a female patient with a family history of breast and ovarian cancer and no BRCA1 or BRCA2 variants detected via direct-to-consumer testing (39.13% correct for the pre-course survey to 57.14% correct for the post-course survey), and how to interpret a variant of uncertain significance (13.04% to 28.57%).

There is evidence suggesting that about one third of genetic tests ordered by non-genetic providers are ordered inappropriately because the provider did not follow guidelines, gave false reassurances to patients, or did not recognize differential diagnoses (Klitzman et al., 2013; Montanez et al., 2020; Shields et al., 2008). Participants in this study struggled to know who to test first in a family with a history of breast cancer. This problem has been reported in the literature. Bensend et. al. reported that health care providers do not always know who the best person is to test first when there is a family history of cancer (2014). The survey questions asked who would be best to test first: the unaffected patient, the mother diagnosed with breast cancer at age 45, a first cousin diagnosed with breast cancer at age 35, or a paternal aunt diagnosed with breast cancer

at age 65. Based on national guidelines, the mother should be tested first given her diagnosis of cancer and her relationship to the patient (NCCN, 2022).

Participants also had difficulty in identifying the most appropriate test for a 5-year-old girl with dysmorphic features, developmental delay, microcephaly, and a history of seizures. Participants were told that this clinical presentation was suggestive of a microdeletion syndrome, yet a majority of participants thought a neuromuscular disorder panel or karyotype was the best test. Guidelines recommend microarray or exome sequencing as first tier testing in such circumstances when individuals have developmental delays or congenital anomalies (Miller et al., 2010).

Additionally, participants struggled with understanding the clinical significance of direct-to-consumer (DTC) testing, which is a concern primary care physicians share (Powell et al., 2012). Primary care physicians were surveyed about their knowledge and understanding of DTC testing, and a majority reported feeling unprepared to answer patient questions concerning DTC testing (Powell et al., 2012). In the survey question, a woman with a family history of breast and ovarian cancer undergoes DTC testing and is not found to have a BRCA1/2 mutation. Four participants would tell the patient to follow general population screening guidelines, while two participants would tell the patient that she is not at increased risk to develop breast cancer compared to the general public. The participants may have selected the incorrect response thinking that DTC is clinically diagnostic, however DTC should not be used for clinical management and the result needs to be validated in clinical lab (Moscarello, Murray, Reuter, & Demo, 2019). Additionally, participants may have not recognized the limitations of DTC genetic testing including lack of comprehensive testing. Moreover, the woman in the clinical scenario has a family history of breast and ovarian cancer, which increases her lifetime risk to develop breast and ovarian cancer.

The average correct score for the knowledge assessment section for the post-course survey was 71.1%, suggesting that participants' genetic knowledge in certain areas is insufficient after completing the Human Genetics course. Insufficient genetic knowledge is associated with deficiencies in evaluating family history, recognizing genetic diagnoses, and making referrals to genetic counseling services, which are topics the participants struggled to answer correctly (Thurston et al., 2007). These deficiencies can contribute to non-genetic providers inappropriately ordering genetic testing, misinterpreting results, and providing inappropriate or no genetic counseling (i.e. pre-test and/or post-test counseling) (Bensend et al., 2014). These errors can result in unnecessary cost to patients, inappropriate care, inaccurate information, and emotional harm, which is why additional education and training are needed to improve health care providers' genetic knowledge.

3.4.3 Improvements Regarding Education and Resources

Based on the participants' responses to the surveys, modifications in the curriculum may help improve medical students' genetic knowledge and enhance their ability to apply their knowledge in future clinical experiences. For example, one possible explanation for the difference in confidence and knowledge scores in this study could be lack of clinical exposure and understanding how to apply genetic knowledge in a clinical setting. Studies have suggested that medical schools integrate genetic curriculum throughout the four years and teach students how to apply genetic knowledge in the clinical setting (Greb et al., 2009; Plunkett-Rondeau et al., 2015).

Formal and informal education such as seminars are required for health care providers to keep up-to-date with current genetic knowledge, especially knowledge related to daily practice and with a focus on clinical application (Harding et al., 2019). Additionally, collaboration between

non-genetic and genetic providers is an opportunity to enhance knowledge and provide support while optimizing patient care in an informal educational manner. Non-genetic providers and genetic counselors have expressed a desire to work together to help patients have access to genetic testing by collaborating in ordering testing and interpreting test results (Bensend et al., 2014; Carroll et al., 2016). This partnership could help non-genetic providers navigate the evolving field of genetics with the support of genetic professionals.

3.4.4 Study Limitations

The study had a number of limitations. The most importation limitation was the low response rate. The pre-course survey had a 15.2% response rate, and the post-course survey had an 8.9% response rate. Additionally, only fourteen students out of 158 participated in both the pre-course and post-course surveys (a response rate of 7.6%). The participation rate may have dropped for the post-course survey because the survey was sent towards the end of the semester and students may have been busy with preparing for the end of the semester and winter break. Also, individuals who did not perform well in the Human Genetics course might have been reluctant to participate in the post-course survey.

The chance to win a $25 Amazon gift card was offered as incentive for the first-year medical students who participated in either the pre-course or post-course surveys. While the incentive doubled the response rate from the survey offered to the Class of 2024 (6.8%), additional incentives may be needed in future studies. Improving the response rate is important because the small sample size may not accurately represent the knowledge and opinions of medical students at the University of Pittsburgh.

Additionally, selection bias may be present in the survey. Individuals who are interested in genetics or had genetic experience may have been more likely to participate in the survey. There is also the possibility that students who performed well in the course were more likely to participate in the post-course survey, compared to individuals who did not enjoy the course or who did not perform well. Lastly, there is also the possibility of that the COVID-19 pandemic negatively impacted the response rate.

3.4.5 Future Research

This study was distributed before and after the Human Genetics course in the Fall of 2021 at the University of Pittsburgh. The course is required for all first-year medical students. The goal of the survey was to identify changes in the medical students' understanding of clinical genetics and genetic testing following completion of the Human Genetics course. Understanding how medical students acquire genetic knowledge can be useful in informing curriculum changes. A future study could survey the medical students again during their fourth year to measure the retention of knowledge. Measuring the knowledge retention of medical students during their fourth year could determine how their overall training and clinical experiences affect their genetic knowledge. Additionally, medical students have the option to take additional genetic courses and will have exposure to clinical genetics during rotations at the University of Pittsburgh. Understanding how these supplementary educational opportunities and clinical rotation affect medical students' genetic knowledge may be beneficial. Additional studies could show how medical student's genetic knowledge changes over time and could possibly identify any gaps in their knowledge. The School of Medicine at the University of Pittsburgh could use the information to alter curriculum and clinical rotation experiences.

3.5 Conclusion

For the Class of 2025, there was a difference between the participants' confidence in their knowledge and their actual genetic knowledge when comparing the participants self-assessed knowledge scores against their knowledge assessment scores. The average confidence score for the post-course survey was 46.0 out of 60 (76.7% confident), while the average correctness score of the knowledge assessment section was 71.1%. It is possible that the medical students overestimate their genetic knowledge.

The self-assessment and knowledge assessment responses indicate the need for more education that relates to a clinical setting, which has been previously reported in the literature (Harding et al., 2019). Overall participants had a higher self-assessed knowledge score and average knowledge assessment score after completion of the Human Genetics course. Participants' self-assessment scores suggested they were confident in their knowledge but then had difficulty answering questions correctly about clinical scenarios. After completion of the Human Genetics course, participants scored the best in the inheritance section, and scored the lowest in the clinical genetics scenario section.

Participants struggled with choosing the most appropriate test to order, identifying the most appropriate person to test, interpreting and determining medical management based on the results of direct-to-consumer testing, and interpreting variants of uncertain significance, which are all skills that require genetic knowledge. The results of the study indicate a need for educational and policy changes to improve medical students' genetic knowledge and help integrate the use of genetic testing into clinical settings. The integration of genetic testing into non-genetic clinics is important due to the shortage of genetic professionals, patients' limited access to genetic clinics, and long wait times for patients (Jenkins et al., 2021).

Studies have shown that multiple classes and clinical experiences are beneficial to increasing genetic knowledge. While this study supports previous results that one genetics course can improve an individual's genetic knowledge, additional educational courses and integration of genetics into the clinical setting may increase health care providers' confidence and knowledge regarding genetic and genomic information.

While it is hard to determine if the survey responses are representative of the class due to the low response rate, the data are supportive of additional education and training on how to apply genetic knowledge in a clinical setting. Surveying the University of Pittsburgh's Medical School Class of 2025 during their final year would be beneficial to determine the effectiveness of the program and the retention rate of medical students' genetic knowledge. Further investigation of medical students' acquisition of genetic knowledge may provide information to guide curriculum changes and standardize training programs.

4.0 PUBLIC HEALTH AND GENETIC COUNSELING SIGNIFICANCE

Genetic professionals encounter challenges keeping up with the demand for genetic testing, which is why non-genetic providers will likely continue to be involved with the provision of genetic testing (Brothers & Knapp, 2018). Additionally, patients have a long-term relationship with their primary care physicians and the established level of trust may enhance patient's willingness to discuss genetic-related concerns and genetic testing with their primary care provider (Ormond, 2009; Powell et al., 2012). Updates to medical school curriculum are needed to help increase the knowledge of non-genetic providers to ensure that patients have access to appropriate genetic information and services. This study is relevant to public health because non-genetic providers require a certain level of genetic knowledge to provide appropriate patient care. The significance of this study to public health can be examined through the evaluation of two core functions of public health: assessment and policy development.

Non-genetic providers struggle to incorporate genetic testing into their clinical practice for several reasons, including lack of knowledge, confidence, time, and guidelines (Brothers & Knapp, 2018; Harding et al., 2019; Mikat-Stevens et al., 2015; Suther & Goodson, 2003). Non-genetic providers have listed a number of barriers that have prevented the adequate implementation of genetic testing into the non-genetic clinical setting with lack of confidence and knowledge of genetic and genomic concepts being the most important (Harding et al., 2019; Powell et al., 2012). Non-genetic providers should have a solid understanding of inheritance patterns, the sensitivity of testing, how to collect and assess a three-generation family history, indications of common genetic conditions, potential psychosocial concerns related to genetic testing, and the ways in which genetic test results can inform approaches to management (Ormond, 2009). This study surveyed

medical students' confidence and knowledge on relevant genetic concepts to assess their understanding.

The results of the assessment from the study have the potential to inform curriculum and policy changes. While most medical schools teach a genetics course during the first year, this may not be sufficient for medical students to obtain the genetic knowledge they need in the clinic (Hofman et al., 1993; Ormond, 2009). Non-genetic providers have critiqued the genetic content covered in medical schools, citing the need for more relevant training instead of focusing on rare conditions. For example, genetic information should be integrated in clinical rounds, case discussions, and course examinations (Harding et al., 2019; Telner et al., 2008). Genetic counselors can also assist in the training of medical students by demonstrating their genetic skills and how they work with different providers to help provide care of patients. Lastly, while medical schools should teach students the fundamentals of genetics, they should also teach students how to apply that knowledge in various clinical settings and how to identify resources for learning genetic information on their own as the field of genetics is constantly evolving (Plunkett-Rondeau et al., 2015; Robinson & Fong, 2008). Educational and policy changes are needed to improve the genetic knowledge of non-genetic providers during and after medical school, and to increase the accessibility of genetic testing to patients by incorporating genetic testing into non-genetic clinical settings (Harding et al., 2019).

Additionally, there are clinical genetics workforce shortages and capacity limitations that prevent patients from receiving genetic services. For example, some institutions report job vacancies for clinical geneticists that are unfilled for more than three years and capacity limitations can lead to long wait times (Jenkins et al., 2021). Increasing the recruitment of clinical genetics trainees and genetic counselors, and enhancing collaborative practices can help decrease barriers

related to the genetic workforce shortages and limitations (Jenkins et al., 2021). Collaboration between health care providers and genetic providers would allow genetic providers to act as a resource and share their genetic knowledge. Healthcare providers and genetic counselors have expressed a desire to develop professional partnerships to help better serve patients (Bensend et al., 2014; Carroll et al., 2016). If non-genetic physicians and genetic professionals work together, physicians may improve their ability to obtain informed consent, order appropriate testing, and correctly interpret genetic test results (Ormond, 2009). This is relevant to genetic counseling practices because genetic counselors collaborate with multiple health care providers and are involved in education efforts with non-genetic providers. Understanding the genetic information needs of health care providers can help genetic counselors adjust their educational efforts and provide clinically relevant information.

5.0 PUBLIC HEALTH ESSAY

5.1 Introduction to Raw Genetic Data

Direct-to-consumer (DTC) genetic tests are publicly advertised and can be sold directly to consumers without involving a healthcare professional or insurance companies. DTC companies like 23andMe, AncestryDNA, My Heritage, and Family Tree DNA, provide consumers with information regarding ancestry, risks of developing certain conditions, carrier status, and more (Tandy-Connor et al., 2018). Individuals may find DTC genetic testing attractive because it can help those with a limited family history, it can be cheaper than clinical genetic testing, and can be easier to access since testing can be purchased online (Tandy-Connor et al., 2018). A majority of individuals report wanting to learn more about their genetic make-up and ancestry when using DTC genetic testing (Nelson, Bowen, & Fullerton, 2019; Wang et al., 2018). Some studies have even seen positive behavioral and health changes based on DTC test results. For example, a meta-analysis found that 23% of consumers reported a positive lifestyle change (Stewart et al., 2018).

While some consumers are interested in learning more about their health, many are unaware that DTC tests are not diagnostic and are not comprehensive, meaning that results often need to be confirmed by a certified clinical lab and the patient could be at risk for other conditions or have a variant in a gene not covered by DTC companies (Tandy-Connor et al., 2018). Some DTC companies are restricted by the Food and Drug Administration (FDA) from "offering products that function as diagnostic tests," which is why the genes associated with different health conditions are usually not "comprehensively sequenced or analyzed in DTC tests, nor do the tests include all the genes that have been associated with these health conditions" (Tandy-Connor et al.,

2018). Diagnostic tests means that the results of the genetic test are supposed to help guide management and surveillance of the condition, which is not the purpose of DTC tests.

In 2013, the FDA ordered 23andMe "to discontinue marketing of the Personal Genome Service (PGS)," which led to the removal of health information from 23andMe's genetic reports. 23andMe was able to provide consumers their raw genetic data, which created the opportunity for third-party interpretation companies to fill in this gap of missing health information (Wang et al., 2018). Some third-party interpretation companies charge consumers a fee to interpret their raw genetic data and provide additional information that DTC companies did not provide. Raw data refers to uninterpreted genetic data (Nelson et al., 2019).

Additionally, in 2014 the Health Insurance Portability and Accountability Act (HIPAA) allowed patients the right to have full access to laboratory records, including access to uninterpreted genetic sequence information (Nelson & Fullerton, 2018). The updated policy allows patients to have access to their raw genetic data. Consumers can obtain their uninterpreted genetic data from DTC genetic tests, researchers, or clinical testing labs and then seek out for a third-party tool for interpretation of their raw data (Nelson & Fullerton, 2018). Third-party interpretation (TPI) companies, such as Promethease, Interpretome, LiveWello, Codegen.eu, and Enlis Personal, arose, in part, due to stricter regulation of DTC genetic testing companies to provide additional information from raw genetic information (Badalato, Kalokairinou, & Borry, 2017).

Additionally, third-party interpretation companies have increased due to the growing availability of raw DNA data from DTC testing companies and the desire of consumers to learn how their raw data may inform their risks of certain health conditions. It is expected that third-party interpretation services will continue to grow particularly because of the All of Us Research Program, which is anticipated to provide participants with their raw sequence data (Nelson et al.,

2019; Wang et al., 2018). However, DTC and third party interpretation companies have caused concerns about the "appropriate use of healthcare resources, clinical utility, provider and patient understanding of limitations, and psychosocial impact on consumers" (Moscarello et al., 2019). For example, in 2017, DTC companies started to return health risk information based on updated guidelines from the FDA (Wang et al., 2018). At the time, the FDA allowed 23andMe Personal Genome Service Genetic Health Risk (GHR) to market testing for 10 diseases or conditions: Parkinson's disease, late-onset Alzheimer's disease, celiac disease, alpha-1 antitrypsin deficiency, early-onset primary dystonia, factor XI deficiency, Gaucher disease type 1, glucose-6-phosphate dehydrogenase deficiency, hereditary hemochromatosis, and hereditary thrombophilia (FDA, 2017).

5.2 Interpretation by Third-Party Companies

One study found that 67% of individuals who purchased DTC testing used a third-party interpretation company to analyze their raw genetic data and obtain additional health information that was not included in the original DTC report (Wang et al., 2018). The raw genotyping data can include variants associated with conditions not reported by DTC companies (Tandy-Connor et al., 2018).

It is important to note that raw genetic data are typically accompanied by a disclaimer that states the data are not validated nor accurate, and should not be used to make decisions concerning medical management because third-party interpretation (TPI) services are not approved to be used as diagnostic testing (Tandy-Connor et al., 2018). Additionally, consumers and health care providers should be aware that third-party interpretation companies differ in the bioinformatic

technology, type of information returned, and the level of transparency about analysis and interpretation (Nelson & Fullerton, 2018).

TPI companies use different analytical and bioinformatic methods to generate different genetic information. When comparing an individual's raw data with publicly available SNP information, some TPI companies will go an extra step to contextualize the consumer's results with a given population to provide a risk estimate or recommendation (Nelson & Fullerton, 2018). SNP genotyping is similar to spot checking a gene at a particular site rather than performing full sequencing or deletion/duplication analysis, which are used by clinically certified laboratories for diagnostic purposes. Consumers can become confused or concerned with their results because some SNPs are associated with protection against a condition while others may be associated with risk for the condition. Some TPI companies create an algorithm to sum up the overall level of risk associated with SNPs to give consumers a better idea because of this conflicting information (Nelson & Fullerton, 2018).

The type of information provided to consumers from TPI companies differs based on the company. Nelson at al. 2018 analyzed 23 TPI companies and found that 16 companies provide information about health and wellness, eight companies offered information about genetic ancestry, and five companies reported information about genealogy. Companies can also differ on the specific details in each category. For example, of the 16 companies that provided information about health and wellness, only some reported information about carrier status, pharmacogenetics, diet and fitness, and various physical and personality traits (Nelson & Fullerton, 2018).

TPI companies also use different methods to interpret results, typically using a variety of scientific publications and publicly available databases (Nelson & Fullerton, 2018). Despite concern in the accuracy of classifications from publicly available databases, third-party companies

may use publicly available databases to report the classification of a variant. For example, some publicly available databases may report a certain single-nucleotide polymorphism (SNP) as pathogenic despite clinical laboratories reporting the variant as benign or a variant of uncertain significance (Badalato et al., 2017; Tandy-Connor et al., 2018). Third-party companies also do not consider interpretation factors like classification discrepancies (Tandy-Connor et al., 2018).

5.3 Potential Consequences of Raw Genetic Data Interpretation

TPI result reports raise concerns about "genotype accuracy, data privacy and security, reliability of health-related information, potential for false positives or false negatives, and down-stream consumption of limited health care recourses" (Nelson et al., 2019). Additional consequences associated with raw data include false positive results, misunderstanding of test results due to poor genetic literacy of consumers and health care providers, and the possibility of conflicting information by different TPI companies.

A number of individuals have pursued DTC testing to learn more about their health and have received positive pathogenic findings from third-party interpretation tools. However, a recent study estimated that 40% of genetic variants discovered by DTC raw data are false positives (Tandy-Connor et al., 2018). In an effort for individuals to clinically confirm a variant, they may undergo unnecessary evaluation and waste healthcare dollars. False-positive and misclassified variants can result in unnecessary stress, medical procedures, and family member testing (Tandy-Connor et al., 2018). There is a financial and psychological cost to false-positive variants that many consumers and physicians are unaware of; for example, a false-positive variant that aligns with an individual's symptoms may lead some patients to request multiple professional opinions

and referrals to specialists, and even to seek testing of additional family members for the benign variant result (Moscarello et al., 2019). There are concerns about who is liable for negative health outcomes that stem from raw data interpretation (Marchant, Barnes, Evans, LeRoy, & Wolf, 2020; Nelson et al., 2019). More research is needed to better understand the experiences of patients with false-positive variants and the possible harms associated with raw data interpretation (Moscarello et al., 2019). While some studies have suggested that the level of anxiety and distress with DTC testing is lower than previously reported and a majority of consumers reported feeling satisfied with the information from TPI companies (Stewart et al., 2018), more than a third of consumers reported feeling confused by the information (Nelson et al., 2019).

Healthcare providers need to be prepared for patients to share their raw genetic data interpretation as studies estimate that 20-30% of consumers will share this information with one or multiple providers (Moscarello et al., 2019; Stewart et al., 2018; Wang et al., 2018). While consumers have reported being satisfied with the decision to analyze their raw data, they also experience challenges with understanding the results, which is why consumers may reach out to their health care providers (Wang et al., 2018). This is a concern because non-genetic providers have reported experiencing difficulty understanding DTC reports, which are shorter and less complicated than TPI reports (Nelson et al., 2019).

This thesis study associated with this essay showed that medical students had difficulty applying genetic knowledge in a clinical setting and interpreting results. When first year medical students were asked about how to interpret a negative DTC result with a strong family history of breast cancer, students struggled with providing the appropriate recommendations for screening. While more than half of the students selected the correct answer of referring the patient to a genetic counselor, some students selected the choice to tell the patient that her chance to develop breast

cancer was at the general population risk. The study supports the need for additional education about how health care providers should handle DTC genetic testing and TPI results.

One study found that 73% of consumers also used more than one company to interpret their raw DNA data, which then leads to the possibility for conflicting reports given the discrepancy of SNP interpretation between third-party companies (Nelson et al., 2019; Tandy-Connor et al., 2018; Wang et al., 2018). Another study found that more than half of consumers that used a TPI service, used a different TPI tool to help provide additional analysis, suggesting that consumers need help understanding the results of TPI reports (Nelson et al., 2019).

While DTC genetic results can lead to improved health changes, the limitations and misconceptions surrounding DTC raw data can cause negative emotions like confusion, anxiety, and disappointment (Moscarello et al., 2019; Tandy-Connor et al., 2018). Additionally, false-positive variants from DTC testing can lead to misunderstandings in consumers and non-genetic providers, which then contributes to inaccurate assessment and incorrect medical management (Moscarello et al., 2019).

5.4 Additional Ethical Concerns of Raw Genetic Data Interpretation

Increased oversight for DTC genetic testing companies has opened the door for third-party interpretation (TPI) companies to offer consumers additional health information based on the individual's raw data. However, lack of regulation and policy guidelines for how TPI companies can operate has led to several ethical concerns. Additionally, while changes to genetic information policy have occurred over the years and patients have the right to request their raw genetic data, there are concerns about how patients will react to this uninterpreted and unexplained information

(Nelson et al., 2019). A study by Badalato et al. analyzed five TPI companies (Codegen.eu, Interpretome, LiveWello, Enlis Personal, and Promethease) that primarily use SNP-based technology to provide health information and compared their practices. The researchers focused on ethical concerns related to clinical utility, informed consent, medical supervision, claims and disclaimers, and data usage and privacy (Badalato et al., 2017). Ethical concerns and consequences of false positive results, misunderstanding of test results due to poor genetic literacy of consumers and health care providers, and the possibility of conflicting information were previously discussed in the prior section.

Several issues have been raised concerning the clinical validity and utility of TPI companies. The results from raw data analysis by TPI companies have scientific shortcomings from utilizing SNP-based technology methods because the SNP-based technology is not as thorough as full sequence and deletion/duplication analysis. TPI companies present a health risk for individual SNPs, which can be overwhelming and confusing to consumers. Even though the raw data report may be more realistic of the factors that predict multifactorial conditions, the information is complex and confusing and may include information on genes associated with rare, inherited disorders (Badalato et al., 2017). Additionally, while TPI companies have been portrayed as an alternative to gain information not provided by DTC companies and a way to learn more about an individual's health, there is concern about the clinical utility of testing. Experts consider the results more in the realm of research than generating information that can direct medical care of patients (Badalato et al., 2017).

There is also a question of the ethics surrounding informed consent and autonomy by TPI companies because websites typically use check boxes to agree to terms instead of providing elements included in a more formal consent process. As the study by Badalato et al. showed, TPI

websites did not clearly express how the information obtained may impact the individual (Badalato et al., 2017). There is limited data on the genetic literacy of consumers who use TPI; some believe the genetic literacy is higher in TPI consumers because of their interest in genetic information, however genetic services and consent processes should not rely on this assumption. Additionally, many TPI companies do not require an age limit to use their services and do not have any policies regarding the ability to submit someone else's raw data for interpretation (Badalato et al., 2017). One study found that a third of DTC consumers submitted another person's sample for testing, with or without consent (Clayton, Evans, Hazel, & Rothstein, 2019). The lack of policy surrounding ownership and consent for TPI companies is ethically concerning and needs to be addressed for consumers in order for consumers to have a better understanding of the risks, benefits, and limitations of raw data interpretation.

Badalato et al. also examined the concern of potentially irrelevant information being misinterpreted to make medical health decisions and relevant information being ignored due to the lack of medical supervision in ordering TPI services (Badalato et al., 2017). For example, there is the potential for consumers to misunderstand a result, experience inappropriate follow-up care, and unnecessarily use healthcare resources (Badalato et al., 2017). Even though TPI companies often recommend that consumers discuss their results with their healthcare providers, research has shown that non-genetic providers report a lack of confidence in their genetic knowledge, which can led to misinterpretation of the results (Badalato et al., 2017; Collier, 2012).

The Badalato et al. study also compared claims, advertising, and disclaimers amongst TPI companies and to DTC companies. Overall, TPI companies tend to have "fewer exaggerated advertising claims, less promotional material, and less skewed information" compared to DTC genetic testing companies (Badalato et al., 2017). While claims and advertising benefits tended to

lower, TPI companies had minimal disclaimers about risk and vague information. For example, TPI websites had scarce information about to the "potential hazards associated with receiving genetic information, including anxiety, genetic discrimination, or impact on family members" (Badalato et al., 2017). However, the study did not address if TPI websites stated how an individual's employment and insurance may be protected or vulnerable to genetic discrimination.

There is also concern about the privacy, protection of consumer data, and data usage policies of TPI companies as there is the potential for privacy breaches and some TPI companies may sell or share user data or retain data long term (Badalato et al., 2017). However, some TPI companies do not retain user data long term which could be considered a protective feature (Badalato et al., 2017). Therefore, specific privacy policies and a discussion of the risk of a potential breach and downstream consequences is needed to promote adequate understanding in consumers.

It has been argued that genetic data sharing policies should be shared with consumers because there are benefits and consequences related to this practice. For example, data sharing can help multiple researcher projects and reduce the burden on research participants because their information would be shared without having to participate in multiple studies, but there is also the concern for patient privacy (Sorani et al., 2014). While the Health Insurance Portability and Accountability Act (HIPAA) and the Genetic Information Nondiscrimination Act are designed to limit access and discrimination of sensitive information such as HIPAA's list of 18 identifiers that must be suppressed, there are still concerns about anonymized data being connected to a specific individual, especially since HIPAA does not apply to DTC testing (Clayton et al., 2019; Sorani et al., 2014).

5.5 Recommendations for the Future

Despite the relatively low clinical utility of DTC genetic testing, consumers are still interested in obtaining information about health. Non-genetic providers should be prepared to help explain the benefits and limitations of DTC genetic testing and possible next steps for the patient. When patients share raw genetic data interpretations, providers need to clinically confirm the genetic variant to determine the accuracy of the test results (Moscarello et al., 2019). Genetic test results should be interpreted by professionals with genetic knowledge who will analyze factors such as the medical and family history of the patient (Tandy-Connor et al., 2018). Lastly, there is a need for resources to educate non-genetic providers about DTC genetic testing and third-party raw data interpretation, policies of companies that are relevant for patients and providers, and improved transparency regarding communication between TPI companies and consumers.

Even though raw genetic data includes disclaimers about the validity and accuracy of the information, the data can still be misinterpreted or misused by consumers and medical providers (Tandy-Connor et al., 2018). The National Human Genome Research Institute (NHGRI) is one example of a resource dedicated to educating health care providers about DTC testing and TPI companies. However, it was challenging to find other resources directed at health care providers that outline information in a visually appealing manner. The NHGRI has a website dedicated to genomic educational resources for health care providers. The NHGRI provides resources on pharmacogenetics, interpreting genomic reports, pedigree analysis, and direct-to-consumer (DTC) testing (NHGRI, 2022). The Direct-to-Consumer Genetic Test FAQ for Healthcare Professionals is a resource that describes types of test results, limitations, pharmacogenetics, raw data and third-party interpretation services, and how to find genetic providers. However, the resource may appear dense and may lead to health care providers missing information. Creating shorter, more

comprehensive resources to highlight the important information about DTC testing and raw data interpretation may be more beneficial to providers who are often busy and have limited time to engage with educational materials.

Figure 3 is an example of a condensed factsheet that is intended to help non-genetic providers understand the meaning of raw data, the clinical utility, and possible next steps for the patient. The NHGRI website was used as a source to develop material for the factsheet. The goal of creating a raw genetic data factsheet for non-genetic providers is to highlight the facts about raw genetic data interpretation and to describe the limitations of the information. Highlighting the facts of DTC testing and TPI reports is important because the myths surrounding the genetic data can potentially lead to negative outcomes. Some myths around raw genetic data include full genomic coverage, accurate variant calls, and same level of quality between different labs. The factsheet was designed using Canva with the goal of being visually appealing and a resource that providers could use efficiently in a clinical setting. The factsheet has a Flesch-Kincaid Grade Level readability of 9.4. While the recommended reading level for health information is around a 6th grade reading level for the general population, this factsheet was designed for medical professionals who tend to have higher health literacy (Hutchinson, Baird, & Garg, 2016). Additionally, the factsheet includes a link to the NHGRI's Direct-to-Consumer Genetics Testing FAQ for Healthcare Professionals website to provide supplementary information if providers are interested.

A goal would be to distribute the factsheet to primary care physicians because they are more likely to see DTC and TPI genetic results (Moscarello et al., 2019; Stewart et al., 2018; Wang et al., 2018). The factsheet could also be shared with national organizations to increase awareness and accessibility of DTC genetic testing and TPI resources. One option to evaluate the factsheet

would be to survey primary care physicians' knowledge about DTC and TPI reports before sending out the factsheet and then surveying the physicians again after six months to see if the factsheet did increase providers knowledge and awareness of DTC and TPI reports.

Non-genetic providers have requested additional resources to help increase their genetic knowledge. If non-genetic providers have a better understanding of how to handle variants from raw genetic data, then hopefully patient experiences can improve when they receive a positive result. Additional education and resources are needed to assist non-genetic providers care for their patients to help prevent misunderstanding and inappropriate care. Non-genetic providers can improve their knowledge through changes in medical curriculum or through post-medical school education modules and resources. Guidelines and policies are needed to help non-genetic providers manage raw genetic data results as more patients access this information through clinical or consumer testing.

Figure 3. Factsheet for Non-genetic Providers Based on NHGRI Resource

Additionally, policies should recognize the rights of patients to have their raw data while also ensuring that testing companies provide validated data and correct test interpretations. Improving the communication of how variants are interpreted, their potential significance, and the limitations of raw data will help minimize the potential negative psychological impacts and reduce unwarranted healthcare costs (Moscarello et al., 2019). More policies and guidelines need to be updated to address the growing access consumers have to their genetic information and to identify who is liable for negative outcomes that stem from raw data interpretation (Marchant et al., 2020; Nelson et al., 2019). For example, the HIPAA Privacy Rule does not typically apply to DTC testing, which is designed to protect health information (Clayton et al., 2019). Most DTC and TPI companies are largely self-regulated and operate outside the policies such as HIPPA and Clinical Laboratory Improvement Amendments (CLIA). Stricter regulation of third-party interpretation companies is needed to help protect patients and providers.

TPI companies also need to improve their communication with consumers. Despite about half of TPI companies categorizing their services as connecting consumers to scientific literature instead of genetic data interpretation, consumers still value the results and assume they are accurate (Nelson & Fullerton, 2018). There is a need for TPI companies to describe to consumers the risks, benefits, and limitations of raw data interpretation. Should this happen, then perhaps, consumers will recognize that TPI companies act more as a bridge to connect consumers to additional publication and databases. This has the potential to enhance consumers' understanding of the type of results they receive (Nelson & Fullerton, 2018).

5.6 Conclusion

TPI companies arose, in part, due to stricter regulation of DTC genetic tests to provide health information (Badalato et al., 2017). Consumers can obtain a copy of their raw genetic data from DTC companies, researchers, or clinical testing labs and then seek out a TPI company to interpret their raw genetic data (Nelson & Fullerton, 2018). DTC tests and TPI companies can then provide consumers with information regarding ancestry, risks of developing certain conditions, carrier status, and more (Tandy-Connor et al., 2018).

While some consumers are interested in learning health-related information, many are unaware that DTC tests are not diagnostic and are not comprehensive, meaning that results often need to be confirmed by a certified clinical lab and the patient could be at risk for other conditions or have a variant in a gene not covered by DTC companies (Tandy-Connor et al., 2018). Additionally, there are other ethical concerns surrounding third-party interpretation including clinical utility, informed consent, medical supervision, claims and disclaimers, privacy and data usage, potential for false positives or false negatives, and down-stream consumption of limited health care recourses (Badalato et al., 2017; Nelson et al., 2019). Improving the communication of how the variants are interpreted, and their potential significance, as well as the limitations of raw data interpretation will help minimize the negative psychological impacts and reduce the unnecessary use of healthcare resources (Moscarello et al., 2019).

Increasing educational efforts and creating resources may help health care providers improve their genetic knowledge. Primary care physicians were surveyed about their knowledge and understanding of DTC testing, and a majority reported feeling unprepared to answer patient questions concerning DTC testing (Powell et al., 2012). Increasing health care providers' knowledge of DTC testing and TPI companies, may help decrease the occurrence of potential

consequences such as inaccurate assessment and incorrect medical management (Moscarello et al., 2019). The goal of the factsheet is to address health care providers concerns regarding the testing methodologies, the meaning of the results, and next steps for patients in a concise educational resource. Additionally, information should be created for the general public, especially for individuals with low health literacy in order to prevent misunderstandings and reduce the waste of health care resources. There is a need for TPI companies to describe the risks, benefits, and limitations of raw data interpretation. This would allow consumers to recognize that TPI companies primarily serve as a bridge to connect consumers to additional publication and databases (Nelson & Fullerton, 2018).

This essay is significant to Public Health because health care providers need to be prepared for patients to share their raw data interpretation, as studies estimate that 20-30% of consumers will share this information with one or multiple providers (Moscarello et al., 2019; Stewart et al., 2018; Wang et al., 2018). Also, because of their long-term relationship with providers, some patients may want providers to be directive and give advice about what to do when facing decisions related to genetic testing (Geller & Holtzman, 1995). Health care providers may be in a clinical setting to provide guidance to patients and need to have sufficient genetic knowledge to make appropriate health care recommendations for the patient. The thesis study associated with this essay showed that medical students had difficulty applying genetic knowledge in a clinical setting and interpreting results, which may suggest a need for changes to the education and training of medical students, as well as additional post-medical school educational resources.

Appendix A Supplemental Figures

Table 11. Self-Assessment: Overall Confidence Ratings for the Pre-Course Survey

Participant ID	Self Assessment: Pre-Course Confidence Rating by Statement												Total Confidence Score
A	2	2	1	1	1	1	1	1	1	1	1	1	14
B	4	5	3	2	3	1	3	1	2	1	3	1	29
C	4	4	4	2	3	2	2	2	1	4	2	2	32
D	4	4	4	2	2	2	2	1	4	1	3	2	31
E	3	4	4	4	4	2	2	2	2	2	2	2	33
F	4	5	4	1	1	1	3	2	2	3	2	2	30
G	4	4	4	3	4	2	3	2	2	3	3	3	37
H	4	4	3	1	1	1	1	4	4		5	1	29
I	5	4	4	5	4	5	5	5	5	5	5	5	57
J	4	5	3	1	2	1	4	2	1	1	2	1	27
K	2	4	4	1	1	2	3	1	1	2	1	2	24
L	5	5	5	1	4	2	3	2	3	2	2	5	39
M	4	5	2	3	3	4	4	5	3	5	4	5	47
N	4	5	4	3	2	1	4	4	2	2	3	1	35
O	4	5	4	2	2	2	3	1	3	4	3	3	36
P	4	4	3	2	3	1	1	1	1	1	1	3	25
Q	5	5	4	2	4	1	4	4	4	4	4	4	45
R	4	5	4	4	4	3	3	4	4	5	2	4	46
S	4	5	4	1	1	1	1	1	3	1	4	1	27
T	4	4	4	4	4	4	4	2	2	2	2	2	38
U	4	4	3	3	4	3	3	2	4	4	3	3	40
V	4	4	2	2	1	2	3	2	1	3	1	3	28
W	4	4	2	2	2	2	2	2	2	2	2	2	28
X	5	5	4	4	5	3	5	4	5	4	5	3	52
Mean Score	3.95833333	4.375	3.45833333	2.33333333	2.70833333	2.04166667	2.875	2.375	2.58333333	2.69565217	2.70833333	2.54166667	34.54166667

Table 12. Self-Assessment: Overall Confidence Ratings for the Post-Course Survey

Participant ID	Self Assessment: Post-Course Confidence Rating by Statement												Total Confidence Score
A	4	3	1	1	2	1	1	1	2	2	1	3	22
B	5	5	5	4	5	4	4	4	3	4	4	5	52
C	5	5	4	4	5	4	4	4	5	5	4	4	53
D	4	4	4	4	4	4	4	4	4	4	4	4	48
E	5	5	5	5	5	3	4	4	4	4	4	4	52
F	5	4	4	2	4	5	5	4	5	3	4	5	50
G	4	5	4	4	4	4	3	4	3	4	4	4	47
H	5	5	4	4	4	4	3	4	5	5	5	5	53
I	1	1	1	1	1	1	1	1	1	1	1	1	12
J	1	1	2	3	2	3	2	4	3	4	2	3	30
K	4	5	5	5	5	5	5	5	4	5	5	5	58
L	5	5	5	5	5	5	5	5	5	5	5	5	60
Y	5	5	5	5	5	5	5	3	5	5	5	5	58
Z	5	5	4	5	5	3	5	3	2	4	4	4	49
Mean Scores	4.14285714	4.14285714	3.78571429	3.71428571	4	3.64285714	3.64285714	3.57142857	3.64285714	3.92857143	3.71428571	4.07142857	46

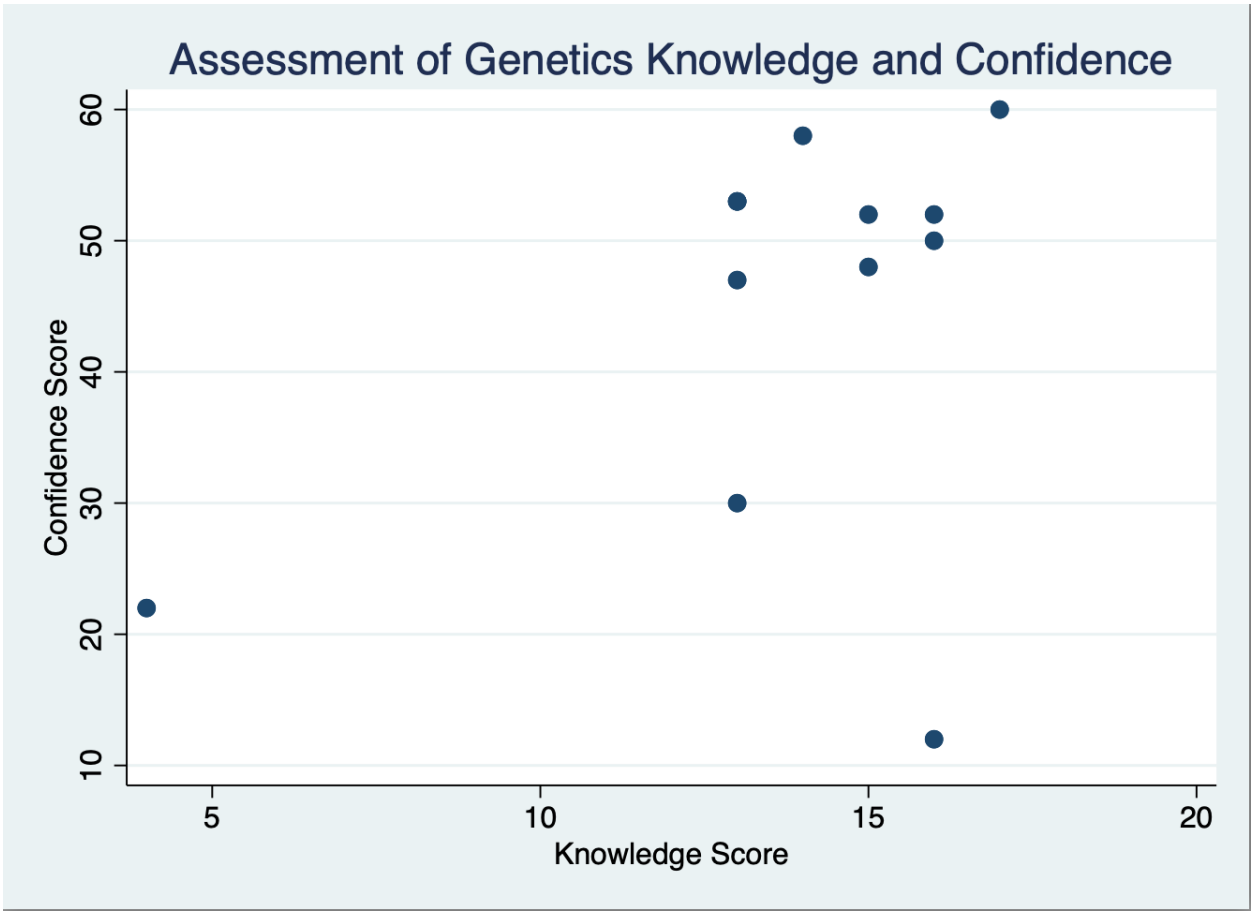

Figure 4. Comparison of Genetics Knowledge and Confidence Scores

Maximum Knowledge Score = 20; Maximum Confidence Score = 60

Appendix B IRB Approval Letter

University of Pittsburgh | Institutional Review Board
Office of Research Protections

EXEMPT DETERMINATION

Date:	August 19, 2021
IRB:	MOD20070423-002
PI:	Robin Grubs
Title:	Genetic literacy and the acquisition of clinical genetics knowledge in medical students
Funding:	None

The Institutional Review Board reviewed and determined the above referenced study meets the regulatory requirements for exempt research under 45 CFR 46.104.

Determination Documentation

Determination Date:	8/19/2021
Exempt Category:	(2)(ii) Tests, surveys, interviews, or observation (low risk)

Approved Documents:	• Genetic_Literacy_in_Medical_Students_Survey_Updated_8-12-21.docx

If you have any questions, please contact the University of Pittsburgh IRB Coordinator, Emily Bird.

Please take a moment to complete our Satisfaction Survey as we appreciate your feedback.

Appendix C Research on Medical Students (ROMS) Committee Approval

PittPRO | Pitt Protocol Review Online

My Inbox | Home | IRB | Meetings

IRB > Genetic literacy and the acquisition of clinical genetics knowledge in medical students > Modification / Update #1 for Study Genetic literacy and the acquisition of clinical genetics knowledge in medical students

<< Return to Workspace < Prev 1 / 7 Next >

Activity Details (Comment Added) Comment visible to all with read access to the submission.

Author:	Bill Yates (U of Pgh | School of Medicine | Otolaryngology)
Logged For (IRB Submission):	Modification / Update #1 for Study Genetic literacy and the acquisition of clinical genetics knowledge in medical students
Activity Date:	8/18/2021 10:42 AM

Form:

Activity Details

Your comment is visible to anyone with access to this submission.

1. **Comment:**
The ROMS committee discussed the revised proposal this morning. The identifier proposed is acceptable. However, there are concerns about the communication plan. All communications must be handled through the Office of Medical Education (OMED). Please contact Katie Maietta (kmaietta@medschool.pitt.edu) to send the email. A maximum of three emails is acceptable.

The Medical School is reluctant to identify the medical leaders to you, and we cannot request advertisement of the survey on social media. The only permitted advertisement will be emails through OMED.

2. **Supporting documents:**

Name	Description
There are no items to display	

3. **Who should receive an e-mail notification?**
PI/PI Proxy/Primary Contact
Study Team
IRB Coordinator

Appendix D Vincent Exemption Form

University of Pittsburgh
Institutional Review Board

Office: 3500 Fifth Avenue
Pittsburgh, PA 15213
Phone: 412.383.1480
Fax: 412.383.1508

Approval of Vincent™ Exception Request: "Man on the Street" Payment Option

Date: August 25, 2021
IRB Number: **STUDY20070423**
Investigator: Robin Grubs
IRB Protocol Title: Genetic literacy and the acquisition of clinical genetics knowledge in medical students

Thank you for submitting a request to make payments using the "Man on the Street" option and for an exception to the requirement to collect social security numbers for subjects receiving payments for participating in the above referenced research study. I have carefully reviewed all of the materials provided to me about this project and on that basis, approve your requests. Both exceptions are applicable to this research study only.

Please note that we are granting exceptions as part of a feasibility study that examines the extent to which subjects participate in multiple research studies over the course of a calendar year and obtain $600 or more in incentive payments. The $600 limit is the IRS threshold that requires the paying organization to report this other income to both the taxpayer and the IRS on Form 1099-MISC. Should we subsequently discover that subjects in this 'exception' program have reached that IRS reporting threshold, we may modify or disband this program. If that happens, you will be notified in a timely manner.

You have also requested permission to use the "Man on the Street" payment option. Based on the small payment and the subject population and nature of the study, I am also happy to approve that request for this research study only.

The PI or designate will obtain funds through a Vincent™ card issued in their name for distribution to study subjects. A separate record must be maintained in sufficient detail to account for all payments (e.g., a subject receipt log initialed by the recipient of the payment) should be prepared and maintained by the PI as necessary for audit purposes.

The University of Pittsburgh's Office of Finance can answer detailed questions about the Vincent™ system.

If you have any other questions, please don't hesitate to contact the IRB Office.

Dana DiVirgilio
Research Review Specialist
University of Pittsburgh | Human Research Protection
3500 Fifth Avenue, Hieber Building, Suite 106 Pittsburgh, PA 15213
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Appendix E Pre-Course Recruitment Email

Subject Line: Genetic Literacy Survey for Medical Students

Hello,

My name is Haley Soller and I am currently a graduate student in the University of Pittsburgh Genetic Counseling Program.

As a University of Pittsburgh medical student who is taking Human Genetics during the Fall 2021 semester, you are eligible to complete a survey that is designed to assess knowledge of clinical genetics and genetic testing. Ultimately, we hope this survey will inform efforts to improve and integrate graduate level genetics curriculum for future physicians. Please consider taking this anonymous survey before and after the Human Genetics course. This information will deepen our understanding of the current gaps and limitations of genetics education in medical school. The link for precourse survey is below and a link to the postcourse survey will be sent after the course is over.

Each survey should take about 20-30 minutes to complete. There are minimal risks associated with participation in the surveys, including but not limited to the infrequent risk of a breach of confidentiality. You will have the chance to win a $25 Amazon gift card after completion of the surveys. Four participants will be chosen at random to be awarded a gift card after completing the survey prior to the course and then four more participants will be chosen at random

to be awarded a gift card for completing the survey after the course. You will need to enter your email address at the end of the survey to be given the opportunity to be chosen at random for the gift card; this email address will not be linked with your responses. Participating in this survey will not positively or negatively impact your academic standing within the University of Pittsburgh School of Medicine.

This is an anonymous questionnaire, and your responses will not be identifiable. All responses are confidential, and results will be secured electronically. Your participation is voluntary. You may skip questions or stop the survey at any time by exiting the survey, though all responses submitted up until the point of exit will be maintained. If you choose to withdraw from this study, all data collected prior to the date of withdrawal will continue to be used.

This study has been approved by the University of Pittsburgh IRB.

Should you have any questions, please feel free to email me at: HAS199@pitt.edu. Thank you for considering taking this survey and I appreciate your assistance in providing information that has potential to enhance genetics education in medical school.

The following link: https://pitt.co1.qualtrics.com/jfe/form/SV_aY0x6zegwyH4Epo
will direct you to the survey.

Appendix F Pre-Course Reminder Email

Subject Line: Genetic Literacy Survey for Medical Students

Hello,

My name is Haley Soller and I am a graduate student in the University of Pittsburgh Genetic Counseling Program. Recently, I invited you to participate in a survey that is designed to assess knowledge of clinical genetics and genetic testing before and after completing the Fall 2021 Human Genetic course. Your response to this survey will inform efforts to improve and integrate graduate level genetics curriculum for future physicians. The link for the survey is below.

As a reminder, the survey should take about 20-30 minutes to complete and all responses are confidential. You will have the chance to win a $25 Amazon gift card after completion of the survey. Four participants will be chosen at random to be awarded a gift card after completing the survey. Participating in this survey will not positively or negatively impact your academic standing within the University of Pittsburgh School of Medicine. The deadline to complete the pre-course survey is October 10, 2021.

This study has been approved by the University of Pittsburgh IRB.

Should you have any questions, please feel free to email me at: HAS199@pitt.edu Thank you for considering taking this survey and I appreciate your assistance in providing information that has potential to enhance genetics education in medical school.

The following link: https://pitt.co1.qualtrics.com/jfe/form/SV_aY0x6zegwyH4Epo will direct you to the survey.

Please disregard questions that relate to the genetics course at this time. Questions related to the genetics course can be answered after completion of the course in the post-course survey.

Thank you,

Haley

Appendix G Post-Course Recruitment Email

Subject Line: Genetic Literacy Survey for Medical Students

Hello,

My name is Haley Soller and I am currently a graduate student in the University of Pittsburgh Genetic Counseling Program.

As a University of Pittsburgh medical student who completed Human Genetics during the Fall 2021 semester, you are eligible to complete a survey that is designed to assess knowledge of clinical genetics and genetic testing. Ultimately, we hope this survey will inform efforts to improve and integrate graduate level genetics curriculum for future physicians. You were sent a survey prior to the course that was intended to assess your genetics knowledge before you completed the course. This survey is designed to assess your genetics knowledge now that you completed the course. This information will deepen our understanding of the current gaps and limitations of genetics education in medical school. The link for the survey is below.

The survey should take about 20-30 minutes to complete. There are minimal risks associated with participation in the survey, including but not limited to the infrequent risk of a breach of confidentiality. You will have the chance to win a $25 Amazon gift card after completion of the survey. Four participants will be chosen at random to be awarded a gift card after completing

the survey. You will need to enter your email address at the end of the survey to be given the opportunity to be chosen at random for the gift card; this email address will not be linked with your responses. Participating in this survey will not positively or negatively impact your academic standing within the University of Pittsburgh School of Medicine.

This is an anonymous questionnaire, and your responses will not be identifiable. All responses are confidential, and results will be secured electronically. Your participation is voluntary. You may skip questions or stop the survey at any time by exiting the survey, though all responses submitted up until the point of exit will be maintained. If you choose to withdraw from this study, all data collected prior to the date of withdrawal will continue to be used.

This study has been approved by the University of Pittsburgh IRB.

Should you have any questions, please feel free to email me at: HAS199@pitt.edu Thank you for considering taking this survey and I appreciate your assistance in providing information that has potential to enhance genetics education in medical school.

The following link: https://pitt.co1.qualtrics.com/jfe/form/SV_8dbDHj3cauyt0O2
will direct you to the survey.

Appendix H Post-Course Reminder Email

Reminder Email- Postcourse Survey

Subject Line: Genetic Literacy Survey for Medical Students

Hello,

My name is Haley Soller and I am a graduate student in the University of Pittsburgh Genetic Counseling Program. Recently, I invited you to participate in a survey that is designed to assess knowledge of clinical genetics and genetic testing before and after completing the Fall 2021 Human Genetic course. Your response to this survey will inform efforts to improve and integrate graduate level genetics curriculum for future physicians. The link for the survey is below.

As a reminder, the survey should take about 20-30 minutes to complete and all responses are confidential. You will have the chance to win a $25 Amazon gift card after completion of the survey. Four participants will be chosen at random to be awarded a gift card after completing the survey. Participating in this survey will not positively or negatively impact your academic standing within the University of Pittsburgh School of Medicine.

This study has been approved by the University of Pittsburgh IRB.

Should you have any questions, please feel free to email me at: HAS199@pitt.edu Thank you for considering taking this survey and I appreciate your assistance in providing information that has potential to enhance genetics education in medical school.

The following link: https://pitt.co1.qualtrics.com/jfe/form/SV_8dbDHj3cauyt0O2 will direct you to the survey.

The post-course survey will close on December 1, 2021.

Thank you,

Haley

Appendix I Survey

Thesis Survey Questions

Start of Block: Unique ID

Q1 To allow us to link your pre-course and post-course survey in an anonymous manner, please create an identifier in the following way: please enter your year of birth, followed by the first letter of your first name, followed by the last four digits of your phone number. For example, a person with the name of Haley Smith who was born in 1998 and whose phone number is 412-123-4567 would enter: 1998H4567

○ Year of birth (1) _____

○ First letter of your first name (2)

_____

○ Last four digits of your phone number (3)

_____

End of Block: Unique ID

Start of Block: Self-Assessment of Clinical Genetics Knowledge and Skills

Q2 Please rate your knowledge relating to each genetics-based competency on a 5-point scale (1 = Strongly agree; 5 = Strongly disagree)

	Strongly agree (1)	Somewhat agree (2)	Neither agree nor disagree (3)	Somewhat disagree (4)	Strongly disagree (5)
I understand the foundational concepts of genome organization. (1)	○	○	○	○	○
I understand the foundational concepts of genetic inheritance. (2)	○	○	○	○	○

I understand how the fundamentals of population genetics relate to modern patient populations. (3)	○	○	○	○	○
I can gather a detailed family history for a genetic indication. (4)	○	○	○	○	○

I can assess genetic risk based on the information within a family history. (5)	○	○	○	○	○
I am comfortable identifying indications for referral to a genetics specialist. (6)	○	○	○	○	○

I can apply knowledge of genetic principles to effectively communicate with patients who have limited genetic literacy. (7)	○	○	○	○	○
I am familiar with clinical genetics resources and databases. (8)	○	○	○	○	○

I am knowledgeable about the principles of cytogenetics and molecular genetic techniques (9)	○	○	○	○	○
I can describe the benefits, risks, and limitations of genetic testing to a patient. (10)	○	○	○	○	○

I have thorough knowledge of genetics relating to the development, diagnosis, and treatment of cancer. (11)	○	○	○	○	○
I am aware of methods for prenatal diagnosis of genetic conditions. (12)	○	○	○	○	○

End of Block: Self-Assessment of Clinical Genetics Knowledge and Skills

Start of Block: Inheritance

Q3 What is the chance that a healthy child whose sibling has an autosomal recessive genetic condition will be a carrier?

- 25% (1)
- 50% (2)
- 66% (3)
- 75% (4)

Q4 A woman marries her 1st cousin, once-removed. Which scenario is most likely?

- Their child is at increased risk to develop an autosomal dominant condition (1)
- Their child is at increased risk to develop an autosomal recessive condition (2)
- Their child is at increased risk to develop an X-linked dominant condition (3)
- Their child is at increased risk to develop an X-linked recessive condition (4)

Q5 A healthy man whose brother has an autosomal recessive genetic condition marries a woman with no family history of this condition. The carrier frequency in the general population for this condition is 1/25, i.e., 1 in 25 individuals in the general population carries one pathogenic variant for this autosomal recessive condition. What is the probability that their child would be affected by this condition?

- 1/75 (1)
- 1/150 (2)
- 1/200 (3)
- 1/400 (4)

Q6 Select the statement that best describes X-linked recessive inheritance:

- The children of affected males are not at risk for being affected with the condition (1)
- The children of carrier females are not at risk for being affected with the condition (2)
- Both males and females are affected equally (3)
- Females are usually more severely affected than males (4)

Q7 True or False: For multifactorial conditions, when the phenotype is more common in one sex, the risk is higher for relatives of the proband of the less susceptible sex.

- ○ True (1)
- ○ False (2)

Q8 What is the chance for a male with deletion of the 22q11.2 region, otherwise known as DiGeorge syndrome, to have a child with this same condition?

- ○ Less than 1% (1)
- ○ 25% (2)
- ○ 33% (3)
- ○ 50% (4)

Q9 A pregnant woman comes for genetic counseling because the father of her female fetus has Leber's hereditary optic neuropathy (LHON), a mitochondrially inherited genetic condition. What is the chance that this fetus is affected with LHON?

- ○ 0% (1)
- ○ 25% (2)
- ○ 33% (3)
- ○ 50% (4)

End of Block: Inheritance

Start of Block: Clinical Genetics Scenario

Q10 A female patient with a family history of hereditary breast and ovarian cancer shows you her results from direct-to-consumer testing. The results show that the patient does not have a mutation in the BRCA1 or BRCA2 genes. What would you recommend as next step for the patient?

○ Refer the patient to appropriate genetic counseling through a genetic counselor or physician. (1)

○ Tell the patient that she does not have an increased risk to develop cancer compared to the general population risk. (2)

○ Tell the patient that general population screening recommendations for cancer prevention are appropriate for her. (3)

○ Repeat the testing through the direct-to-consumer testing company to confirm the results. (4)

Q11 A 21 year old woman reports that her mother had a BRCA1 mutation and provides you with the report confirming this information. She is unwilling to undergo genetic testing at this stage in her life, but is fearful of developing cancer. How do you counsel this patient?

○ Refer her to a high-risk breast cancer screening and management program. (1)

○ Address the psychosocial concerns of the patient. (2)

○ Discuss lifestyle modification, medication, and surgical recommendations (3)

○ All of the above (4)

Q12 A 30-year-old woman comes to the genetics clinic for BRCA1 and BRCA2 testing. She does not have breast cancer, but her mother was diagnosed with breast cancer at age 45, her

first cousin was diagnosed with breast cancer at age 35, and her paternal aunt was diagnosed with breast cancer at age 65. To clarify the woman's risk, which of the following individuals should be tested first?

- The woman (1)
- Her mother (2)
- Her first cousin (3)
- Her aunt (4)

Q13 A woman with hereditary nonpolyposis colorectal cancer, an adult-onset condition, wants her 14 year old daughter to be tested for the known familial mutation. What do you tell this woman and her daughter?

○ Reassure the mother that her daughter is not likely to develop cancer in the next ten years, therefore genetic testing is unnecessary. (1)

○ Genetic testing for her daughter is not warranted unless her daughter develops cancer before age 30. (2)

○ Genetic testing for her daughter is appropriate at this time, as childhood cancers are common in Lynch syndrome. (3)

○ Genetic testing for Lynch syndrome is typically not recommended for children younger than 18 but can be considered once she reaches adulthood. (4)

Q14 A 5 year old girl presents to your clinic with dysmorphic features, developmental delay, microcephaly, and a history of seizures suggestive of a microdeletion syndrome. What is the most appropriate first genetic test to order for this child?

○ Direct-to-Consumer genetic testing (1)

○ Microarray or exome sequencing (2)

○ Genetic testing for her daughter is appropriate at this time, as childhood cancers are common in Lynch syndrome. (3)

○ Genetic testing for Lynch syndrome is typically not recommended for children younger than 18 but can be considered once she reaches adulthood. (4)

Q15 When is it LEAST appropriate to order a karyotype?

○ If you are concerned about a translocation due to a parental history of multiple miscarriages. (1)

○ If you suspect the patient has Down syndrome. (2)

○ If your patient has multiple congenital anomalies. (3)

○ If you suspect the patient has a sex chromosome disorder. (4)

Q16 A woman is referred to your clinic at 19 weeks gestation because her amniocentesis, performed for advanced maternal age, revealed a karyotype of 47XXY (Klinefelter syndrome).

The woman and her partner are tearful, and are debating whether to terminate the pregnancy. How would you discuss this result with the couple?

- ○ Tell the couple that it would be in their best interest to continue the pregnancy. (1)
- ○ Provide a wealth of detailed information about the features of Klinefelter syndrome. (2)
- ○ Remind the couple that Klinefelter syndrome is not associated with a decrease in life expectancy. (3)
- ○ Individually explore the couple's thoughts about the various outcomes of this pregnancy. (4)

Q17 Non-Invasive Prenatal Testing (NIPT) has a very high detection rate for Down syndrome, therefore, diagnostic testing is not needed following a positive NIPT. Is this statement true or false?

- ○ True (1)
- ○ False (2)

End of Block: Clinical Genetics Scenario

Start of Block: Interpretation of Genetic Test Results

Q18 A couple whose child had a positive newborn screen for cystic fibrosis presents to your clinic for counseling. The child's sweat test returns negative and genetic testing reveals one mutation: a F508 deletion. What do these results mean for the child?

- The child has cystic fibrosis. (1)
- The child has CFTR-Related Metabolic Syndrome (CRMS). (2)
- The child is a carrier for cystic fibrosis (3)
- The child is not a carrier for cystic fibrosis (4)

Q19 An infant with deletion of the 22q11.2 region, otherwise known as DiGeorge syndrome, is evaluated by medical genetics. Neither of the child's parents carry the deletion. The parents are interested in having more children and want to know their risk of having another

affected child. What information would you provide when discussing recurrence risk for future pregnancies?

- ○ The parents are at slightly increased risk to have a child with DiGeorge syndrome due to the possibility of germline mosaicism (1)
- ○ If they have another child with DiGeorge syndrome, that child would have the same features of DiGeorge syndrome as their first child. (2)
- ○ The parents are not at increased risk to have another child with DiGeorge syndrome. (3)
- ○ The parents have a 50% chance to have another child with DiGeorge syndrome (4)

Q20 A genetic test report reveals a "variant of unknown significance". What does this result mean for the patient?

- ○ Changes in medical management are warranted depending on the exact variant. (1)
- ○ Ordering providers are not required to inform patients of such a result. (2)
- ○ Medical management decisions should not be made based on a variant of unknown significance. (3)

Q21 Which of the following methods can be used to determine the clinical meaning of a variant of uncertain significance?

- Repeat the test. (1)
- Test other affected family members to see if the variant tracks with the phenotype of interest in the family. (2)
- Test another tissue type (instead of blood use skin fibroblasts or buccal swab). (3)
- All of the above. (4)

Q22 If a fetus has an increased nuchal translucency and an atrioventricular septal heart defect, which of the following karyotype results is the most likely to be found on amniocentesis?

- 45, X (1)
- 45, X/46, XX (2)
- 46, XX (3)
- 47, XX, +21 (4)

End of Block: Interpretation of Genetic Test Results

Start of Block: Demographics

Q23 The following questions will ask about your experience in Dr. Khan's Human Genetics course.

Q24 How challenging was this course?

- ○ Extremely challenging (1)
- ○ Very challenging (2)
- ○ Moderately challenging (3)
- ○ Slightly challenging (4)
- ○ Not challenging at all (5)

Q25 How much did you learn from this course?

- ○ A great deal (1)
- ○ A lot (2)
- ○ A moderate amount (3)
- ○ A little (4)
- ○ Nothing at all (5)

Q26 How could this course be improved?

_____

Q27 What topics in genetics interest you the most?

_____

Q28 Did you take a genetics course during your undergraduate education?

- Yes (1)
- No (2)
- Not sure (3)

Q29 Do you have any prior work experience with genetics (laboratory positions, research, clinical observation)?

- Yes (1)
- No (2)
- Not sure (3)

Display This Question:

If Do you have any prior work experience with genetics (laboratory positions, research, clinical obs... != No (2)

Q30 Please explain your prior work experience with genetics.

_____

Q31 What is your gender?

- ○ Male (1)
- ○ Female (2)
- ○ Transgender (4)
- ○ Other: (5) _____

End of Block: Demographics

Start of Block: Raffle Question

Q32 Would you like to enter the raffle to win a $25 Amazon gift card? Your responses will still remain anonymous.

- ○ Yes (1)
- ○ No (2)

End of Block: Raffle Question

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