

**Genetic Literacy and the Acquisition of Clinical Genetics Knowledge in Medical Students**

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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

University of Pittsburgh

2021

UNIVERSITY OF PITTSBURGH

GRADUATE SCHOOL OF PUBLIC HEALTH

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University of Pittsburgh, 2021

## **Abstract**

Many physicians report minimal clinical genetics education and feel ill-prepared to discuss genetic information with their patients.<sup>1,2</sup> This study assessed the clinical genetics knowledge of University of Pittsburgh medical students through an online survey. The students were asked to rate their confidence in their knowledge of clinical genetics concepts and then answer multiple-choice questions that elicited knowledge concerning inheritance, clinical scenarios, and genetic test selection. The survey was distributed three months after the students took a 21-day Human Genetics course, required for all first year medical students at the University of Pittsburgh.

Out of 147 medical students, 10 completed the survey (a response rate of 6.8%). Medical students' responses suggested they are confident in their understanding of foundational genetic concepts such as the central dogma and inheritance but are less confident in collecting family histories and identifying indications for genetics referral. Contrary to the respondents' confidence levels, the knowledge assessment revealed that students often incorrectly answered knowledge questions pertaining to inheritance and appropriate test selection. Students had lower confidence scores and lower knowledge scores for clinical genetics resources, testing strategy, and test interpretation. Most students reported experience with molecular genetics through undergraduate coursework; a minority reported genetics-related clinical or research experience. There was no significant difference between respondents who reported prior genetics clinical or research

experience and those who did not, suggesting that all medical students would benefit from learning the breadth of both molecular and clinical genetics in medical school curriculum.

These results signify a need for genetics education that is pertinent to advancements in clinical genetics. This study is significant to public health because physicians with limited formal genetics education are at increased risk of accidentally ordering the wrong genetic test, failing to refer a patient in need of genetic services, or unintentionally providing misinformation during results disclosure, which can jeopardize the quality of care for patients and limit equitable access to healthcare.<sup>3-6</sup> To build a skilled public health workforce, medical students must possess basic knowledge of clinical genetics concepts and resources to make appropriate decisions regarding genetic information in the clinical setting as future physicians.

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## **1.0 INTRODUCTION**

### **1.1 Background and Specific Aims**

Recent advances in genetic testing have provided a wealth of genetic information not accessible in years past. To provide diagnostic information for patients with suspected genetic conditions, genetic testing in clinical settings is becoming more commonplace, with the outcomes of those test results impacting patient care and extending beyond the patient to their family. In addition to clinical genetic testing, consumers have access to personal genomic, or direct-to-consumer (DTC) testing services, which provide personal health and ancestry information, though the utility of this information is debatable.<sup>7</sup> Genetics is more accessible than ever before, yet a large portion of the population demonstrates limited genetic literacy, presenting challenges for health care providers in communicating genetic information, which is often complex.<sup>8</sup> The future of medicine is intertwined with advances in genetics, presenting ethical dilemmas concerning informed consent and the privacy of genetic information. To prepare for this future, health care providers must learn to incorporate genetic concepts, such as inheritance patterns, family history, and awareness of genetic conditions into their practice alongside full disclosure of the ethical concerns related to genetic testing.

Despite this reality, health care providers, particularly physicians, report little formal genetics education and feel ill-prepared to discuss genetic information with their patients.<sup>2</sup> Studies have shown that providers without formal genetics education are at increased risk of accidentally ordering the wrong genetic test, failing to refer a patient in need of genetic services, or unintentionally providing misinformation.<sup>3,9,10</sup> While most studies to date have surveyed

physicians directly, there is little information regarding the genetic literacy of medical students at the beginning of their training as compared to when they graduate. Additionally, most tools used to assess genetic literacy assume a limited familiarity with genetics terminology. Since medical students are a health literate population and are presumably familiar with words like “gene” and “chromosome”, genetics knowledge can be used as a proxy for genetic literacy

To assess the genetic knowledge of soon-to-be physicians, a survey was administered to 147 first-year University of Pittsburgh medical students. The survey was designed to assess knowledge of clinical genetics and genetic testing, as well as self-confidence in those genetic concepts, in relation to their Human Genetics course, a 21-day course that is required for all first-year medical students at the University of Pittsburgh. The information gained from this study has the potential to influence the content of medical student’s genetic education by identifying areas in which student’s knowledge is lacking.

While this study addresses the first iteration of the survey, distributed three months following the conclusion of the Fall 2020 course with the goal of getting preliminary data on content retention, future studies will aim to track medical students’ improvements in knowledge over time during their training. Detailed information concerning knowledge gaps will inform future efforts to further integrate and expand genetics in medical school curriculum.

### **1.1.1 Specific Aim I**

To develop a survey to assess the University of Pittsburgh medical students’ genetic literacy and clinical genetics knowledge as well as their familiarity with clinical genetics concepts.

### **1.1.2 Specific Aim II**

To evaluate the process by which medical students acquire genetic knowledge during their training.

## **2.0 LITERATURE REVIEW**

### **2.1 Defining Genetic Literacy**

Genetic literacy, a subset of health literacy, is defined as “sufficient knowledge and appreciation of genetics principles to allow informed decision-making for personal well-being and effective participation in social decisions on genetic issues”.<sup>11</sup> According to Joseph McInerney, former executive vice president of the American Society of Human Genetics, genetic literacy is vital to “understanding the history and nature of life on earth, as well as understanding the future of health care, including the ethical, legal, and social aspects of health care and the genetic contributions to health care”.<sup>12</sup>

Though a number of Americans have some familiarity with genetics through its coverage in media, this awareness of genetics does not constitute being genetically literate. A minority of Americans are considered to have a sufficient degree of genetic literacy necessary to make medical management decisions based on genetic information. In essence, many American citizens are conversationally familiar with genetics but lack the fundamental scientific framework to contextualize genetic information and this can result in an unintentional overestimation of understanding.<sup>13</sup>

Despite the lack of genetic literacy in the general population, genetics has a growing impact on healthcare, serving as a major checkpoint in the diagnostic odyssey for many with acute and chronic health conditions. A considerable proportion of the population is affected by a genetic disorder. Around 1 in 50 people have a single-gene disorder, while 1 in 263 have a chromosomal

condition.<sup>14</sup> Even genetic conditions that are defined as “rare” are relatively common; when rare disorders are considered collectively, 1 in 21 people in the general population are affected.<sup>14</sup>

While there is still much to be discovered about the role of genes in health and disease, genetic testing in clinical settings is becoming more commonplace, with the outcomes of those test results impacting patient care and extending beyond the patient to their family. As advances in healthcare progress towards precision medicine, there is a need for genetics education for both the public and healthcare providers. Bridging the patient-provider literacy gap can allow for more in-depth discussions of genetic risk and provide the opportunity for appropriate informed consent.

## **2.2 Genetic Literacy in the General Population**

Demographic factors such as older age, limited education, lower income, and status as a non-native English speaker are known to be associated with low health literacy and may also be associated with low genetic literacy.<sup>8,15,16</sup> Other individual risk factors include limited understanding of biology and poor numeracy (particularly concerning probability, statistics, and risk), which may not be immediately obvious to the provider during the first encounter with a patient.

Individuals with low genetic literacy have a tendency to use “gene”, “chromosome”, and “DNA” interchangeably without knowing the biological nuance of such terminology.<sup>17</sup> Similarly, patients may not recognize that all humans share the same number of genes; it is variation within the genes that influences an individual’s risk for disease. This misconception can be identified by a patient stating that they have the “gene” for a condition, rather than a genetic change within the gene. Another common misconception is the erroneous assumption that genetic factors alone

influence risk for common multifactorial conditions, rather than the complex interplay of genetic factors and environment. Patients may, for instance, believe that there is a “gene” that causes diabetes, a known multifactorial condition, given that the condition exists in several family members. Other common fallacies include the environment consisting solely of influences from the natural world instead of including an individual’s lifestyle choices, as well as the idea that genes exist solely in the brain or gonads rather than distributed throughout most cell lines in the body.<sup>13</sup>

A common misconception about genetic literacy is that individuals with average or high health literacy also possess high genetic literacy. In one study of health literate individuals at high risk to develop type 2 diabetes, 30% of participants had limited health numeracy and 38% had limited genetic literacy.<sup>18</sup> Similarly, an international study using the International Genetic Literacy and Attitudes Survey (iGLAS) found that genetics knowledge was generally poor (average genetics knowledge test score = 65.5%) regardless of demographic factors i.e. country of origin, profession, education level and religious affiliation.<sup>19</sup> While there is a positive correlation between education and genetics knowledge, even college-educated individuals are not always genetically literate, leading to concerns about the degree of genetic literacy achieved in both undergraduate and graduate education. One cohort of college undergraduate students pursuing degrees outside of the biological sciences scored only 45% on average using the Genetic Literacy Assessment Instrument.<sup>11</sup>

### **2.2.1 Tools to Assess Genetic Literacy**

In evaluating a patient’s degree of genetic literacy, one approach is to consider E.M. Rogers’ hierarchy of knowledge, which describes the diffusion of a novel concept such as genetics

into the everyday life of an average person. Rogers' framework maintains that basic familiarity with genetic terminology is obtained first, followed by being able to contextualize basic genetic information for informal personal application; the highest order of the framework is understanding the underlying biological principles and mechanisms of genetics.<sup>20</sup> Consider an example of a patient reading a genetic test report that reveals a *BRCA1* pathogenic variant. The patient may be somewhat familiar with the term "gene" or "DNA" (the "what"). If they have achieved the next order of knowledge, the patient may be able to comprehend the notion that this mutation will increase their lifetime risk for certain cancers and alter their medical management, as well as understand that certain other relatives are at risk to have inherited this mutation ("how-to"). Few patients will understand the mechanisms of disease at the molecular level, in this case the *BRCA1* protein's role in transcription and double strand break repair ("why").<sup>21</sup>

The Rapid Estimate of Adult Literacy in Genetics (REAL-G) assessment addresses the "what" of Rogers' hierarchy.<sup>21</sup> REAL-G was created in 2007 to aurally screen for low genetic literacy in patient populations in clinical or research settings by asking subjects to read standard genetic terminology aloud to assess fluency.<sup>22</sup> Similarly, the Genetic Literacy and Comprehension measure (GLAC) evaluates genetic literacy by asking participants to rank familiarity with 8 commonly used genetic words and concepts: Genetic, Chromosome, Susceptibility, Mutation, Variation, Abnormality, Heredity, and Sporadic using a 7-point scale (strongly agree to strongly disagree with the statement "I am familiar with this term").

REAL-G and GLAC have both been utilized in research that addresses the first portion of Rogers' hierarchy in regards to genetic literacy, but are more applicable to the general population when compared to individuals immersed in health and scientific pursuits.<sup>22,23</sup> In other words, these instruments address literacy rather than genetics knowledge and evaluation of content in

educational settings. As one author argues, evaluating an individual's genetic literacy, particularly in the context of highly educated individuals, should more heavily emphasize the practical skills and factual knowledge portions, as these are more salient to the interpretation and clinical application of risk information.<sup>21</sup> Practical skills and factual knowledge can be assessed using scenario-centered questions and multiple choice or true/false statements, respectively.

In the academic setting, the Genetics Literacy Assessment Instrument (GLAI) has been used to evaluate genetics education at both the undergraduate and medical school level. The GLAI was developed to evaluate the factual knowledge component of genetic literacy in undergraduate students taking introductory biology courses.<sup>11</sup> This survey is a 31-item multiple-choice test that addresses 17 concepts identified as central to genetics literacy, including the ASHG-mandated six concept areas for genetic literacy for non-science majors at the undergraduate level (described in further detail below). The GLAI was created to evaluate genetic literacy as relevant to everyday life at the undergraduate level, particularly for non-biology majors, but the authors suggest that the survey may be helpful in assessing the genetic literacy of other populations.

To evaluate genetic literacy internationally, the International Genetic Literacy and Attitudes Survey (iGLAS) was developed by a collaborative team from Goldsmiths, University of London, Tomsk State University, and The Accessible Genetics Consortium (TAGC). iGLAS has four sections: knowledge, attitudes, a personality measure, and demographics. The demographics section includes sex, education level, employment, parental status (number of children), country of secondary education, country of residence, religious affiliation, religiosity level, spirituality level, and political ideology. The anonymous online survey was developed in English and Russian and has been administered to thousands of participants. Translations are currently available in

Spanish, French, Italian, Romanian and Albanian. The latest version of the study can be found at <http://tagc.world/iglas/>.

While previously mentioned studies have assessed genetics knowledge alone, other studies have attempted to find correlations between genetics knowledge and attitudes towards genetics. A recent study examined the knowledge and attitudes towards medical genetics in students of the Medical Faculty in Rijeka, Croatia. Students at this institution are required to take a medical genetics course during their 5th year; the impact of this course was evaluated based on the change in knowledge, attitudes, and personal assessment of knowledge in medical genetics, all of which were found to have improved after taking the genetics course.<sup>24</sup> Positive attitudes were correlated with higher levels of knowledge, implying that exposure to needs-based theoretical and practical education results in a strong foundation in genetics knowledge, which improves student's self-confidence in providing genetics services in a clinical setting. The student's self-confidence was reflected in their greater willingness to work directly with patients, a positive view of their own education, and the ability to clearly convey information about genetic conditions while respecting the patient's autonomy.

### **2.3 Outcomes of Limited Genetic Literacy in Patient-Provider Interactions**

Assessing a patient's genetic literacy level when preparing to have a conversation about genetics can be a challenge for healthcare providers. Experienced and genetically literate health care providers may be able to identify specific signs of low genetic literacy, which in some cases may also be signs of low health literacy. Regardless, these misunderstandings have the potential to complicate diagnosis and treatment as well as diminish patient satisfaction, as patients with low

genetic literacy are more likely to have poor information recall following a genetics-oriented conversation with a health care provider.<sup>16,25</sup> This puts the patient at increased risk for potentially problematic misconceptions of the natural history, surveillance, and treatment of their genetic condition, and may lead to over- or underestimations of the risk to other family members.<sup>26,27</sup> Consequently, individuals may hold harmful misconceptions about genetics and genetic testing. They may be unaware of trustworthy scientific resources to educate themselves, making them vulnerable to false or inaccurate information encountered online or in daily life. Patients who lack the biological framework for understanding a genetic diagnosis are more likely to experience confusion and frustration, confounding their care and contributing to feelings of depression and isolation.<sup>8</sup> Though assumption of a patient's genetic literacy level may be a sensitive topic, it is crucial for providers to recognize characteristics of a patient that may indicate low genetic literacy and to err on the side of caution when explaining genetic terminology and its relevance to the patient's health.

There are methods by which health-care providers can counter health and genetic illiteracy. Simplifying patient reading materials (i.e., patient letters, test reports, and pamphlets) can increase patient recall by providing a legible resource to reference at a later date and to share with relatives who may have varying degrees of health and genetic literacy. Strategies for more effective written communication include defining genetic terminology, replacing medical jargon with common language, and including images to illustrate difficult to understand concepts. Perhaps the most common verbal technique for reinforcing a difficult to grasp concept is the "teach-back" method of asking the patient to share her/his understanding of the information. Ultimately, by providing clear definitions and context for a patient's unique situation, healthcare providers can enable the opportunity for understanding and informed consent for the patient and family members.

## 2.4 Genetic Literacy and Clinical Genetics Knowledge in Physicians

In 2017, there were approximately 75,000 genetic tests on the market, with the majority being prenatal genetic tests and hereditary cancer genetic tests.<sup>1,28,29</sup> As the number of patients who undergo genetic testing increases, so too does the need for not only genetic counselors, geneticists, and other genetics clinicians, but also for genetically literate healthcare providers outside of clinical genetics. Given that many non-genetics affiliated healthcare providers (HCPs) are likely to encounter patients in need of genetic counseling, it is important to consider what education HCPs receive concerning genetics and genetic testing, as well as who is involved with the provision of genetic services in healthcare. There is a distinct connection between a provider's genetic literacy and their clinical genetics knowledge; measuring a provider's clinical genetics knowledge serves as a proxy for genetic literacy in an already health literate, highly educated population.

Unfortunately, many HCPs, particularly physicians, report little formal genetics education and feel ill-prepared to discuss genetic information with their patients.<sup>2</sup> Through analysis of three types of knowledge related to genetic literacy (awareness, "how-to", and principles), one systematic review of twenty-one studies found that genetic literacy in oncologists is limited across all three knowledge types, only one such example of a significant trend revealing a lack of genetics education in non-genetics affiliated physicians.<sup>30</sup> One survey of internists reported that 65% had counseled patients on genetic issues, but more than 70% of the internists described their personal knowledge of genetics as "very/somewhat poor", particularly in the context of counseling patients, selecting an appropriate test, and knowing the guidelines for a genetics referral.<sup>1</sup> Conversely, a different study found that despite confusion surrounding interpretation of variants of uncertain significance (VUS) and management of patient emotions, up to 61% of non-genetics healthcare

providers had a positive attitude towards their knowledge of genetic testing options for hereditary cancer with almost half of respondents ordering more than 30 of these tests per year.<sup>3</sup>

#### **2.4.1 Clinical Genetics Knowledge in Primary Care Physicians**

A significant amount of research has examined the genetic literacy of primary care providers' given their role as a patient's first point of contact for health care. Despite the critical services primary care physicians (PCPs) provide, deficiencies in several key skills essential to provision of genetic services have been identified, most notably ethical, legal, and social implication (ELSI) issues related to screening for genetic conditions, and basic knowledge of clinical genetics.<sup>31,32</sup> There is a need for the expansion of PCP's understanding of fundamental genetic principles, genetic test characteristics, and professional guidelines regarding testing, as well as promoting effective patient communication strategies about genetic risk and testing, specifically with regards to hereditary cancer genetic testing.<sup>31</sup> Patients should always take part in a thorough discussion for informed consent before electing to proceed with a genetic test. This discussion may include ELSI issues such as the clinical and personal utility of information garnered from a genetic test, the impact on medical management, federal protections related to genetic discrimination, the distinction between testing for clinical care and testing for research purposes, the possibility of secondary or incidental findings, among others.<sup>33</sup> Partnerships with genetic professionals can pave the way for improving access to genetics education of healthcare providers.

Commonly cited barriers to integration of genetics services in primary care include a lack of knowledge about genetics and genetic risk assessment, concern for patient anxiety, and a lack of time both to counsel patients and to learn about genetic concepts.<sup>34</sup> Fortunately, this problem

may be rectified through the provision of continuing education experiences by academic institutions, medical institutions, and professional societies. Providers can be incentivized to pursue these opportunities through continuing education credits and other paid trainings. Both web-based modules and traditional continuing education experiences are effective in educating PCPs. Some evidence suggests that web-based content results in improved knowledge retention and preference for shared decision making, a two-way communication model where the provider and patient develop a partnership to make a decision based on empathy and respect for the patient's belief system and level of genetic literacy.<sup>35,36</sup>

Since PCPs have established relationships within the community and well-defined roles as providers of preventative medicine and health education, they are ideal candidates for genomics education efforts. In addition to promoting open and effective patient-provider communication about genetic risk and genetic testing, addressing the educational needs and role of genetics in primary care may improve genetics risk assessment, increase genetics specialist referral rates, and provide a platform for the integration of precision medicine.<sup>31,37-39</sup> Genomics education moving forward should take a multi-pronged approach through forging partnerships between PCPs and genetics professionals, providing educational genetics experiences in the context of the field of primary care, and pursuing further research to tailor these educational strategies.<sup>37</sup>

#### **2.4.2 Clinical Genetics Knowledge in Pediatricians**

Early identification of a genetic condition in a child is crucial for promoting growth and development. In many cases, the first sign of a genetic condition in a child is Global developmental delay (GDD), which affects 1% to 3% of children.<sup>40</sup> Unfortunately, genetic testing is underutilized in pediatrics due to a lack of information surrounding testing guidelines. One survey from 2018

identified that 68% of pediatricians were not familiar with any genetic testing guidelines for a patient with global developmental delay (GDD). Although a majority of the 225 participants had ordered genetic testing for children with GDD, the study found that almost all providers would order genetic testing if a child presented with dysmorphic features and GDD, but only a minority (20.6%) would order testing for a case of isolated GDD.<sup>41</sup> This is contrary to the American Society of Human Genetics and the American College of Medical Genetics and Genomics (ACMG) position statements recommending chromosomal microarray as a first-tier clinical diagnostic test for individuals with apparent non-syndromic developmental disabilities and GDD.<sup>42,43</sup>

### **2.4.3 Clinical Genetics Knowledge in OB/GYNs**

Uncertainty has long been a factor of prenatal genetic counseling, though the vast wealth of information accessible through new prenatal genetic technologies deepens that uncertainty further than ever before.<sup>44</sup> For instance, the rise of cell-free DNA (cfDNA) screening from a maternal blood sample has resulted in an increased ability to detect common aneuploidies and even certain microdeletion syndromes as early as 10 weeks gestation.<sup>45</sup> In addition, the American College of Obstetrics and Gynecology (ACOG) has recommended that prenatal chromosomal microarray analysis is the standard of care offered to patients with a fetus with one or more major structural abnormalities identified on ultrasonographic examination and who is undergoing invasive prenatal diagnosis (chorionic villus sampling or amniocentesis).<sup>46</sup> The use of advanced genetic diagnostic tools in the event of a suspected fetal anomaly may provide answers for expecting parents, but understandably may cause distress. Carrier screening, whether ethnic-based or expanded, can provide couples with risks for certain autosomal recessive conditions prior to conceiving.

While more than 90% of OB/GYNs offer ethnic-based carrier screening, many OB/GYNs do not routinely offer expanded carrier screening (ECS) to their patients.<sup>47</sup> Contrary to the American College of Obstetricians and Gynecologist's statement that expanded carrier screening should be offered as part of preconception and pregnancy care, one survey of OB/GYNs from 2016 found that only 27% of practicing OB/GYNs offer expanded carrier screening to their patients, though notably, reproductive endocrinology/infertility and maternal fetal medicine specialists were significantly more likely to offer expanded carrier screening (80 and 70% offer ECS, respectively).<sup>47,48</sup> Similarly, another survey of OB/GYNs found that while all were familiar with cfDNA screening, or noninvasive prenatal testing (NIPT) the vast majority of these respondents (91%) felt that they needed more education on NIPT before offering the expanded version of NIPT to their patients.<sup>49</sup> One place to start expanding genetic testing education would of course be residency, however as of 2019 only 14.3% of OB/GYN residency programs have incorporated a medical genetics and genomics rotation; these rotations were generally shorter compared to other rotations such as family planning or ultrasound.<sup>50</sup>

Evidence suggests that the genetic literacy of pregnant women, as assessed by the Genetic literacy and Comprehension Measure (GLAC), does not impact their use of prenatal screening or diagnostic tests.<sup>51</sup> However, a patient with limited genetic literacy may struggle to communicate with and understand recommendations from their healthcare provider. As a result, patients may experience frustration or confusion, or worse, may make inappropriate management decisions based on miscommunication of genetic test results.<sup>52</sup> Therefore, healthcare providers involved with prenatal screening and diagnosis of genetic disorders should be prepared to counsel women of varying levels of genetic literacy and provide appropriate pre- and post-test counseling.

#### 2.4.4 Clinical Genetics Knowledge in Oncologists

Hereditary cancer predisposition syndromes are caused by pathogenic germline variants, most often in tumor suppressor genes. Early identification of a cancer predisposition syndrome can significantly impact medical care by providing therapeutic options, syndrome-specific surveillance, and prevention guidelines alongside disease management recommendations. Moreover, identifying a cancer predisposition may provide a long-sought explanation for the “family disease” and therefore initiate cascade testing for relatives of the affected individual. To discern between hereditary, familial, and sporadic forms of cancer, providers must utilize thorough risk assessment alongside knowledge of current genetic testing guidelines. Oncologists and other specialists who are providing care to patients with a personal and/or family history of cancer should have a working knowledge of hereditary forms of cancer. Patients with hereditary breast/ovarian and hereditary non-polyposis colorectal cancer (HNPCC) syndromes, while uncommon in the general population, can present in standard oncology practices.

Despite this reality, numerous studies demonstrate limited knowledge of genes associated with hereditary cancers in many non-genetics healthcare providers, including but to a lesser degree oncologists.<sup>5,6,53</sup> Many providers are familiar with *BRCA1/2* but are unaware of other genes associated with hereditary forms of breast cancer, which often necessitates the need for multigene panel testing rather than *BRCA1/2* alone. In accordance with NCCN guidelines, multigene panel testing for both high- and moderate- risk breast cancer genes are indicated in many patients.<sup>54</sup> Still, there are instances where oncologists have failed to test even for *BRCA1/2* mutations in a patient with a family history suggestive of hereditary breast and ovarian cancer (HBOC), resulting in missed opportunities for preventative treatment, surveillance of at-risk relatives, and therapeutic opportunities such as the use of PARP inhibitors and other targeted therapies.<sup>2,10,55-57</sup> Conversely,

one study found that in families with known pathogenic variants, where single-site testing of *BRCA1/2* would be appropriate, fewer than 35% of physicians correctly ordered single-site testing and instead ordered panel testing, resulting in excess medical costs to the patient.<sup>58</sup> This study did reveal that oncologists were the most likely specialty to correctly select single-site testing (38% of oncologists surveyed), but a significant portion opted for more expensive measures including *BRCA1* sequencing or comprehensive *BRCA* analysis.

*BRCA1/2* testing has existed since the late 1990's, but studies conducted within the last decade have shown that genetic counseling referral rates for women with epithelial ovarian cancer can vary between medical centers. While some hospitals report referral rates for women high-grade serous ovarian cancer as high as 95%, other institutional referral rates are as low as 31%.<sup>55,59,60</sup> One 2015 study found that only 31% of 104 epithelial ovarian cancer patients received a referral for genetic counseling from their oncologist. Similarly, genetic counseling referral rates from oncologists for male breast cancer, a rare cancer also correlated with pathogenic variants in *BRCA1/2*, are low, highlighting the need for provider education about cancer risks in males associated with hereditary predisposition syndromes.<sup>61</sup>

Other hereditary cancer etiologies are known to manifest with extra-oncological findings that could be identified through consultation with a genetic counselor. For instance, individuals with *PTEN* hamartoma tumor syndrome may present with learning disabilities, acral keratoses, and macrocephaly in addition to an increased incidence of breast, endometrial, and thyroid cancers, among others. Instances of physicians missing this potential diagnosis on the basis of not taking a detailed family history and/or lack of familiarity with the condition have been reported.<sup>62</sup> The National Comprehensive Cancer Network (NCCN) offers evidence-based risk assessment and

referral guidelines for these and many other hereditary cancer syndromes. Oncologists can utilize these and other resources to make a referral to cancer genetics when appropriate.

## **2.5 Consequences of Limited Genetic Literacy in Physicians**

In recent years, non-genetics healthcare providers, most commonly oncologists and obstetricians/gynecologists, have ordered significantly more genetic tests as part of their practice.<sup>1,28</sup> Evidence suggests that up to one-third of these tests were inappropriately ordered, either because they did not comply with practice guidelines, provided false reassurance to the patient, or failed to cover all involved differential diagnoses.<sup>63</sup>

Physicians with limited formal genetics education are at increased risk of accidentally ordering the wrong genetic test, failing to refer a patient in need of genetic services, or unintentionally providing misinformation during results disclosure.<sup>3-6</sup> These mistakes could result in harm to the patient and point toward the need for more physician training in selecting the appropriate genetic test, recognizing when referral to genetic services is necessary, as well as for utilization management through review of tests orders by a certified genetic counselor or genetics specialists.

Research has identified that medical management decisions have been based upon the misunderstanding of a variant of uncertain significance (VUS) as causative of disease including the recommendation that family members be tested for an identified variant of uncertain significance.<sup>5,6,53</sup> The American College of Medical Genetics states that testing for these variants is unnecessary because by their very definition, they do not impact patient care.<sup>64</sup> However, evidence suggests that non-genetics healthcare providers would recommend or have recommended

that family members be tested for a VUS.<sup>5,6,53</sup> Education on genetic testing including the interpretation of results would conceivably reverse this trend.

## **2.6 Workforce Data on Genetics Specialists**

Workforce data on medical genetics specialists have revealed a stark contrast between the increasing demand for genetic testing and the number of available genetics providers, particularly geneticists. One survey of medical genetics providers revealed that 25% of geneticists reported that they expect to retire in the next 5 years.<sup>65</sup> Given the aging workforce, genetics residency programs are attempting to recruit more applicants, but their efforts have yielded little success. In fact, genetics residency programs are currently reporting a lack of applicants; over the past several years many programs have not had enough applicants to fill all spots within the program.<sup>66</sup> The shortage of both current and aspiring medical geneticists points to an impending magnification of the current situation, which is already critical. For instance, wait times for combined genetic counselor and geneticist appointments, an arrangement necessary for many pediatric and adult indications, frequently exceed 4 months.<sup>67,68</sup> While the genetic counseling profession is rapidly expanding and genetic counselors are utilizing their scope of practice in new roles, the demand for genetic counseling still far exceeds the supply. A recent study on the genetic counseling workforce indicated a shortage of genetic counselors engaged in direct patient care, with the supply and demand not expected to reach equilibrium until sometime between 2024 and 2030.<sup>67</sup>

Different service delivery and practice models have been proposed to ameliorate the genetic specialist shortage. For example, efforts have focused on providing medical genetics training to mid-level providers (such as nurse practitioners and physician assistants) who are

licensed to perform physical examinations. Roles for physician assistants (PAs) and nurse practitioners (NPs) within clinical genetics have existed for decades but are often secondary to their official job duties within a broader department, for instance, oncology or maternal fetal medicine. The expansion of full-time genetics specialization would introduce more PAs and NPs to the profession. In addition, there has long been a need in the genetic counseling profession for increased autonomy independent of physicians, which can be achieved through federal policies such as expansion of licensure and recognition of genetic counselors as healthcare providers by Medicare and Medicaid services, which would allow them to be reimbursed under Medicare.<sup>38</sup> Meanwhile, in order to keep all genetics professionals working “at the top of their scope”, hiring additional support staff (i.e. genetic counseling assistants) can serve to improve workplace efficiency, as well as provide a pathway for aspiring genetics professionals to enter the field.<sup>38,68</sup>

## **2.7 Access to Genetic services**

To better prepare for a future where genetics is expected to play a greater role in clinical care, non-genetics healthcare professionals will need to incorporate genetic concepts, such as inheritance patterns, family history, and basic awareness of genetic conditions into their practice. Yet integration of genetics services has been slow to progress.

Non-genetics healthcare providers should not be expected to fulfill the same roles as genetics specialists. Individualized practice-based competencies (PBCs) are established for various professions with a role in providing care to individuals with genetic conditions. Currently, PBCs are easily accessible through the Genetics and Genomics Competency Center (G2C2) for physicians, genetic counselors, pharmacists, physician assistants, and nurses. In the case of genetic

counselors and nurses, PBCs were crafted through their respective accrediting body (Accreditation Counsel for Genetic Counseling; American Nurses Association) while those for physician assistants and pharmacists were created through a conglomerate of several professional organizations.<sup>69-71</sup> At the most basic level, providers should be able to identify patients in need of genetic services through basic knowledge of the characteristics of genetic conditions and inheritance patterns. Health care institutions could foster connections between primary care doctors and genetics teams to create open lines of communication for questions and continuity of patient care. Finally, if a provider chooses to refer a patient to genetics, the provider should explain to the patient why they are being referred and how genetics could impact the course of care.

### **2.7.1 Barriers to Genetic Counseling Services**

Numerous factors have been cited for the lethargic integration of genetics into health care, including access to and knowledge of genetic counseling. As with generalized medical care, but perhaps to a greater degree, physical and financial barriers continue to impede patient access to genetic counseling services despite expansion of different care delivery models.<sup>38,72</sup> As of 2020, genetic counselors are still concentrated in large, urban medical centers. Patients living in rural areas may have to travel a considerable distance to meet with a genetic specialist, despite efforts to expand care through rural outreach programs and telemedicine. Some patients continue to have inadequate access to technology for telemedicine. Scheduling conflicts, out-of-pocket costs, and long wait times continue to be barriers, especially for lower-income patients. In low-income populations, health and genetic literacy is often lower. It is not uncommon for individuals with limited health or genetic literacy to present for a genetic counseling appointment with little to no understanding as to why they were referred to genetics. When so many seemingly insurmountable

barriers exist, from the patient's perspective the benefit of attending a genetic counseling appointment can appear low, especially if the patient does not understand how genetics impacts their course of care.<sup>73</sup>

Patients often cite emotional or familial reasons for deferring genetic testing and not seeking genetic counseling services.<sup>72</sup> Some patients prefer to direct questions about genetic testing towards their general practitioner prior to or instead of seeking the services of a genetic professional with whom they do not have a professional relationship.<sup>74</sup> This may be related to the limited public familiarity with the genetic counseling profession, though recent efforts to increase public awareness of the field, a nationwide growth in the number of genetic counselors and greater public familiarity with genetic conditions, may change this perception in time. However, as described in the previous section, there remains a nationwide shortage of geneticists that continues to hamper access to genetic services for patients in need of a physical examination, which genetic counselors are not licensed to perform, and coordination of care with other specialists.

## **2.8 The Current Status of Genetics Education**

### **2.8.1 Recommendations and Guidelines for Undergraduate Education**

Research has assessed the impact of undergraduate education in understanding genetic information. In a 2002 survey of undergraduate biology course instructors, the respondents expressed that they felt undergraduate students lack both depth in understanding of genetic concepts and the ability to relate genetics to everyday life. In response, 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.<sup>12,75</sup> Other researchers have criticized these domains as emphasizing Mendelian genetics too heavily, less focus on important concepts related to multifactorial inheritance, variable expressivity and penetrance, polygenic traits, and other aspects of complex genetic disorders.<sup>76</sup>

## **2.8.2 Recommendations and Guidelines for Medical School Curriculum**

To acknowledge and confront the widening gap between clinical incorporation of genetics into educational efforts and the pace at which genomic medicine is evolving, the National Human Genome Research Institute assembled a working group: The Inter-Society Coordinating Committee for Physician Education in Genomics (ISCC-PEG). 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."<sup>77</sup> In 2014, the ISCC was first tasked with developing a framework for genomics practice-based competencies for physicians.<sup>78</sup> Each practice-based competency falls 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: medical knowledge, patient care, interpersonal and communications skills, practice-based learning and improvement, professionalism, and systems-

based practice. The ACGME broad competencies were in turn translated into core curriculum competencies for standard medical genetics education by the Association of Professors of Human and Medical Genetics (APHMG). The APHMG core curriculum utilizes deductive and empirical skills in genetics for the medical student as opposed to the memorization of symptoms associated with particular genetic diseases while also educating students on appropriate molecular genetic test selection, bioinformatics tools, and specialist referral.<sup>79</sup> Most medical genetics course directors report using the APHMG core curriculum to guide and evaluate their own curriculum content.<sup>80</sup>

### **2.8.3 Current Status of Genetics Education in Medical Schools**

There are a limited number of studies examining the curricula across medical schools nationwide. In 2005, 46% (52/112) of course directors and curricular deans reported that medical genetics was taught as a stand-alone course at their medical schools, and 54% (60/112) indicated that it was integrated into other courses, with most of these courses being taught in the first or second year.<sup>81</sup> As evidenced by 80% of respondents indicating that these courses consisted of fewer than 40 contact hours, exposure to genetics education during medical school is limited.<sup>82</sup> A minority of programs reported continuing genetics education into the third and fourth years. While genetics has advanced considerably in the past fifteen years, research has found that little has changed in the amount of time dedicated to genetics in medical school curriculum. A more recent study from 2013-2014 found similar trends in that most schools primarily teach genetics during the first 2 years, with an increase in the number of integrated curricula compared with a standalone medical genetics course.<sup>80</sup> Only 26% of institutions reported formal genetics teaching during years 3 and 4 of medical school. Interestingly, most medical genetics course directors from the 2013 survey felt the amount of time spent on genetics was insufficient preparation for clinical practice.

Trends in the topics addressed during medical genetics have changed over time, with personalized medicine, direct-to-consumer testing, and pharmacogenomics being covered more frequently, whereas eugenics, linkage analysis, and evolutionary genetics have been removed from curriculum.<sup>80</sup>

Certain institutions have attempted to tackle genetics education in unique and innovative ways. For example, Baylor College of Medicine recently began offering a “Genetics Track Curriculum” for medical students with a special interest in genetics. In addition to the standard curriculum, which includes 12 genetics education contact hours in Year 1 and 22 genetics education contact hours in Year 2, students are provided with additional didactic sessions, small group discussions, longitudinal clinical experiences, clinical and laboratory rotations, community outreach, and scholarly projects related to genetics.<sup>9</sup> Other institutions and medical schools offer medical genetics “Special Interest Groups” (SIGs) to students interested in genetics.<sup>83</sup>

Some medical schools have educated medical students on the benefits and pitfalls of personal genotyping considering the widespread availability of direct-to-consumer tests (DTC), or genetic tests that can be ordered at-will by a consumer without supervision from a healthcare provider. These tests typically involve a saliva sample with results made available online. The rapid growth of the direct-to-consumer testing market is remarkable, with up to 100 million people expected to undergo DTC testing by 2021.<sup>84</sup> Consumers may be interested in DTC tests for a number of reasons, including but not limited to information regarding ancestry, lifestyle/fitness, entertainment, health information (i.e. the Jewish pathogenic BRCA1/2 variants), or access to raw genomic data files.<sup>85</sup>

Direct-to-consumer tests have limited clinical utility in part because they are largely based upon single nucleotide polymorphism (SNP) genotyping rather than comprehensive whole gene

sequencing.<sup>86</sup> DTC results that are deemed clinically significant are recommended to have follow-up diagnostic testing conducted through a health care provider. Contrary to the fact that DTC tests can be ordered without the oversight of a healthcare provider, companies offering DTC testing services often encourage discussing results with health care providers. Many patients view physicians as credible sources of information regarding their DTC test results, which raises the question of how physicians are equipped to handle these requests.<sup>87</sup>

One study found that medical student perspectives on DTC testing shifted after taking a core genetics course that incorporated personal genotyping. After taking part in personal genotyping through the course, students were less likely to believe that information provided by DTC tests were useful in impacting medical management in terms of diagnosis and treatment of medical conditions, though many expressed that they would consider personal genotyping out of general curiosity.<sup>88</sup> Additionally, approximately 50% of medical students who took part in personal genotyping expressed concern about confidentiality of results. While general genetics knowledge improved after taking the course, the students still struggled with clinical interpretation of DTC results when provided with scenarios.

While many medical schools see the value in educating future physicians about genomics, there is the constraint of including additional content into an already rigorous and demanding curriculum. However, medical students have expressed a desire for additional genetics education given the integration of personalized genomic medicine into clinical care, with many expressing limited understanding of genomic concepts, reflected by low genetics knowledge scores.<sup>89</sup> In response, certain programs have strived to provide unique educational experiences to maximize content retention. One approach is to allow students to perform DNA sequencing on themselves using portable DNA sequencers to learn about next-generation sequencing (NGS).<sup>90,91</sup> Discussion

about such results may result in improved genetic literacy, which is often incompletely attained during undergraduate education. Additionally, hands-on learning experiences using NGS technology appear to result in a greater willingness to learn how to interpret genetic test results and a greater appreciation of the patient experience.<sup>91</sup>

#### **2.8.4 Medical Genetics Education during Residency**

Some physicians receive additional training in genetics and genomics during residency, depending on their chosen specialty. However, even among medical students who choose to specialize in medical genetics, 32% had not taken a medical genetics elective prior to entering the medical genetics residency.<sup>92</sup>

The Council on Resident Education in Obstetrics and Gynecology (CREOG) provides educational objectives for medical genetics education within an OB/GYN residency, which were last updated in 2020. Such topics include prenatal counseling, implications of genetic test results, knowledge of genes associated with hereditary cancer, and criteria for referral to a genetic counselor.<sup>93</sup> One recent study reviewed OB/GYN residency programs' websites during the month of December 2016. Out of 238 American Council for Graduate Medical Education (ACGME)-accredited OB/GYN residency programs for which rotations schedules were publicly available, only 34 programs (14.3%) had a formal medical genetics and genomics education rotation.<sup>50</sup> Out of these, only one program had a full month-long rotation dedicated entirely to medical genetics, whereas the other 33 were combined with another rotation, most commonly ultrasound. These observations challenge the assumption that medical students who pursue careers in specialties that rely on considerable genetics knowledge will receive thorough genetics training in residency. This has the potential to result in a limited understanding of genetics and its relationship to women's

health , though interactive genetics curriculum during residency training has proven to be both easy to implement and effective in educating residents.<sup>94</sup>

## 3.0 MANUSCRIPT

### 3.1 Background

Genetic literacy, a subset of health literacy, is defined as “sufficient knowledge and appreciation of genetics principles to allow informed decision-making for personal well-being and effective participation in social decisions on genetic issues”.<sup>11</sup> The majority of the general population in the United States has not achieved genetic literacy.<sup>8,15,16</sup> Though many Americans express familiarity with genetic terminology, few possess the fundamental scientific framework to contextualize genetic information in terms of their own health and medical management, resulting in a possible unintentional overestimation of understanding.<sup>13,17</sup> Misconceptions about genetic testing rooted in limited genetic literacy have the potential to confound discussions concerning genetic information between patients and providers, a scenario which is becoming more common as genetics and precision medicine continues to become integrated into healthcare. Patient misunderstandings of genetic information have the potential to complicate diagnosis and treatment as well as diminish patient satisfaction, as patients with low genetic literacy are more likely to have poor information recall following a genetics-oriented conversation with a health care provider.<sup>16,25</sup> This puts the patient at increased risk for potentially problematic misconceptions of the natural history, surveillance, and treatment of their genetic condition, and may lead to over- or underestimations of the risk to other family members.<sup>26,27</sup>

As genetics services become more routine, non-genetics affiliated healthcare providers (HCPs), most commonly oncologists and obstetricians/gynecologists (OB/GYNs), have ordered significantly more genetic tests as part of their practice.<sup>1,28</sup> Given that many non-genetics HCPs

are likely to encounter patients in need of genetic counseling, it is important to consider what education HCPs receive concerning genetics and genetic testing, as well as who is involved with the provision of genetic services in healthcare. While there is a positive correlation between higher education, genetics knowledge, and a high degree of health literacy, even college-educated individuals are not always genetically literate, leading to concerns about the genetic literacy of healthcare providers themselves.<sup>11,18</sup> There is a distinct connection between a provider's genetic literacy and their clinical genetics knowledge; measuring a provider's clinical genetics knowledge serves as a proxy for genetic literacy in an already health literate, highly educated population.

Unfortunately, many HCPs, particularly physicians, report little formal genetics education and feel ill-prepared to discuss genetic information with their patients and interpret genetic test results.<sup>1,2,30</sup> Up to one-third of genetic tests ordered by non-genetics healthcare providers were inappropriately ordered, either because they did not comply with practice guidelines, provided false reassurance to the patient, or failed to cover all involved differential diagnoses.<sup>63</sup> Primary care physicians have cited a lack of knowledge about genetics and genetic risk assessment, concern for patient anxiety, and a lack of time both to counsel patients and to learn about genetic concepts as barriers to the integration of genetic services in primary care.<sup>34</sup> Pediatricians have reported limited familiarity with genetic testing guidelines for children with common indications such as developmental delay, which affects between 1-3% of children.<sup>40-43</sup> Similarly, the rollout of expanded carrier screening and expanded noninvasive prenatal testing (NIPT) has been complicated by a lack of provider education for OB/GYNs about counseling patients for the benefits, risks, and limitations of these tests.<sup>47-49</sup> Evidence suggests that the genetic literacy of pregnant women does not impact their use of prenatal screening or diagnostic tests, yet providers may lack the ability to communicate the nuances of these tests to patients with limited genetic

literacy.<sup>51</sup> Finally, numerous studies demonstrate limited knowledge of genes associated with hereditary cancers in many non-genetics healthcare providers, including but to a lesser degree oncologists.<sup>5,6,53</sup> Many providers are familiar with *BRCA1/2* but are unaware of other genes associated with hereditary forms of breast cancer, which often necessitates the need for multigene panel testing rather than testing only *BRCA1/2* for many patients in accordance with NCCN guidelines.<sup>54</sup> Inappropriate test selection for hereditary cancer may result in missed opportunities for preventative treatment, surveillance of at-risk relatives, and therapeutic opportunities such as the use of targeted therapies.<sup>2,10,55-57</sup>

Physicians with limited formal genetics education are at increased risk of accidentally ordering the wrong genetic test, failing to refer a patient in need of genetic services, or unintentionally providing misinformation during results disclosure.<sup>3-6</sup> These mistakes could result in harm to the patient and point toward the need for more physician training in selecting the appropriate genetic test, recognizing when referral to genetic services is necessary, as well as for utilization management through review of tests orders by a certified genetic counselor or genetics specialists. Unfortunately, workforce data on medical genetics specialists have revealed a stark contrast between the increasing demand for genetic testing and the number of available genetics providers. This current shortage of genetics specialists is exacerbated by the aging workforce of geneticists, the lack of applicants to genetics residency programs, and a lag in the supply of genetic counselors, which is not expected to equalize with demand until the late 2020's.<sup>38,65-68</sup> To communicate complex genetic information to patients with varying degrees of genetic literacy, our healthcare system needs not only more genetic counselors and geneticists, but also more genetically literate non-genetics healthcare providers to bridge the gap between patients and genetics specialists.

As genomics continues to play a greater role in clinical care, non-genetics healthcare professionals will increasingly need to incorporate genetic concepts, such as inheritance patterns, family history, basic awareness of genetic conditions, and genetic testing into their practice. Consequently, medical schools will need to help medical students master these basic clinical genetics concepts. Since undergraduate education in biology largely focuses on molecular and Mendelian genetics, medical school is often a medical student's first exposure to clinical genetics.<sup>12,75,76</sup> The Association of Professors of Human and Medical Genetics (APHMG) core curriculum is used by many medical school genetics course directors, and utilizes deductive and empirical skills in genetics as opposed to the memorization of symptoms associated with particular genetic diseases while also educating students on appropriate molecular genetic test selection, bioinformatics tools, and specialist referral.<sup>79</sup> However, most medical schools devote fewer than 40 contact hours to genetics education, which studies have suggested is insufficient preparation for clinical practice.<sup>80-82</sup> While many medical schools see the value in educating future physicians about genomics, there is the constraint of including additional content into an already rigorous and demanding curriculum. Though certain programs have strived to provide unique educational experiences to maximize content retention such as patient-led educational sessions, opportunities to join special interest groups, and even allowing students to perform direct-to-consumer testing on themselves, medical students have still expressed a desire for additional genetics education given the integration of genomic medicine into clinical care.<sup>88,90,91</sup>

Previous studies have shown that medical students have a limited understanding of genomic concepts, reflected by low genetics knowledge scores.<sup>89</sup> This study is an updated assessment of current genetics educational exposures unique to the University of Pittsburgh School of Medicine with the goal of better understanding how students feel about their knowledge of

clinical genetics concepts through self-assessment, followed by a knowledge questionnaire. This and other studies are intended to provide additional evidence for the further integration of clinical genetics into medical school curriculum.

### **3.1.1 Specific Aim I**

To develop a survey to assess the University of Pittsburgh medical students' genetic literacy and clinical genetics knowledge as well as their familiarity with several clinical genetics topics.

### **3.1.2 Specific Aim II**

To evaluate the process by which medical students acquire genetic knowledge during their training.

## **3.2 Methods**

### **3.2.1 Study Population**

The target population for survey distribution consisted of all first year medical students at the University of Pittsburgh School of Medicine (UPSOM) during the 2020-2021 academic year. Students were eligible to take the survey if they had participated in the School of Medicine's Human Genetics course during the Fall 2020 semester. This 21-day course is required for all first year medical students at UPSOM.

### 3.2.2 Survey Development

Prior to recruitment efforts and distribution, exempt IRB approval was obtained from the University of Pittsburgh (see Appendix B). The study was also approved by the University of Pittsburgh Research on Medical Students (ROMS) Committee (see Appendix C). The study survey was developed and distributed using the Qualtrics survey system, which was accessed through a University of Pittsburgh license. The survey included three major sections. The Self-Assessment section asked students to rate their familiarity and understanding of several clinical genetics topics on a 5-point Likert-scale. The Knowledge section was split into three portions: Inheritance, Clinical Genetics Scenarios, and Interpretation of Genetic Test Results. Questions within the Knowledge section were multiple choice questions with 3-4 possible responses and true/false questions. Finally, the UPSOM Human Genetics Course Assessment and Prior Experience in Genetics section asked participants about the perceived degree of difficulty of the UPSOM medical genetics course as well as any prior experience in the field of genetics.

All survey questions (see Appendix E) were newly developed but were informed by instruments used in studies that surveyed similar student populations, specifically the Genetic Literacy Assessment Instrument (GLAI) developed by Bowling et al, the International Genetic Literacy and Attitudes Survey (iGLAS), Ormond et al.'s study concerning direct-to-consumer genetic testing, and Pearl et al.'s study involving knowledge assessment of a medical school's clinical neurogenetics curriculum.<sup>11,19,88,89</sup> Confidence topics were derived from questions in Bowling et al and iGLAS since these studies target the general population. Clinical knowledge questions were generated based on questions presented in Ormond et al and Pearl et al, both of which are focused on the opinions of medical and graduate students. In developing the survey, multiple physicians and genetic counselors were consulted for input on perceived gaps in genetics

education of medical students. Survey questions ascertained knowledge on prenatal, pediatric, and cancer genetics and covered content that was included in the UPSOM Human Genetics course. Survey questions were reviewed for clarity by four genetic counselors, an MD, and a statistical geneticist. The survey was piloted by 10 genetic counseling students. Based upon their feedback, minor modifications to the wording of several questions were made for clarity.

### **3.2.3 Recruitment and Survey Distribution**

Survey distribution was facilitated by a contact within the University of Pittsburgh School of Medicine Office of Education (OME). The study coordinator contacted this individual in advance of the survey distribution and provided the survey invitation (see Appendix D). The OME contact sent the survey invitation to all email addresses belonging to current first year medical students at the University. The survey opened to participants on February 5, 2021 and concluded on March 5, 2021. A reminder email was sent to the students on February 23, 2021. Data was collected anonymously through the Qualtrics survey system.

### **3.2.4 Statistical Methods**

Descriptive statistics were used to indicate how frequently each response was selected. Microsoft Excel and Qualtrics were used to generate descriptive statistics. Composite scores for Likert scale Self-Assessment questions were generated to assess confidence with various genetic concepts. Similarly, composite scores were generated in the knowledge section. Nonparametric T-tests (Wilcoxon rank-sum) were used to study the association between knowledge, confidence,

and prior experience. 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 147 first year medical students at the University of Pittsburgh. We received 21 total responses, yielding a response rate of 14.3%. However, only 15 participants completed the Self-Assessment. The six incomplete responses who did not complete the Self-Assessment were excluded from all analyses. Two participants started but did not complete the Knowledge Assessment. Only 10 participants completed the entire survey, yielding a response rate of 6.8%.

#### **3.3.2 Self-Assessment of Knowledge**

Participants were asked to rate their knowledge in twelve genetic concepts. The statements used were positively framed, i.e. “I can do this task” or “I am knowledgeable in this concept” and were assessed using a 5-point Likert scale (1=strongly disagree; 5= strongly agree). Responses were used to generate composite scores to yield a total maximum “confidence score” of 60. The term “confidence” or “confidence score” is a measure of the student’s perceived knowledge or ability to perform a skill related to a clinical genetics concept. For the fifteen respondents who

completed the Self-Assessment, the average confidence score was 47.93/60 (79.8% confident) (see Appendix A: Table 7).

Table 1 shows the responses for the fundamental genetic concepts portion of the Self-Assessment. 81% of respondents (n=13/15) answered “Strongly Agree” in rating their knowledge of the central dogma and inheritance. Participants also reported a high level of understanding of population genetics (93% “Strongly” or “Somewhat” agree; n=14/15). With regards to molecular and cytogenetic techniques, only one respondent felt strongly confident in their knowledge, with 66% of respondents somewhat agreeing and 26% neither agreeing nor disagreeing.

**Table 1. Self-Assessment: Fundamental Genetic Concepts**

Genetic Concept	Number of Participants (N=15)
<b>I understand the relationship between DNA, RNA, and protein.</b>	
Strongly agree	13
Somewhat agree	1
Neither agree nor disagree	0
Somewhat disagree	0
Strongly disagree	1
<b>I understand the foundational concepts of genetic inheritance.</b>	
Strongly agree	13
Somewhat agree	1
Neither agree nor disagree	0
Somewhat disagree	0
Strongly disagree	1
<b>I understand how ancestry, genetic drift, and natural selection relate to modern patient populations.</b>	
Strongly agree	9
Somewhat agree	5
Neither agree nor disagree	0
Somewhat disagree	0
Strongly disagree	1
<b>I am knowledgeable about the principles of cytogenetics and molecular genetic techniques.</b>	
Strongly agree	1
Somewhat agree	10
Neither agree nor disagree	3
Somewhat disagree	0
Strongly disagree	1

Responses were more variable for self-assessment of clinical skills (see Table 2). 87% of participants (n=13/15) “agreed” or “somewhat agreed” that they were capable of taking a family history for a genetics indication, while 73% “agreed” or “somewhat agreed” (n=11/15) that they

felt confident enough to assess risk for a genetic condition based on a family history. Only 60% (n=9/15) felt comfortable or somewhat comfortable identifying indications for referral to a genetics specialist. Knowledge of clinical genetics resources was varied; 53% of respondents (n=8/15) were not familiar with clinical genetics resources or databases. Participants rated their ability to describe the benefits, risks, and limitations of genetic testing positively (87% “Strongly” or “Somewhat” agree; n=13/15).

**Table 2. Self-Assessment: Genetic Concepts Involving Clinical Skills**

Genetic Concept	Number of Participants (N=15)
<b>I can gather a detailed family history for a genetic indication.</b>	
Strongly agree	3
Somewhat agree	9
Neither agree nor disagree	1
Somewhat disagree	2
Strongly disagree	0
<b>I can assess genetic risk based on the information within a family history.</b>	
Strongly agree	4
Somewhat agree	7
Neither agree nor disagree	0
Somewhat disagree	3
Strongly disagree	1
<b>I am comfortable identifying indications for referral to a genetics specialist.</b>	
Strongly agree	3
Somewhat agree	6
Neither agree nor disagree	4
Somewhat disagree	2
Strongly disagree	0
<b>I can apply knowledge of genetic principles to effectively communicate with patients who have limited genetic literacy.</b>	
Strongly agree	8
Somewhat agree	4
Neither agree nor disagree	2
Somewhat disagree	0
Strongly disagree	1
<b>I am familiar with clinical genetics resources and databases.</b>	
Strongly agree	2
Somewhat agree	5
Neither agree nor disagree	3
Somewhat disagree	3
Strongly disagree	2
<b>I can describe the benefits, risks, and limitations of genetic testing to a patient.</b>	
Strongly agree	7
Somewhat agree	6
Neither agree nor disagree	1
Somewhat disagree	0
Strongly disagree	1

Lastly, Table 3 shows that 66% of respondents (n=10) rated their knowledge of genetics and genetic testing in relation to cancer positively. Participants ranked their knowledge higher for methods of prenatal diagnosis (87% “Strongly” or “Somewhat” agree; n=13/15).

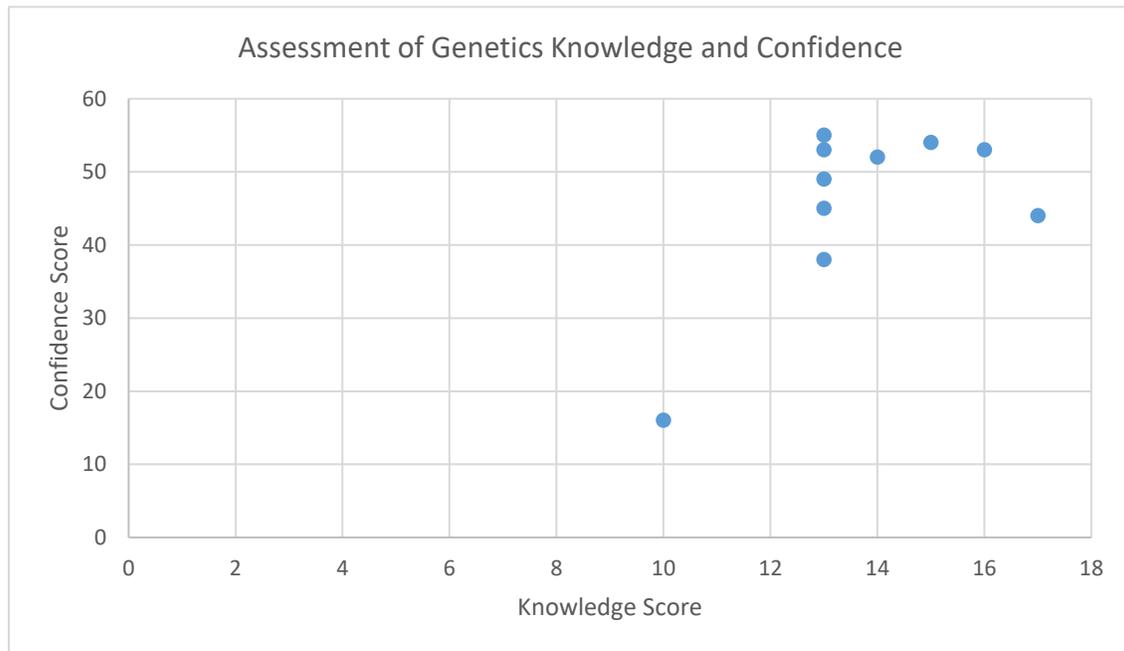
**Table 3. Self-Assessment: Cancer and Prenatal Genetic Concepts**

Genetic Concept	Number of Participants (N=15)
<b>I have thorough knowledge of genetics relating to the development, diagnosis, and treatment of cancer.</b>	
Strongly agree	4
Somewhat agree	6
Neither agree nor disagree	3
Somewhat disagree	1
Strongly disagree	1
<b>I am aware of methods for prenatal diagnosis of genetic conditions.</b>	
Strongly agree	7
Somewhat agree	6
Neither agree nor disagree	0
Somewhat disagree	1
Strongly disagree	1

### 3.3.3 Clinical Genetics Knowledge

In the next section of the survey the participants were assessed on their knowledge of clinical genetics. The average score of all participants for the Clinical Genetics Knowledge section was 72.1%, or 13.7 questions correct out of 19 total knowledge questions. The Clinical Genetics Knowledge section was divided into three portions: Inheritance (six questions), Clinical Genetics Scenarios (eight questions), and Interpretation of Genetic Test results (five questions). The comparison between knowledge composite scores and self-assessment composite scores are shown in Figure 1. There is a positive correlation ( $R = 0.61$ ) between knowledge and confidence. However, this relationship is not as strong after censoring a high leverage point. After removing this datapoint (knowledge score=10, confidence score=16), the correlation is considerably weaker ( $R=0.04$ ), which may point to limitations in this study, which will be addressed in the Discussion section.

**Figure 1. Comparison of Genetics Knowledge and Confidence Scores**



**Maximum Knowledge Score = 19; Maximum Confidence Score = 60**

Table 4 outlines the frequency of correct responses for questions concerning inheritance. All participants (n=12) correctly answered questions asking them to identify characteristics of autosomal recessive and mitochondrial inheritance. Similarly, most participants (91.67%) knew that for multifactorial conditions, when a phenotype is more common in one sex, the risk for having the phenotype is higher for relatives of an affected individual of the less susceptible sex. However, only 8 respondents (66%) were able to correctly identify the carrier risk for a healthy child whose sibling has an autosomal recessive condition (a 66% carrier risk); 4 respondents (33%) incorrectly stated that the sibling's carrier risk would be 50%. When asked about characteristics of X-linked recessive inheritance, only 7 (58.3%) participants correctly indicated that the children of affected males are typically not at risk for being affected with the condition; 4 (33.33%) respondents incorrectly reported that females are usually more severely affected than males and 1 (8.33%) respondent thought that males and females would be affected equally. Participants also

encountered difficulty with a scenario involving autosomal dominant inheritance. When asked what the chance for a male with deletion of the 22q11.2 region, also known as DiGeorge syndrome, to have a child with this same condition, only 7 (58.3%) participants correctly indicated that each child would have a 50% chance to inherit the deletion; 3 (25%) respondents incorrectly reported that the child's risk would be 25% and 2 (16.67%) respondents thought that the risk would be less than 1%.

**Table 4. Knowledge Assessment (Inheritance): Frequency of Correct Responses**

<b>Inheritance</b>		
<b>Question</b>	<b>Correct n (%)</b>	<b>95% Confidence Interval</b>
What is the chance that a healthy child whose sibling has an autosomal recessive genetic condition will be a carrier?	<b>8 (66.67%)</b>	<b>34-90%</b>
A woman marries her 1st cousin, once-removed. Which scenario is most likely?	<b>12 (100%)</b>	-
Select the statement that best describes X-linked recessive inheritance:	<b>7 (58.33%)</b>	<b>28-85%</b>
True or False: For multifactorial conditions, when a phenotype is more common in one sex, the risk for having the phenotype is higher for relatives of an affected individual of the less susceptible sex.	<b>11 (91.67%)</b>	<b>62-99%</b>
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?	<b>7 (58.33%)</b>	<b>28-85%</b>
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?	<b>12 (100%)</b>	-

**Note: 12 respondents completed the Inheritance section.**

The first portion of the Clinical Genetics Scenarios section (see Table 5) elicited respondents' knowledge relating to cancer genetics, with three out of four questions concerning the *BRCA1/2* genes. The first scenario references a female patient with breast cancer who reports that she has undergone genetic testing and was found to have "the gene for breast cancer" but is implied to not have a copy of the genetic test report. Participants were expected to not rely solely on the patient's statement, however, all participants (n=9) selected that it would be reasonable to assume that the patient has a pathogenic variant in a gene associated with an increased risk for breast cancer, even without a copy of the report. Many participants (90.91%) indicated the counseling for a familial *BRCA1* pathogenic variant would include a discussion about lifestyle modification, surgical recommendations, and psychosocial concerns, as well as potential referral to a high-risk breast cancer screening program. In a related scenario where an unaffected 30-year-old woman comes to the genetics clinic for *BRCA1* and *BRCA2* testing, only 4 participants (36.36%) correctly selected the patient's mother, who had breast cancer diagnosed at age 40, as the best person to test; all other participants (n=7; 63.64%) stated that the patient should be tested first. When asked about testing a child for an adult-onset hereditary cancer syndrome, 8 participants (72.73%) correctly said that genetic testing would typically not be recommended until the child is a legal adult.

Questions concerning pediatric scenarios focused on genetic testing strategy. Only 4 participants (36.36%) correctly stated that microarray should be the first genetic test to order for a 5 year old girl with dysmorphic features, developmental delay, and microcephaly; 5 respondents (45.45%) would have ordered Chromosome Breakage studies (DEB analysis) and 2 (18.18%) would have ordered exome sequencing. Similarly, while participants recognized that it would be appropriate to order a karyotype when there is suspicion for Down syndrome, 5 participants

(45.45%) felt that it would not be necessary to order a karyotype if there was concern for a translocation due to a history of multiple miscarriages and 1 participant (9.09%) felt that it would not be necessary to order a karyotype when there was concern for a sex chromosome disorder.

Regarding the prenatal scenarios, 9 participants (81.82%) would use counseling strategies to individually explore a couple's thoughts about the outcomes of their pregnancy following a prenatal diagnosis of Klinefelter syndrome; 2 participants (18.18%) felt it would be necessary to first provide detailed information about the features of Klinefelter syndrome. All participants (n=11) correctly stated that diagnostic testing is needed following a positive NIPT.

**Table 5. Knowledge Assessment (Clinical Genetics Scenarios): Frequency of Correct Responses**

<b>Clinical Genetics Scenarios</b>		
<b>Question</b>	<b>Correct n (%)</b>	<b>95% Confidence Interval</b>
A female patient with breast cancer reports that she has undergone genetic testing and was found to have the "gene for breast cancer". Which of the following is safe to assume based solely on the patient's statement?	<b>0 (0%)</b>	<b>-</b>
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?	<b>10 (90.91%)</b>	<b>59-99%</b>
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 40, her maternal female 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?	<b>4 (36.36%)</b>	<b>11-69%</b>
A woman with hereditary nonpolyposis colorectal cancer, otherwise known as Lynch syndrome, wants her 14 year old daughter to be tested for the known familial mutation. What do you tell this woman and her daughter?	<b>8 (72.73%)</b>	<b>39-94%</b>
A 5 year old girl presents to your clinic with dysmorphic features, developmental delay, and microcephaly. Which of the following is the most appropriate genetic test to order for this child?	<b>4 (36.36%)</b>	<b>11-69%</b>
When is it LEAST appropriate to order a karyotype?	<b>5 (45.45%)</b>	<b>17-77%</b>
A woman is referred to your clinic at 19 weeks gestation because her amniocentesis, performed for advanced maternal age, revealed a karyotype of 47,XXY (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?	<b>9 (81.82%)</b>	<b>48-98%</b>
True or False: Non-Invasive Prenatal Testing (NIPT) has a very high detection rate for Down syndrome, therefore, diagnostic testing is not needed following a positive NIPT.	<b>11 (100%)</b>	<b>-</b>

**Note: 11 respondents completed the Clinical Genetics Scenarios section.**

The Interpretation of Genetic Test Results section, shown in Table 6, asked participants to interpret genetic test results for a variety of genetic conditions. 80% of participants correctly stated that a child with a positive newborn screen for cystic fibrosis with a negative sweat test and a single F508 mutation is a carrier for cystic fibrosis, while 20% suspected that the child would have CFTR-Related Metabolic Syndrome (CRMS). 6 participants (60%) stated that the parents of a child with a confirmed *de novo* 22q11.2 deletion would have a slightly increased risk to have another child with DiGeorge syndrome due to the possibility of germline mosaicism, while 4 participants (40%) would have told the parents that they were not at increased risk. The majority of participants (8 participants; 80%) correctly stated that medical management decisions should typically not be made based on a variant of unknown significance. If one had clinical suspicion that a variant of uncertain significance had clinical meaning, 3 participants (30%) correctly stated that they would test other affected family members to see if the variant tracks with the phenotype of interest in the family; the other 70% of participants would have also repeated the test or tested other tissue types, both of which are costly and unnecessary measures. All participants (n=10) were correct in associating increased nuchal translucency on ultrasound with being a soft marker for Down syndrome.

**Table 6. Knowledge Assessment (Interpretation of Genetic Test Results): Frequency of Correct Responses**

<b>Interpretation of Genetic Test Results</b>		
<b>Question</b>	<b>Correct n (%)</b>	<b>95% Confidence Interval</b>
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?	<b>8 (80%)</b>	<b>44-97%</b>
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?	<b>6 (60%)</b>	<b>26-88%</b>
A genetic test report reveals a "variant of unknown significance". What does this result mean for the patient?	<b>8 (80%)</b>	<b>44-97%</b>
Which of the following methods can be used to determine the clinical meaning of a variant of uncertain significance?	<b>3 (30%)</b>	<b>7-65%</b>
If a fetus has an increased nuchal translucency, which of the following karyotype results is the most likely to be found on amniocentesis?	<b>10 (100%)</b>	<b>-</b>

**Note: 10 respondents completed the Interpretation of Genetic Test Results section.**

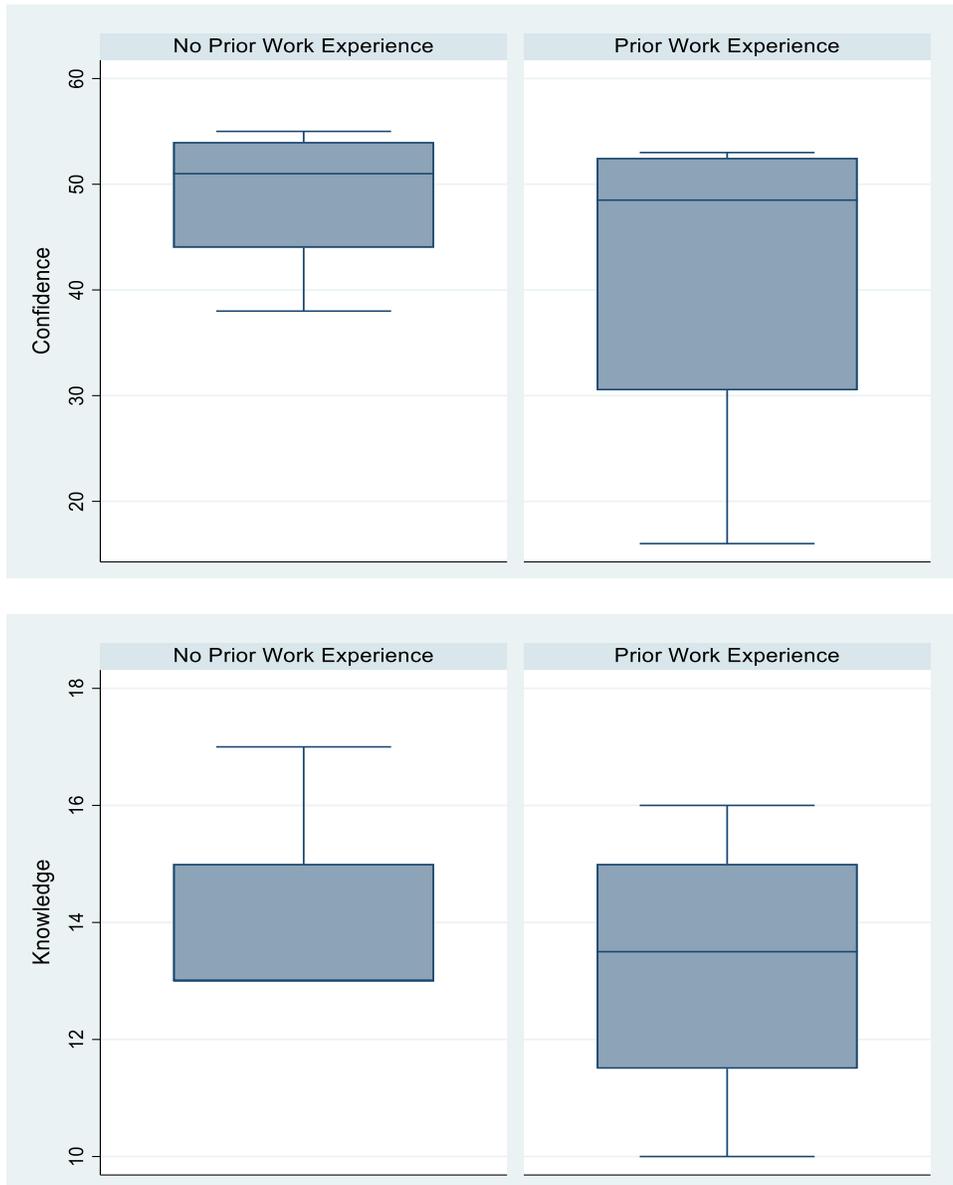
### **3.3.4 UPSOM Human Genetics Course Assessment and Prior Experience in Genetics**

Participants were asked to provide information concerning UPSOM’s Human Genetics course. Seven participants (70%) reported that the course was moderately challenging, while the other 3 participants reported that it was slightly challenging. Eight participants (80%) learned “a moderate amount” to “a lot” from the course and 2 participants only learned “a little”.

The majority of participants (8/10, 80%) reported that they took a genetics course during their undergraduate education. Participants were asked to state if they had any prior work experience in genetics, which was defined as any laboratory position, research, clinical observation, and paid positions relevant to genetics. Four participants reported prior work experience in genetics, which included genetics-based research in molecular genetics, immunology, and infectious disease, as well as multiple undergraduate genetics courses. One participant reported prior work in a clinical setting where genetics was relevant. The other 6 participants reported no prior work experience.

To analyze the knowledge of the participants, a nonparametric t-test was performed to show the differences in self-assessment and knowledge scores between respondents who had prior work experience in genetics and those who did not. There was no statistically significant difference between confidence scores for respondents with prior work experience in genetics and those who did not ( $p = 0.4542$ ). Similarly, there was no statistically significant difference between knowledge scores for respondents with prior work experience in genetics and those who did not ( $p = 0.8201$ ). A box-plot of the distribution of scores in each of the two groups is shown in Figure 2.

**Figure 2. Confidence and Knowledge Scores Segregated by Prior Work Experience**



### 3.4 Discussion

This survey of medical students noted discrepancies between student's overall confidence and knowledge. The average confidence score was 47.93/60 (79.8% confident), while the average score for the Clinical Genetics Knowledge section was 72.1%, or 13.7 questions correct out of 19 total knowledge questions. Per personal communication with the course director of the University of Pittsburgh Human Genetics course, the medical students generally score around the 80<sup>th</sup> percentile on examinations (S Khan 2021, personal communication, 9 April). A 7.9% difference between confidence and knowledge, while not a large discrepancy, suggests that medical students may be somewhat overconfident in their knowledge of genetics concepts.

Overconfidence in genetic knowledge has been observed in physicians, with one study finding that despite confusion surrounding interpretation of genetic tests and implications for medical management, up to 61% of non-genetics healthcare providers had a positive attitude towards their knowledge of genetic testing options for hereditary cancer.<sup>3</sup> In contrast, many physicians have reported feeling ill-prepared to discuss genetic information with their patients, particularly in the context of counseling patients, selecting an appropriate test, and knowing the guidelines for a genetics referral.<sup>1,2</sup>

Most participants were confident in their knowledge of fundamental concepts involving molecular genetics and inheritance, but the Self-Assessment of clinical genetics skills section responses varied. 87% of participants reported feeling confident in their ability to take a family history and 73% indicated that they felt confident enough to assess risk for a genetic condition based on a family history. These results are discrepant with the findings of a study of primary care providers that utilized a standardized patient roleplay involving a case of early-onset breast cancer. Wilkes et al. found that primary care providers infrequently performed key counseling behaviors

related to inherited breast cancer such as taking the family history of cancer, including asking about the age of onset of breast cancer, which diminishes their ability to perform a proper risk assessment and represents limited familiarity with the utility of these skills.<sup>35</sup> Respondents to this survey felt confident taking a family history and performing a risk assessment which is likely influenced by the fact that these students recently completed coursework in genetics, but conversely may represent overconfidence in their abilities.

Only 60% of respondents felt comfortable identifying indications for referral to a genetics specialist and only 47% expressed confidence in their familiarity with clinical genetics resources. These findings are consistent with previous studies of medical students, which found that only half were familiar with the Online Mendelian Inheritance in Man (OMIM) database, a commonly used tool for any genetics specialist.<sup>89</sup> The Association of Professors of Human and Medical Genetics (APHMG) core curriculum currently recommends that all medical students should be able to obtain reputable current information about genetics online using websites such as OMIM, National Human Genome Research Institute (NIH/NHGRI), and MedlinePlus (formerly Genetics Home Reference).<sup>79</sup> These findings are also consistent with the notion that physicians often do not refer patients for genetic counseling due to uncertainty of when it is appropriate to refer and that this uncertainty is rooted in physicians' limited clinical genetics knowledge in conjunction with a lack of awareness of clinical genetics resources, including clinical guidelines, and tools to help make appropriate decisions regarding their patient's medical management. For example, the genetic counseling referral rates for women with epithelial ovarian cancer vary widely between medical centers and referral rates are especially low in the case of rare cancers, such as male breast cancer.<sup>55,59-61</sup> While up to 74% of non-genetics health professionals are familiar with web-based

cancer risk assessment models, additional training on cancer risk assessment and the utility of these models is desired.<sup>53,82</sup>

Participants correctly answered questions about characteristics of autosomal recessive, multifactorial, and mitochondrial inheritance, but may have encountered difficulty in calculating carrier risks, with 33% of respondents incorrectly stating that a healthy child whose sibling has an autosomal recessive genetic condition would have a 50% chance of being a carrier, rather than 66% (66.67% correctly answered; 95% CI 34-90%). Additionally, there may have been confusion surrounding characteristics of X-linked recessive inheritance, with 7 (58.3%; 95% CI 28-85%) participants correctly indicating that the children of affected males are typically not at risk for being affected with the condition; 4 (33.33%) respondents incorrectly reported that females are usually more severely affected than males and 1 (8.33%) respondent thought that males and females would be affected equally.

Studies have suggested that physicians demonstrate knowledge of autosomal dominant inheritance through familiarity with the *BRCA* genes.<sup>5</sup> This familiarity in theory would aid a physician in assessing risk for other conditions following autosomal dominant inheritance in the clinic. However, these results show that students may not recognize more nuanced examples of autosomal dominant inheritance. For example, 41.7% of respondents failed to recognize that chromosomal deletions follow autosomal dominant inheritance, therefore the recurrence risk of a chromosomal deletion or duplication, with one chromosome altered and the other intact, would be 50%. Information about the clinical characteristics of the specific deletion or duplication was irrelevant in this context. Similarly, 60% of participants correctly stated that the parents of a child with a confirmed de novo 22q11.2 deletion would have a slightly increased risk to have another child with DiGeorge syndrome due to the possibility of germline mosaicism, while 40% of

participants would have told the parents that they were not at increased risk. While respondents were confident in their understanding of inheritance (81% answered “Strongly Agree” in rating their knowledge of inheritance), based on the responses to knowledge scores it appears there remains a need for improved education regarding risk assessment, chromosomal conditions, and X-linked inheritance.

Respondents were given a scenario where a female patient with breast cancer reports that she has undergone genetic testing and was found to have “the gene for breast cancer” but is implied to not have a copy of the genetic test report. Participants were expected to not rely solely on the patient’s statement, however, all participants (n=9) selected that it would be reasonable to assume that the patient has a pathogenic variant in a gene associated with an increased risk for breast cancer, even without a copy of the test report. It is worth considering that medical students may be overestimating a patient’s genetic literacy, however, this may also reflect poor wording of the survey question.

Respondents also encountered difficulty with identifying the best individual in a family to test for a familial variant. In a scenario where an unaffected 30-year-old woman comes to the genetics clinic for *BRCA1* and *BRCA2* testing, only 4 respondents (36.36%) correctly selected the patient’s mother, who had breast cancer diagnosed at age 40, as the best person to test; the other respondents (63.64%) stated that the patient should be tested first. This confusion over genetic testing strategy has been identified in research with physicians. One study found that in families with known pathogenic variants, where single-site testing of *BRCA1/2* would be appropriate, fewer than 35% of physicians correctly ordered single-site testing and instead ordered comprehensive *BRCA* analysis or panel testing, resulting in excess medical costs to the patient.<sup>58</sup> Reassuringly, a majority of participants in this study (90.91%) indicated that counseling for a familial *BRCA1*

pathogenic variant would include a discussion about lifestyle modification, surgical recommendations, and psychosocial concerns, as well as potential referral to a high-risk breast cancer screening program, suggesting that medical students recognize that identification of a hereditary cancer syndrome involves comprehensive counseling and management.

The majority of participants (8 participants; 80%) correctly stated that medical management decisions should typically not be made based on a variant of unknown significance, a response consistent with the joint recommendations of the American College of Medical Genetics and Genomics (ACMG) and the Association for Molecular Pathology (AMP).<sup>64</sup> In contrast, studies reveal confusion surrounding medical management decisions and variants of uncertain significance by physicians.<sup>2,5,41,58</sup> One study found that when presented with a case of a *BRCA1* variant of uncertain significance, 82% of physicians recommended testing of at-risk relatives and 13% recommended oophorectomy for the affected patient based on the VUS, with no statistically significant difference between physicians with and without prior *BRCA1/2* testing experience.<sup>57</sup> In some cases however, particularly in the pediatric setting, laboratories may offer to perform family studies to assist the lab in future classification of the variant. When asked about approaches to determining the clinical meaning of a variant of uncertain significance, 3 participants (30%) correctly stated that they would test other affected family members to see if the variant tracks with the phenotype of interest in the family; the other 70% of participants would have also repeated the test or tested other tissue types, both of which are costly and unnecessary measures that would still yield inconclusive results.

Several survey questions addressed pediatric genetic testing. While ACMG recommends microarray as the first-line genetic test for any child with dysmorphic features or developmental delay,<sup>95</sup> only 4 participants (36.36%) correctly stated that microarray should be the first genetic

test to order for a child with dysmorphic features, developmental delay, and microcephaly. Instead, respondents favored Chromosome Breakage studies (DEB analysis) or exome sequencing. While it may one day be feasible to implement exome as the first genetic test for children with this phenotype, at this time, exome is often cost-prohibitive and not the recommended first-line genetic test. The respondents' answers are consistent with studies indicating that there is confusion surrounding testing strategy among non-genetics healthcare providers. One survey from 2018 identified that 68% of pediatricians were not familiar with any genetic testing guidelines for a patient with global developmental delay (GDD), signifying that genetic testing guidelines are not well disseminated, particularly if they are issued by other specialties.<sup>41</sup> Of those 31.9%, most were familiar with the American Academy of Pediatrics (AAP) recommendations. The AAP recommendations were the most well-known: 27% were familiar with AAP recommendations whereas only 2.8% were familiar with the American College of Medical Genetics and Genomics (ACMG) guideline on cytogenetic tests. Similarly, while participants recognized that it would be appropriate to order a karyotype if there is suspicion for Down syndrome, 5 participants (45.45%) felt that it would not be necessary to order a karyotype when there was concern for a translocation due to a history of multiple miscarriages and 1 participant (9.09%) felt that it would not be necessary to order a karyotype if there was concern for a sex chromosome disorder. These findings suggest that there is possible confusion surrounding the nature of chromosomal conditions and the type of information gained from a karyotype.

The majority of respondents (81.82%) would use counseling strategies to individually explore a couple's thoughts about the outcomes of their pregnancy following a prenatal diagnosis of Klinefelter syndrome. Two participants (18.18%) felt it would be necessary to first provide detailed information about the features of Klinefelter syndrome. While information about the

genetic condition is important, a provider should first assess the parents' emotional state and avoid overwhelming them by going into too much medical or technical detail. All participants were correct in recognizing increased nuchal translucency on ultrasound as being a soft marker for Down syndrome. The respondents' confidence and generally high knowledge scores on topics concerning prenatal genetics may reflect good coverage of these topics during the Human Genetics course, as well as possible utilization of knowledge from other courses.

Among the 10 respondents to complete this survey, 8 reported having taken a genetic course during their undergraduate education. Four respondents, one of who did not take a genetics course during their undergraduate education, reported prior work experience in genetics, which included genetics-related laboratory research and genetics related work in a clinical setting. There was no statistically significant difference between confidence scores for respondents with prior work experience in genetics and those who did not. Similarly, there was no statistically significant difference between knowledge scores for respondents with prior work experience in genetics and those who did not. These findings suggest that all medical students, even those who report prior genetics work experience in a research setting, would benefit from learning the breadth of both molecular and clinical genetics in medical school curriculum. Additionally, the small sample size may have negatively affected the chance of detecting statistically significant results (or relationships).

In 2005, most medical schools devoted fewer than 40 contact hours to genetic education.<sup>81</sup> A more recent study from 2013-2014 found that the mean number of total genetics contact hours for medical students is 36 hours, with 75% of medical school genetics course directors reporting that genetics education is integrated into other courses such as biochemistry, metabolism, or cellular biology.<sup>80</sup> The University of Pittsburgh School of Medicine Human Genetics course

provides students with 44 contact hours of genetics education, which includes both lectures and interactive patient-led educational sessions. Respondents were given the opportunity to write in suggestions to improve UPSOM's Human Genetics course and topics they would like to focus on. Suggestions included more discussion of recommended changes to medical management based on genetic test results and additional patient-led educational sessions. Respondents reported that they are most interested in cancer genetics, prenatal genetics, and personalized medicine, which suggests that they view genetics as being essential to future practice as a physician in their chosen specialty, rather than a tangential field for specialists.

### **3.4.1 Study Limitations**

This study had several limitations, with the most important being the low response rate. The low number of respondents only allowed for a limited analysis. No statistically significant findings were identified and the small sample may have adversely impacted the chance to identify statistically significant relationships. Therefore, this survey may not reflect the knowledge and opinions of all University of Pittsburgh medical students. The survey was intentionally distributed more than three months after the Human Genetics course concluded to observe retention of knowledge, however the timing of the survey may have conflicted with the medical student's busy schedule and resulted in the low participation rate. Additionally, participation may have been compromised due to the challenges medical students are currently facing during COVID-19 pandemic.

Selection bias may be present within this study design. Given the lack of compensation for participation in the survey, the language in the survey recruitment may have inadvertently attracted two distinct groups of participants: those with a strong interest in genetics and/or those with

previous genetics experience, and those who were frustrated with their experience in the Human Genetics course. Individuals are more likely to take surveys pertaining to topics that they are interested and proficient in, which may result in higher estimates of confidence and knowledge.<sup>96</sup> In theory, individuals who may not have performed well in the Human Genetics course may have chosen to participate to demonstrate their lack of confidence or knowledge; this may explain the one high leverage datapoint in the dataset.

Survey questions were designed to be relevant to the Human Genetics course material and timeless given the ever-changing nature of the field of clinical genetics. In hindsight, a few of the knowledge questions could have been constructed in a different way to better satisfy these criteria. For example, one question referenced a 5-year-old girl who presents with dysmorphic features. According to current practice guidelines, the correct answer regarding genetic testing for this clinical scenario is microarray. However, as the cost and availability of whole exome sequencing (WES) improves, WES may one day replace microarray as the first-line test for this particular indication. To keep the survey questions timeless, it may be worth reexamining this question. Another question asked about an adult-onset hereditary cancer syndrome. This syndrome was discussed in the student's Human Genetics course, but only briefly. While the intent of the question was for students to recognize that genetic testing for adult-onset conditions in children is not recommended, the Human Genetics course manual did not explicitly mention that this condition was adult-onset, which may have led to several participants thinking that it would be appropriate to test a child in this scenario. In another question, respondents were given a scenario where a female patient with breast cancer reports that she has undergone genetic testing and was found to have "the gene for breast cancer" but is implied to not have a copy of the genetic test report. Participants were expected to not rely solely on the patient's statement, however, all participants

(n=9) selected that it would be reasonable to assume that the patient has a pathogenic variant in a gene associated with an increased risk for breast cancer, even without a copy of the test report. In this scenario, a copy of the genetic test report is necessary to confirm that the patient has a pathogenic variant, not a variant of uncertain significance, and to determine which of the many genes associated with breast cancer the patient is referring to prior to coordinating management and testing of relatives. It is worth considering that medical students may be overestimating a patient's genetic literacy, however, this may reflect poor wording of the survey question. Since the survey did not contain any questions about direct-to-consumer (DTC) genetic testing, this particular question could be replaced by a question that addresses a positive DTC test with the goal of gauging participant's knowledge about the clinical utility of DTC testing.

There was also significant dropout among participants after the Self-Assessment. Those who dropped out upon seeing the Knowledge section may have faced greater time constraints than those able to complete the entire survey. Of course, the Knowledge section requires considerable problem-solving skills and information recall, which given medical student's busy schedules, may have required more time than students were willing to dedicate to complete the survey. Our hope is that this survey can be utilized in future research. To combat the issue of low response rate, we would advise future researchers to compensate students in some manner for completing the survey.

### **3.4.2 Future Directions**

This survey was distributed three months following the conclusion of the Fall 2020 Human Genetics course with the goal of getting preliminary data on long-term clinical genetics content retention. Now that the survey has been both piloted and distributed once, certain questions can be modified to capture knowledge more accurately for the purpose of future research. We hope to

continue this study through distributions to future cohorts of medical students as part of a longitudinal study. One potential study design would be to incorporate the survey into the students' Human Genetics course. The survey could be distributed twice to the same cohort to obtain both a pre-course response and immediate post-course response. This cohort could be followed throughout their training while tracking their personal experiences in clinical genetics. At the University of Pittsburgh, certain medical students will get additional genetics coursework through elective coursework and clinical experiences during rotations in their third and fourth years. This study design will ideally show an evolution of a medical student's understanding of clinical genetics and genetic testing as they complete coursework, however it is possible that gaps in the trainee's knowledge will still be observed. It could also contribute to the analysis of curricular changes over the course of the next few years that is taking place at the University of Pittsburgh School of Medicine.

### **3.5 Conclusion**

The confidence and clinical genetics knowledges of medical students was assessed using a questionnaire which asked them to rate their confidence in their knowledge of clinical genetics concepts and answer knowledge questions concerning clinical genetics that the students may encounter in future practice as physicians. Overall, the students were confident in their perceived knowledge of clinical genetics concepts. However, the knowledge assessment revealed that students often incorrectly answered knowledge questions pertaining to clinical genetics concepts which received higher confidence scores, namely inheritance and risk assessment. This suggests that students may be somewhat overconfident in their knowledge in certain areas. Students

reported lower confidence scores and had lower knowledge scores for clinical genetics resources, testing strategy, and test interpretation. These results signify a need for clinical genetics education that is pertinent to advancements in clinical genetics. While the sample size and ultimately the response rate in this study was small, this study adds to the growing body of literature concerning the gaps in genetic literacy of healthcare providers. In order to address these gaps, a clinical genetics curriculum for medical students should build a solid foundation in basic genetic concepts and promote adaptability to keep pace with the ever-changing nature of the field through awareness of clinical genetics resources and practice guidelines.<sup>89</sup> Dedicating more contact hours to clinical genetics would be beneficial, but in the context of medical student's dense curriculum, this is not always feasible. Rather, it would be worthwhile to incorporate experiences that expose students to the integration of genetics into clinical practice. Suggestions for such experiences include more standardized patient roleplays, patient-led educational sessions, and genetics case presentations.<sup>81</sup> It is imperative that non-genetics healthcare providers possess a strong foundation in basic genetics clinical concepts, as well as maintain standing relationships with genetics specialists, in order to provide the best care for patients with a suspected or an established genetic condition.

#### **4.0 PUBLIC HEALTH AND GENETIC COUNSELING SIGNIFICANCE**

This study addresses the genetics knowledge of medical students, which forms the basis of their ability to communicate effectively to inform and educate future patients about genetics as it relates to their personal health and their health of the family members. In considering the three core functions of public health, this study focuses on assurance, namely by identifying barriers to building and supporting a skilled public health workforce and assuring an effective healthcare system that enables equitable access for all patients. To build a skilled public health workforce, medical students must possess basic knowledge of clinical genetics concepts and resources to make appropriate decisions regarding genetic information in the clinical setting as future physicians. The current iteration of the Association of Professors of Human and Medical Genetics (APHMG) core curriculum, used by most medical school human genetics course directors, emphasizes that students have sufficient knowledge of basic genetic principles including inheritance, genome organization, and genetic variation, as well as the ability to apply those skills by demonstrating the ability to gather family history information, construct and interpret a family pedigree, assess risk for a genetic disorder, and determine when a complete genetics evaluation is appropriate.<sup>79</sup> This study determined that medical students' basic clinical genetics knowledge is incomplete, with a possible overconfidence in that knowledge, which suggests that the amount of time devoted to genetics education in medical school may be insufficient. Studies have shown that physicians with limited formal genetics education are at increased risk of accidentally ordering the wrong genetic test, failing to refer a patient in need of genetic services, or unintentionally providing misinformation during results disclosure.<sup>3-6</sup> These scenarios jeopardize the quality of care for

patients, particularly those with limited health and genetic literacy, which does not equate to equitable access to healthcare for all members of the general population.<sup>13</sup>

Genetic counselors can play a pivotal role in genetics education for medical students and physicians. Genetic counselors receive specialized training to communicate complex genetic information to individuals of all backgrounds, from patients with low genetic literacy to highly trained physicians, and they are utilizing their skills in new roles, one of which is the education of physicians and other non-genetics healthcare providers. Many healthcare systems have already instituted utilization management programs to implement review of genetic test orders by a genetic counselor prior to request for insurance authorization. These programs mitigate unnecessary genetic testing expenditures, foster relationships between physicians and genetic specialists, and serve as a feedback loop for physicians in selecting the appropriate genetic tests.<sup>38</sup> However, physicians should also be receiving more comprehensive genetics education during the course of their training, which can be supplemented by continuing education coursework and clinical experience in the clinic. Featuring genetics specialists more prominently in medical school Human Genetics courses, or even having genetics clinicians teach genetics courses, could promote the field and lead to a greater recognition of the ways in which genomics is being integrated into clinical practice. Genetic counselors are well suited to lead continuing education opportunities to help practicing healthcare providers develop their genetics knowledge. As the profession continues to expand, genetic counselors should be encouraged to take on roles in the education of non-genetics healthcare professionals to shift the perception of genetics as a field of rare disease, to one that is both pertinent and accessible to many patients.

## Appendix A Supplemental Figures

**Table 7. Self-Assessment: Overall Confidence Ratings**

Participant ID	Confidence Rating													Total Confidence Score
A	4	5	5	4	5	4	5	4	4	5	5	5	55	
B	5	5	5	2	4	4	5	5	4	5	4	5	53	
C	5	5	4	4	2	2	4	1	3	4	2	2	38	
D	1	1	1	2	1	2	1	3	1	1	1	1	16	
E	5	5	5	4	4	5	4	3	5	4	4	5	53	
F	5	5	5	4	4	4	4	3	4	4	3	4	49	
G	5	4	4	4	4	3	3	2	4	4	3	5	45	
H	5	5	5	4	2	3	5	1	3	3	4	4	44	
I	5	5	4	4	5	3	4	4	4	5	5	4	52	
J	5	5	4	5	4	5	5	4	4	5	4	4	54	
K	5	5	5	4	5	5	5	2	4	5	5	5	55	
L	5	5	5	4	4	3	3	4	3	5	4	5	50	
M	5	5	5	4	4	4	5	5	4	4	4	4	53	
N	5	5	5	4	2	4	5	2	4	4	3	4	47	
O	5	5	4	4	5	4	5	4	4	5	5	5	55	
Mean Score	4.667	4.667	4.4	3.8	3.667	3.667	4.2	3.133	3.667	4.2	3.733	4.133	47.93	

## Appendix B IRB Approval Letter



### EXEMPT DETERMINATION

Date:	January 11, 2021
IRB:	STUDY20070423
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:	1/11/2021
Exempt Category:	(2)(ii) Tests, surveys, interviews, or observation (low risk)

Determinations:	<ul style="list-style-type: none"><li>• Students / Employees</li></ul>
Approved Documents:	<ul style="list-style-type: none"><li>• Genetic_Literacy_in_Medical_Students_Survey.docx, Category: Data Collection;</li><li>• 1st survey run Script_Version_0.01.docx, Category: Recruitment Materials;</li><li>• 2nd survey pre-course run Script_Version_0.01.docx, Category: Recruitment Materials;</li><li>• HRP-721 - WORKSHEET - Exemption_Tests Surveys Public Behavior_Version_0.01.docx, Category: IRB Protocol</li></ul>

If you have any questions, please contact the University of Pittsburgh IRB Coordinator, [Chelsea Michelessi](#).

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 Hello, Ravelia Raker ▾

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[IRB](#) > Genetic literacy and the acquisition of clinical genetics knowledge in medical students

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**Activity Details (Submitted Ancillary Review)** Submits an ancillary review.

---

**Author:** Bill Yates (U of Pgh | School of Medicine | Otolaryngology)

---

**Logged For (IRB Submission):** Genetic literacy and the acquisition of clinical genetics knowledge in medical students

---

**Activity Date:** 1/11/2021 7:00 AM

**Form:**

**1. \* Select the review you are submitting:**

Organization	Person Review Type	Required
U of Pgh   School of Medicine   Office of the Dean   Medical Education	Medical School Review	yes

**2. \* Do you accept the proposed study?**  
 Yes  No

**3. Comments:**  
The study has been modified in accordance with the requests of the ROMS committee

**4. Supporting documents:**  
Name  
There are no items to display

**Documents:**

[<< Return to Workspace](#)

## **Appendix D Recruitment Email**

Subject Line: Genetic Literacy Survey for Medical Students

Hello,

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

As a University of Pittsburgh medical student who took Human Genetics during the Fall 2020 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, which will deepen our understanding of the current gaps and limitations of genetics education in medical school.

The survey should take about 20-30 minutes to complete. There are minimal risks associated with participation in this survey, including but not limited to the infrequent risk of a breach of confidentiality. There are no direct benefits to you in return for your participation. You will not receive any form of compensation as part of this study. 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: [RAR175@pitt.edu](mailto:RAR175@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\\_7VYHFYBds92BcTr](https://pitt.co1.qualtrics.com/jfe/form/SV_7VYHFYBds92BcTr) will direct you to the survey.

## Appendix E Survey

# Genetic Literacy in Medical Students

---

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

Q1 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)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I understand the foundational concepts of genetic inheritance. (2)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I understand how the fundamentals of population genetics relate to modern patient populations. (3)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I can gather a detailed family history for a genetic indication. (4)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

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)

Start of Block: Inheritance

Q2 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)



Q3 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)
-



Q4 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?

1/150 (1)

1/400 (2)

1/75 (3)

1/200 (4)



Q5 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)
- 

Q6 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)
-

Q7 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)
- 

Q8 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 Scenarios

Q9 A female patient with breast cancer reports that she has undergone genetic testing and was found to have the "gene for breast cancer". Which of the following is safe to assume based solely on the patient's statement?

- That she has received appropriate genetic counseling through a genetic counselor or physician. (1)
  - That she has a pathogenic variant in a gene associated with an increased risk for breast cancer. (2)
  - That the genetic testing ordered for this patient was sufficient to cover all known causes of hereditary breast cancer. (3)
  - None of the above (4)
-

Q10 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)
- 

Q11 A 30-year-old woman with 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)
-

Q12 A woman with hereditary nonpolyposis colorectal cancer, otherwise known as Lynch syndrome, 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)
-

Q13 A 5 year old girl presents to your clinic with dysmorphic features, developmental delay, microcephaly, prominent jaw, and a history of seizures. What is the most appropriate genetic test to order for this child?

- Whole exome sequencing (1)
  - Microarray (2)
  - FISH testing for 22q (3)
  - Methylation studies (4)
- 

Q14 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)
-

Q15 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)
- 

Q16

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)

Start of Block: Interpretation of Genetic Test Results

Q17 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)
- 

Q18 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)
- 

Q19 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)
-

Q20 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)
- 

Q21

If a fetus has an increased nuchal translucency, 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

Q22 The following questions will ask about your experience in Dr. Khan's Human Genetics course.

---

Q23 How challenging was this course?

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

Q24 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)
- 

Q25 How could this course be improved?

---

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---

---

Q26 What topics in genetics interest you the most?

---

Q27 Did you take a genetics course during your undergraduate education?

Yes (1)

No (2)

Not sure (3)

---

Q28 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... = Yes*

*Or Do you have any prior work experience with genetics (laboratory positions, research, clinical obs... = Not sure*

Q29 Please explain your prior work experience with genetics.

---

---

Q30 What is your gender?

Male (1)

Female (2)

Non-binary (3)

Transgender (4)

Other: (5) \_\_\_\_\_

End of Block: Demographics

---

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