

Exploring Experts' Attitudes, Preferences, and Perceived Challenges in the Implementation of Multi-Cancer Early Detection (MCED) Testing

by

Mehr-un-Nisa Usman

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Exploring Experts' Attitudes, Preferences, and Perceived Challenges in the Implementation of Multi-Cancer Early Detection (MCED) Testing

Koç University

Graduate School of Health Sciences

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Mehr-un-Nisa Usman

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Committee Members:

Assist. Prof. Özge Karanfil (Main Advisor)

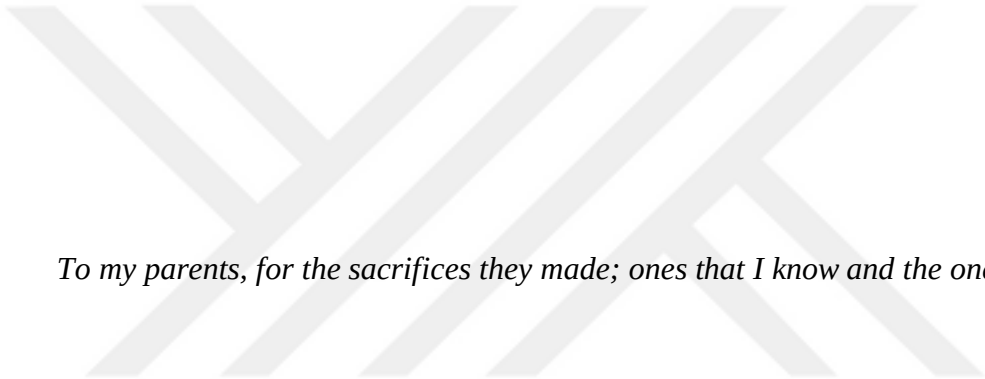
Prof. Zeynep Akşin Karaesmen

Prof. Sibel Kıran

Prof. Sibel Sakarya

Assist. Prof. Mehlika Toy

Date: January 21, 2025



To my parents, for the sacrifices they made; ones that I know and the ones unknown

ABSTRACT

Exploring Experts' Attitudes, Preferences, and Perceived Challenges in the Implementation of Multi-Cancer Early Detection (MCED) Testing

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Multi-Cancer Early Detection (MCED) testing is an emerging medical technology with the potential to revolutionize screening for early detection of cancer. This study uses a mixed-methods, survey-based approach to examine expert stakeholders' attitudes, including those of physicians, academics, and other healthcare professionals, towards its use in clinical practice, as well as to understand how potential challenges can be addressed before its implementation. Using validated scales from literature, we first developed an online survey instrument to explore these aspects on Qualtrics and collected responses over a course of four weeks. We then analysed survey results to investigate how ambiguity aversion, cancer risk perception, and physicians' perceived competence influences experts' attitudes, and test relevant hypotheses. In this context, higher/lower attitude scores reflect more optimistic/pessimistic views toward MCED testing, and its various aspects of its real-life implementation.

Survey results reveal that ambiguity aversion had a moderate negative correlation with attitudes, suggesting that greater aversion to ambiguity led to less optimistic views on future implementation of MCED testing. While experts' risk perception of cancer showed no significant association with attitudes, physicians' perceived competence was positively correlated, indicating that when physicians felt more confident in their ability to educate, guide, and explain MCED test results to patients, they held more optimistic views about its future implementation. Regression analyses confirm physicians' perceived competence and ambiguity aversion as significant predictors of physician attitudes. Qualitative insights provide actionable insights to addressing major implementation barriers such as risk of exploitation, inequities, lack of diagnostic guidelines etc. Overall, our findings underscore the importance of addressing psychological, intangible factors like ambiguity aversion, systemic barriers, and enhancing professional competencies to support the successful adoption of MCED testing for early cancer detection.

ÖZETÇE

Çoklu Kanser Erken Teşhis (MCED) Testinin Uygulanmasında Uzmanların Tutumlarını, Tercihlerini ve Algılanan Zorluklarını Keşfetmek

Mehr-un-Nisa Usman

Program Adı, Yüksek Lisans Küresel Sağlık

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Çoklu Kanser Erken Tanı (Multi Cancer Early Detection, MCED) testi, kanserin erken tespiti ve taranmasında devrim yaratma potansiyeline sahip yeni bir teknolojidir. Bu çalışmada, paydaşların -özellikle hekimler, akademisyenler ve sağlık profesyonelleri- MCED testinin gerçek hayatta uygulanmasına yönelik düşünce ve tutumlarını incelemek ve ayrıca testi uygulama öncesinde ele alınması gereken temel zorlukları anlamak amacıyla karma yöntemler ve anket tabanlı bir yaklaşım kullanılmıştır. Literatürdeki doğrulanmış ölçeklerden yararlanarak, bu unsurları keşfetmek amacıyla öncelikle Qualtrics üzerinde bir çevrimiçi anket aracı geliştirilmiş ve dört hafta boyunca yanıtlar toplanmıştır. Daha sonra, belirsizlikten kaçınma, kanser risk algısı ve hekimlerin algılanan yetkinliklerinin uzmanların tutumlarını nasıl etkilediğini incelemek ve ilgili hipotezleri test etmek için anket sonuçlarını analiz edilmiştir. Bu bağlamda, yüksek/düşük tutum puanları, MCED testine ve bu testin gerçek hayatta uygulanmasının çeşitli yönlerine karşı daha iyimser/kötümser görüşleri yansıtmaktadır.

Anket sonuçları, belirsizlikten kaçınmanın tutumlarla orta düzeyde negatif bir korelasyona sahip olduğunu ortaya koymaktadır; bu da belirsizlikten daha fazla kaçınmanın, MCED testinin gelecekte uygulanmasına yönelik daha iyimser görüşlere yol açtığını göstermektedir. Uzmanların kanser risk algısı ile tutumları arasında anlamlı bir ilişki bulunmazken, hekimlerin algılanan yeterlilikleri pozitif bir korelasyon göstermesi hekimlerin MCED test sonuçlarını hastalara öğretme, rehberlik etme ve açıklama konusundaki yeteneklerine daha fazla güvendiklerinde, testin gelecekteki uygulanmasına yönelik daha iyimser görüşlere sahip olduklarını göstermektedir. Regresyon analizleri, hekimlerin algılanan yeterlilikleri ve belirsizlikten kaçınmanın, hekim tutumlarının önemli belirleyicileri olduğunu doğrulamaktadır. Bulgular, belirsizlikten kaçınma gibi psikolojik ve soyut faktörlerin ele alınmasının yanı sıra mesleki yeterliliklerin artırılmasının, kanserin erken teşhisi için MCED testinin başarılı bir şekilde benimsenmesini desteklemek açısından önemini vurgulamaktadır.

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ABBREVIATIONS

AA	Ambiguity Aversion
ASCO	American Society of Clinical Oncology
CRP	Cancer Risk Perception
ESHPM	Erasmus School of Health Policy & Management
FDA	Food and Drug Administration
FP	False Positive
FPR	False Positive Rate
GLOBOCAN	Global Cancer Observatory
HINTS	Health Information National Trends Survey
HTA	Health Technology Assessment
IMTA	Institute for Medical Technology Assessment
KUTTAM	Koç University Research Center for Translational Medicine
LDCT	Low-Dose Computed Tomography
LMIC	Low- and Middle-Income Countries
MCED	Multi-Cancer Early Detection
NUML	National University of Medical Sciences
PPC	Physicians' Perceived Competencies
TP	True Positive
TP:FP	True Positive/FALSE Positive ratio
WHO	World Health Organization

Chapter 1:

INTRODUCTION

1.1 Overview

Cancer is one of the leading causes of death around the world, posing a significant challenge to global health. The importance of early detection in improving survival rates and treatment efficacy is well-documented. Traditional cancer screening methods, such as mammograms for breast cancer, colonoscopies for colorectal cancer, and Pap smears for cervical cancer, have been instrumental in identifying cancers at an early, more treatable stage. However, these methods are typically limited to single cancer types and often require invasive procedures, which can be a barrier to widespread screening adherence.

In recent years, advancements in genomics and molecular biology have led to the development of Multi-Cancer Early Detection (MCED) tests. These innovative assays leverage DNA methylation patterns and other biomarkers detectable in blood samples to identify multiple types of cancer simultaneously. The potential of MCED tests to revolutionize cancer screening lies in their ability to provide a non-invasive, comprehensive approach to early detection.

Multi-Cancer Early Detection (MCED) testing represents a groundbreaking advancement in the early detection of cancer, with the potential to significantly reduce cancer-related mortality worldwide. However, as an emerging technology that lacks FDA approval and standardized guidelines, its adoption and implementation into health systems remains uncertain. This study aims to explore the perceptions and attitudes of key expert experts; 1. Academic Researchers, 2. Physicians, and 3. Other Healthcare Professionals, toward the implementation of MCED testing, while identifying the factors that shape these perspectives.

A central focus of the study is ambiguity aversion, which can arise from conflicting expert opinions and the absence of established protocols, and its potential impact on physicians' attitudes toward MCED testing. Additionally, we investigate the role of physicians' perceived competence in handling MCED-related scenarios, examining how their confidence in managing such cases influences their attitudes toward MCED

testing. The study also considers cancer risk perception, aiming to understand whether experts' beliefs about cancer causes, prevention, and control influence their optimism regarding the future of MCED testing.

In addition to quantitative analyses, this study includes a qualitative component that explores the key challenges experts identify in the widespread implementation of MCED testing. The study also delves into potential strategies experts propose for addressing these barriers and ensuring the successful adoption of MCED testing.

This research is critical for providing a nuanced understanding of the psychological, professional, and practical factors influencing stakeholder attitudes toward MCED testing. The findings provide critical insights that can inform targeted strategies for physician education, the development of policy frameworks, and the establishment of evidence-based guidelines, all of which are crucial for overcoming the barriers to successful MCED testing implementation in clinical practice.

1.2 Significance of the Study

The significance of this study lies in its ability to address critical knowledge gaps regarding the implementation of Multi-Cancer Early Detection (MCED) testing, a technology with transformative potential for early cancer detection. As MCED testing is still in its early stages, lacking regulatory approval and standardized guidelines, understanding experts' perspectives is essential to ensure its successful integration into healthcare systems. This study goes beyond theoretical discussions by examining real-world attitudes and perceptions of key experts, particularly physicians, who will play a pivotal role in its adoption and use.

By exploring the relationships between ambiguity aversion, cancer risk perception, and perceived physician competencies, this research provides a nuanced understanding of the psychological and professional factors influencing attitudes toward MCED testing. Such insights are critical because attitudes can shape clinical decision-making, patient communication, and overall acceptance of new medical technologies. Furthermore, the inclusion of qualitative data adds depth to the findings, shedding light on perceived challenges such as ethical considerations, health equity, and the need for robust diagnostic guidelines.

Ultimately, this study has the potential to develop strategies that address stakeholder concerns and optimize the implementation of MCED testing, as well as inform targeted strategies for physician education. By doing so, it contributes to ensuring that this innovative technology fulfills its promise of reducing cancer mortality while addressing ethical and practical considerations.

1.3 Research Questions and Objectives

This study is guided by the following research questions:

1. What are the attitudes of experts towards the implementation of MCED testing?
2. How does ambiguity aversion influence experts' attitudes towards MCED testing?
3. How are cancer risk perception and physicians' perceived competence associated with attitudes towards MCED testing?

The primary objectives of this study are:

- To examine experts' attitudes towards the future implementation of MCED testing across key subdomains, including medical benefit or harm, impact on patient experience, health disparities and access, progress toward implementation, personal impact, and overall evaluation.
- To analyze the relationship between ambiguity aversion, cancer risk perception, and perceived physician competence with experts' attitudes.
- To determine whether ambiguity aversion influences attitudes toward MCED testing.
- To assess experts' preferences regarding the implementation of MCED testing, including considerations such as target populations, healthcare settings, and the roles of insurance providers and government in supporting these tests.
- To gather insights from experts on the perceived challenges in adopting MCED testing and potential strategies to address these barriers.

1.4 Hypotheses

Based on our literature review and preliminary research, we developed three main hypotheses. The first hypothesis is regarding the relationship between ambiguity aversion and attitudes of experts. The second hypothesis is regarding the association of cancer risk perception and attitudes of experts. The third hypothesis is regarding the association between physicians' perceived competencies and attitudes of experts.

The main outcome variable is attitudes of experts. The main independent variables are ambiguity aversion, cancer risk perception, and physicians' perceived competence. All variables were measured using validated scales from medical literature.

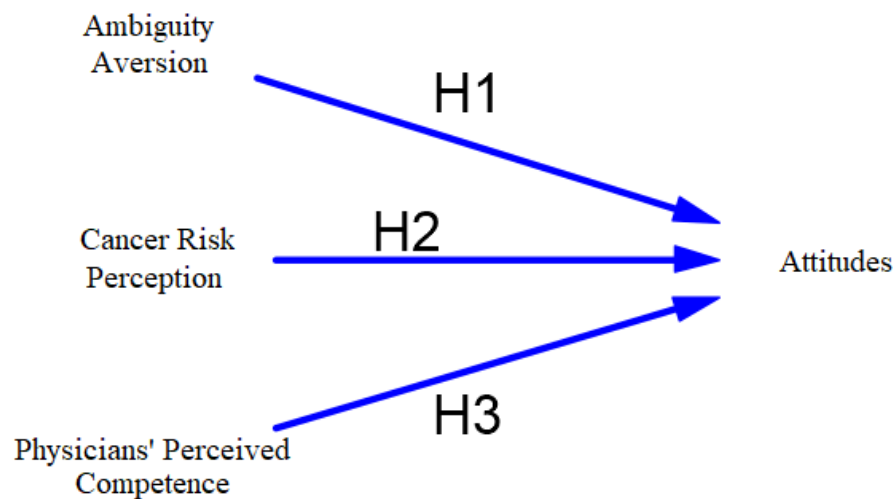


Figure 1-1: Hypotheses

1.4.1 Definitions

The main independent and outcome variables are defined in the table below.

Table 1-1: Definition of Key Variables

Variables	Variable Type	Definition
Attitudes	Main outcome	Attitudes are broadly defined in the literature as evaluative judgments (positive, negative, or neutral) toward an object, concept, or practice. In medical and health research, attitudes refer to individuals' beliefs, feelings, and predispositions toward healthcare

		interventions, technologies, or policies (Ajzen, 1991; Fishbein & Ajzen, 1975; <i>Health Behavior</i>, 2015.). In our research, attitudes refer to participants' overall evaluations and perspectives on the future implementation of Multi-Cancer Early Detection (MCED) testing. This construct encompasses beliefs, expectations, and concerns across six key domains: medical benefits or harms, impact on patient experience, health disparities and access, progress toward implementation, personal impact, and overall evaluation (Horrow et al., 2021). Importantly, in our research, higher scores indicate more favorable attitudes toward MCED testing, while lower scores reflect less optimistic attitudes.
Ambiguity Aversion	Independent	Ambiguity Aversion refers to an individual's tendency to feel discomfort or uncertainty when faced with conflicting or unclear information about medical tests and treatments. It reflects how uncertainty regarding the reliability, credibility, or adequacy of medical risk information influences trust in experts, emotional responses, and decision-making. This construct is measured using the AA-Med scale, which assesses aversion to ambiguity specifically in the healthcare context (Einhorn & Hogarth, 1986; Ellsberg, 1961; Han et al., 2009). Higher scores indicate greater aversion to ambiguity, while lower scores suggest lower aversion to ambiguity.
Cancer Risk Perception	Independent	Cancer Risk Perception refers to an individual's beliefs and feelings about the causes, controllability, and personal relevance of cancer risk. This includes perceptions of behavioral and lifestyle factors in

		cancer development, the complexity of cancer prevention recommendations, and emotional responses to cancer risk information. It also captures avoidance tendencies and fatalistic attitudes toward cancer (Harper et al., 2021.) Higher scores indicate greater cancer risk, while lower scores suggest less perception of cancer risk.
Physicians' Perceived Competence	Independent	Physicians' perceived competence refers to their self-assessed confidence in engaging with patients about Multi-Cancer Early Detection (MCED) testing. This includes their ability to educate patients on MCED testing, facilitate shared decision-making, explain false positive and false negative MCED test results, and guide patients through follow-up diagnostic evaluations after an abnormal MCED test result. This construct is measured using the Perceived Competence Scale (Chambers et al., 2023). Higher scores indicate greater confidence in these competencies, while lower scores suggest less confidence.

1.4.2 Hypothesis 1

Hypothesis 1: Ambiguity aversion predicts attitudes of experts.

Studies have shown that ambiguity aversion can impact individuals' attitudes and behaviors toward medical decisions. For example, in an NIH genome sequencing study, participants who perceived greater ambiguity about their genome sequencing results were less likely to express an intention to learn about them, indicating that ambiguity can influence the willingness to engage with genetic testing (Taber et al., 2015). Similarly, ambiguity aversion has been shown to provoke irrational behaviors in patients using direct-to-consumer genetic tests, leading some to seek unnecessary testing or avoid genetic testing altogether (Felder & Sevim, 2024). These findings suggest that ambiguity

aversion can drive behaviors and perceptions that may not align with optimal medical decision-making.

A study exploring the public's perceptions of ambiguity in cancer prevention recommendations found that perceived ambiguity was inversely related to the perceived preventability of cancer and preventive behaviors such as cancer screening and sunscreen use (Han et al., 2007). This suggests that ambiguity about health information leads to pessimistic judgments and lower engagement in risk-reducing behaviors.

In the context of MCED testing, primary care physicians have expressed negative views due to skepticism about its clinical utility, as well as uncertainty regarding who should be tested and how to interpret results (Samimi et al., 2024). Additional uncertainty about the test's added value for patients may further complicate physicians' decision-making and contribute to hesitation around its widespread adoption (Fagery et al., 2024). These studies suggest that experts are particularly susceptible to ambiguity aversion when confronted with novel technologies like MCED testing, which are often accompanied by high levels of uncertainty and conflicting expert opinions.

Moreover, a study highlighted several factors hindering the clinical implementation of MCED tests, such as the lack of guidelines for handling false positives and negatives, confusion over when and how to use the test, and concerns about standardization (Brito-Rocha et al., 2023). These factors may contribute to the ambiguity that experts face when considering MCED testing, making them more likely to have cautious or negative attitudes.

Based on these findings, Hypothesis 1 suggests that experts' levels of ambiguity aversion, measured by their discomfort with conflicting expert opinions and uncertainty about the reliability of medical tests, are likely to influence their attitudes toward the implementation of MCED testing.

1.4.3 Hypothesis 2

Hypothesis 2: Cancer risk perception is inversely associated with attitudes.

Research suggests that individuals' perceptions of risk significantly influence their trust in and acceptance of new medical technologies. A study on healthcare workers and the general public found that higher perceived risk of medical technologies led to diminished trust and lower adoption rates, as seen with COVID-19 vaccines (Ramot &

Tal, 2024). Similarly, an exploratory study on digital health technologies discusses how fear, confusion, and concern about the effectiveness of new healthcare technologies become barriers to public acceptance (Antes et al., 2021). These findings indicate that uncertainty and worry about new technologies often result in skepticism, negatively shaping attitudes toward their adoption.

Heightened cancer risk perception has also been linked to reluctance toward medical technologies. For instance, ethnic minority groups were less likely to undergo genetic testing for hereditary cancer risk due to cultural fears and lower awareness, suggesting that concerns about cancer risk can lead to skepticism toward such technologies (Hann et al., 2017).

Psychological distress related to cancer has further been shown to impact engagement with medical screening. A study on mammography adherence found that intrusive thoughts and worry about breast cancer significantly predicted lower screening adherence, suggesting that fear and risk perception can act as psychological barriers to preventive medical technologies (Lerman et al., 1993).

Additionally, perceived ambiguity in cancer prevention has been linked to heightened cancer risk perception. Individuals who viewed cancer prevention recommendations as unclear or inconsistent reported greater perceived cancer risk, which influenced their attitudes and decision-making (Han et al., 2006, 2007). This suggests that uncertainty surrounding cancer prevention may amplify risk perception, reinforcing hesitation toward medical technologies.

These findings support Hypothesis 2, suggesting that when individuals with high cancer risk perception, they are less optimistic about medical technologies. Beliefs that cancer is uncontrollable, confusion over prevention guidelines, and fear about cancer may reduce optimism about MGED testing implementation.

1.4.4 Hypothesis 3

Hypothesis 3: Physicians' Perceived Competence is positively associated with attitudes

Research indicates that physicians' self-perceived competence is positively associated with their attitudes toward medical practice. Studies have shown that higher

perceived competence correlates with more positive attitudes in areas such as dementia care (Kaduszkiewicz et al., 2008) and obesity management (Jay et al., 2009).

Physicians generally exhibit positive perceptions of MCED testing. A recent study found that healthcare providers widely recognized the value of MCED testing and anticipated its benefits in complementing existing cancer screening methods (Schroll et al., 2024). Experts also noted that MCED testing could improve screening specificity and reduce strain on healthcare systems by minimizing false positives (de With, 2023). Additionally, most physicians surveyed believed MCED testing would benefit all patients and promote further cancer screening (Clunie et al., 2024).

Perceived competence plays a key role in shaping physicians' attitudes toward MCED testing. A study found that physicians who felt confident in their ability to guide patients through MCED testing were significantly more receptive to its clinical use (C. V. Chambers et al., 2023). Similarly, another study reported that physicians aware of MCED technology and confident in managing its implementation were more likely to adopt it in practice (Hallman et al., 2023).

Together, these findings support Hypothesis 3, suggesting that physicians who perceive themselves as competent in MCED testing are more likely to have positive attitudes toward its adoption.

Chapter 2: **LITERATURE REVIEW**

2.1 Overview

The literature review underscores the promising potential of MCED testing for improving early cancer detection, particularly for cancers lacking existing screening options. MCED tests offer benefits such as higher specificity and the ability to detect cancers at earlier stages, particularly when combined with current screening practices, which could reduce healthcare costs and improve patient outcomes. While many studies explore the concerns regarding widespread implementation of MCED testing, more insights are needed to understand how these barriers can be overcome.

Studies investigating experts' perceptions, particularly physicians, towards MCED testing show conflicting results, as there is high receptivity in some and general pessimism in others. Furthermore, gaps persist in understanding how perceived competencies of physicians impact their perceptions towards the implementation of MCED testing. Moreover, the role of ambiguity aversion in MCED testing remains underexplored.

In summary, while MCED testing holds considerable promise, the existing literature highlights the need for more research to understand experts' attitudes and concerns towards MCED testing, as well as the role of ambiguity aversion, cancer risk perception and perceived competencies of physicians in shaping these attitudes. These gaps must be addressed to better understand the professional, psychological, and general barriers that impact the equitable and effective implementation of MCED testing into health systems.

2.2 Overview of Cancer Incidence and Mortality

Cancer remains a leading global health challenge, with significant disparities in incidence and mortality rates across different regions. According to a study based on Global Cancer Observatory (GLOBOCAN) data, in 2020, there were 19.3 million new cancer cases, with breast, lung, colorectal, prostate, and cervix uteri cancers together accounting for 43.6% of these cases (Sung et al., 2021). The same five cancers were responsible for 41.5% of cancer-related deaths, highlighting their profound impact on global health. Lung cancer emerged as the leading cause of cancer mortality, underscoring

the need for improved early detection and treatment strategies (Filho et al., 2024). The study also revealed that the remaining cancers, which make up 51.6% of cases and 58.5% of deaths, point to a broader, pressing need for diverse research and targeted healthcare interventions to manage the overall cancer burden effectively (Sung et al., 2021).

According to the World Health Organization (WHO), cancer is the second leading cause of death worldwide, following cardiovascular diseases. In 2020, the WHO estimated that there were approximately 10 million cancer-related deaths, which represents about 1 in 6 deaths globally (WHO). According to GLOBOCAN predictions, worldwide cancer incidence is expected to rise up to 35.3 million and cancer mortality to 18.5 million by 2050, making early detection of cancer exceedingly important (WHO). The high mortality rate associated with cancer is attributable to various factors, including late-stage diagnosis, limited treatment options in some regions, and variations in healthcare accessibility (Bray et al., 2018)

Regional disparities further complicate the global cancer burden. High-income countries tend to have higher survival rates due to advanced healthcare systems and early detection technologies, while low- and middle-income countries face greater challenges. For instance, the prevalence of cancers such as breast and prostate cancer is notably high in high-income countries, whereas cancers related to infectious agents, such as cervical and liver cancer, are more prevalent in low-income regions (Bray et al., 2018; Ferlay et al., 2019). This disparity highlights the critical need for tailored cancer prevention and treatment strategies that address the specific needs and resource limitations of different regions.

Additionally, cancer incidence and mortality rates are influenced by a range of factors, including age, sex, lifestyle, and environmental exposures. The incidence of cancer generally increases with age, with most cancers being diagnosed in individuals over the age of 50 (Siegel et al., 2020). Lifestyle factors such as smoking, dietary habits, and physical inactivity play a significant role in cancer risk, as does exposure to environmental pollutants and occupational hazards (Islami et al., 2018; Lauby-Secretan et al., 2015). Understanding these risk factors is essential for developing effective prevention strategies and for informing public health policies aimed at reducing cancer incidence and improving outcomes.

Efforts to reduce the global cancer burden must focus on enhancing early detection and improving treatment options, and advance research through system dynamics

modeling for cancer prevention and control (O. Karanfil et al., 2024; Ö. Karanfil, 2023; Kenzie et al., 2023). Advances in medical research, such as the development of personalized medicine and targeted therapies, offer hope for better outcomes. However, achieving these improvements requires concerted efforts to address healthcare disparities, increase access to care, and promote cancer prevention and education at both the individual and community levels (Hanna et al., 2020; Siegel et al., 2021). Equally important is understanding experts' attitudes toward innovative approaches, as this can reveal challenges such as gaps in evidence-based research, equity concerns, and the need for robust clinical guidelines, which are key factors for successful implementation.

2.3 *Current Cancer Screening Practices and Limitations*

According to WHO's 2019 global survey for assessing national capacity for the prevention and control of noncommunicable diseases, organized population-based screening of breast cancer and cervical cancer programs was available in approximately 73% and 65% of the countries in the European region, respectively (WHO, 2020). Most cancers, however, are detected at a late stage, by which point they have grown aggressive, thereby limiting treatment options significantly. This is why screening practices can significantly reduce cancer mortality by aiding early detection and diagnosis (WHO). However, as organized population-based screening exists for mainly breast, cervical, and colorectal cancers only in the European region, mortality from cancer remains higher than it could be otherwise (Armaroli et al., 2015).

Despite these advancements in screening practices, there are several limitations that impact their effectiveness. One major limitation is the accessibility and coverage of these screening programs. In many low- and middle-income countries (LMICs), organized screening programs are often unavailable or insufficient, leading to a lower rate of early detection and higher mortality rates from cancer. In these regions, the lack of resources, infrastructure, and trained healthcare personnel further exacerbates the situation, leaving many cancers undiagnosed until they reach advanced stages. For instance, less than 30% of low-income countries reported having comprehensive cancer screening programs for cervical cancer, compared to nearly 90% in high-income countries (Torre et al., 2016).

Moreover, even in high-income countries, there are significant disparities in the access to and utilization of screening services. Socioeconomic factors, geographic

barriers, and lack of awareness can prevent individuals from participating in screening programs. For example, individuals from lower socioeconomic backgrounds or those living in rural areas may face difficulties in accessing screening facilities, thereby missing the opportunity for early detection and treatment. A study in the United States found that breast cancer screening rates were significantly lower among women without health insurance (38%) compared to those with private insurance (72%) (Islami et al., 2021).

Another limitation of current screening practices is the specificity and sensitivity of the screening tests themselves. While mammograms, Pap smears, and colonoscopies have been proven effective in detecting breast, cervical, and colorectal cancers respectively, they are not without their flaws. False positives can lead to unnecessary anxiety and medical procedures, while false negatives can result in missed diagnoses. For instance, a study found that approximately 20% of mammography results in false positives, leading to additional tests and biopsies (Smith et al., 2019). Therefore, there is a continuous need for improving the accuracy and reliability of these screening tests. It is also equally important to develop and adhere to evidence-based practice guidelines for screening, keeping in mind that significant variations in clinical practice and fluctuations in test thresholds, test efficiency, and the target screening population can incur harm to individuals (Ö. Karanfil, 2016; Ö. Karanfil & Sterman, 2020; Ö. Karanfil & Sterman, 2023).

Lastly, there is a need for expanding screening programs to cover more types of cancers. Over half of cancer deaths involve cancers with no recommended screening protocols, such as ovarian and pancreatic cancers (Siegel et al., 2023). Currently, organized screening is mainly available for breast, cervical, and colorectal cancers. However, cancers such as lung, prostate, and liver also have high mortality rates and could benefit from early detection through screening. For example, low-dose computed tomography (LDCT) has been shown to reduce lung cancer mortality by 20% among high-risk individuals (de Koning et al., 2020). This underscores the urgent need for innovative screening methods that can address these gaps effectively. Expanding screening programs to include these types of cancers could significantly improve early detection and reduce mortality rates. Such advancements will require the integration of new technologies and methodologies in screening practices.

Alongside the development of new technologies and methodologies, it is crucial to ensure their implementation is effective, efficient, safe, and equitable. For this, experts'

perspectives are essential as they can assist in identification of challenges and help form strategies to ensure successful adoption in diverse healthcare settings.

2.4 Multi-Cancer Early Detection (MCED) Testing

Multi-Cancer Early Detection (MCED) testing represents a significant advancement in cancer screening, enabling the detection of multiple types of cancers from a single blood sample. This approach leverages advances in molecular biology and genomics to identify cancer-related biomarkers that are common across different types of cancer. Unlike traditional screening methods, which are typically cancer-specific, MCED tests aim to provide a broad spectrum of early detection capabilities, potentially identifying cancers before they manifest with symptoms (Brito-Rocha et al., 2023).

Recent advancements in MCED technology involve sophisticated genomic techniques, including the analysis of circulating tumor DNA (ctDNA) and other biomarkers. In recent years, MCED screening tools have emerged, making it possible to detect more than 50 cancers with ease, reliability, and efficiency. These tools are minimally invasive and draw information from specific blood-based cancer biomarkers such as circulating cell-free DNA (cfDNA), cell-free RNA (cfRNA), circulating tumor cells (CTCs), exosomes, proteins, and metabolites (Marrugo-Ramírez et al., 2018). High-throughput sequencing and machine learning algorithms are used to detect cancer signals in the bloodstream, enhancing early detection and intervention (Cohen et al., 2018).

Out of the various MCED approaches, DNA methylation-based MCEDs have gained significant attention due to their ability to detect cancers with high specificity. DNA methylation, a well-studied epigenetic modification, plays a crucial role in regulating gene expression and maintaining cell physiology. In healthy cells, DNA methylation patterns are tightly regulated to ensure proper gene function. However, aberrations in these patterns can lead to genomic instability and contribute to cancer development by either suppressing tumor suppressor genes or activating oncogenes (Kulis & Esteller, 2010).

DNA methylation-based MCED tools utilize blood samples from patients, isolating plasma and extracting cell-free DNA. This DNA is then analyzed for abnormal methylation patterns that are indicative of cancer presence. The integration of Next Generation Sequencing (NGS) with sophisticated machine learning classifiers enables the

creation of a comprehensive library of DNA methylation patterns. By comparing patient samples against this library, these tools can detect multiple types of cancer and identify their tissue of origin, thus offering a promising advancement in cancer screening (Brito-Rocha et al., 2023).

Several studies have demonstrated the potential of MCED tests to improve early cancer detection rates and outcomes. Research published in JAMA Oncology in 2022 highlighted the potential of MCED tests to reduce the incidence of late-stage cancer by identifying tumors at earlier stages (Klein et al., 2021). Moreover, the Galleri test, developed by GRAIL, demonstrated a remarkable ability to detect over 50 different cancers with a sensitivity of 52% and a specificity of 99% in a large-scale clinical trial (Klein et al., 2021). Another example is the PanSeer test, which showed a 95% sensitivity in detecting five different cancers including ovarian and pancreatic cancers, even at early stages (Chen et al., 2020). CancerSEEK, a multi-analyte blood test, was able to detect eight common cancers by assessing circulating proteins and mutations in cfDNA. In a study conducted with 1005 previously diagnosed cancer patients and 850 healthy control individuals, CancerSEEK was able to detect cancer with a 99% specificity and a sensitivity of 78% for stage III, 73% for stage II, and 43% for stage I cancers (Cohen et al., 2018). Furthermore, the SYMPLIFY study reported for cases in which a cancer signal was detected among patients with cancer, the MCED test's prediction of the site of origin was accurate in 85.2% of the cases (Nicholson et al., 2023).

These advancements highlight MCED tests' capacity to provide a broad, high-performance approach to early cancer detection, potentially revolutionizing current screening paradigms. However, as an emerging technology lacking FDA approval and established guidelines, its integration depends on understanding experts' attitudes and concerns, which can reveal critical barriers and challenges that must be addressed to ensure its successful and equitable implementation across healthcare systems.

2.5 Comparison of MCEDs and Current Screening Methods

MCED tests are also described more capable of detecting cancers earlier than traditional methods, particularly those without existing screening options (Samimi et al., 2024). They focus on using specific biological markers for more accurate and efficient disease detection. This shift moves away from one-size-fits-all methods, similar to how

personalized medicine in clinical trials aims for targeted, effective strategies. (Nelson et al., 2014). Moreover, they are done via liquid biopsies, which adopt a noninvasive approach for the detection and monitoring of cancer biomarkers, thereby minimizing pain as well as stress for individuals undergoing it (Rubis et al., 2019). Tissue biopsies, on the other hand, which are considered the gold standard for diagnosing cancer, are performed using endoscopy or needle biopsy, which are invasive procedures that may require sedatives or anesthesia to keep the patient from feeling pain (Corcoran & Chabner, 2018; *Tests and Procedures Used to Diagnose Cancer - NCI*, 2015).

One large large-scale scale clinical validation study conducted to analyze the performance of MCED testing showed that it can predict cancer signal detection with a specificity of 99.5%, thereby suggesting a low false positive rate (FPR) of 0.5% (Klein et al., 2021). In comparison, the FPR of current recommended cancer screenings is much higher; 11.1% for digital screening mammograms for detecting breast cancer (Lehman et al., 2017), 12.8% for low-dose computed tomography (LDCT) for detecting lung cancer (Pinsky et al., 2015). This shows that the comparatively high specificity rate of MCED testing, when complemented with current cancer screening practices, can allow the population cancer detection rate to increase (Klein et al., 2021).

Furthermore, a study by Hackshaw et al., showed that, in the US, for breast, colorectal, cervical and lung cancers found through the recommended screening practices, the TP:FP (true positive vs false positive) ratio is 1:43 (which means that in order to detect one person with any of these four cancers, 43 individuals may have to undergo unnecessary diagnostic procedures. When complemented with MCED testing, however, the TP:FP ratio was projected to be 1:14 (which means that in order to detect one person with breast, colorectal, cervical, or lung cancer, 14 individuals may have to undergo unnecessary diagnostic procedures), thereby leading to less unnecessary diagnostics to detect true positives. (Hackshaw et al., 2021a).

Klein et al., also found the overall sensitivity of cancer detection signal with MCED testing to be 51.5%, with sensitivity increasing with the progression of cancer stages (i.e. stage I: 16.8%, stage II: 40.4%, stage III: 77.0%, and stage IV: 90.1%). The study also showed that MCED testing could detect cancer signal origin (CSO) with an accuracy of 88.7% (Klein et al., 2021). Furthermore, a subgroup analysis also showed that the overall sensitivity for solid tumors for which common screening options were not available was twice (65.6%) as compared to the overall sensitivity for solid tumors which had common

cancer screening options. This led the authors to suggest that MCED testing, when complemented with current screening practices, has the potential to minimize missed detections, thereby not only increasing the absolute number of cases detected, particularly for cancers for which common screening does not exist, but also detecting them at earlier stages (Klein et al., 2021). This is also supported by the study by Hackshaw et al. which shows that the combined implementation of current cancer screening practices and MCED testing can increase the number of true positives from 2.66 per 1000 (from current screening practices only) to 3.43 per 1000, thereby increasing overall cancer detection (Hackshaw et al., 2021a).

An interception model developed to predict the long-term performance of MCED testing showed that it can detect 485 cancers per 100,000 people annually (Hubbell et al., 2021). Among these, 68% of the cases intercepted would have been diagnosed at a late stage (III and IV) without MCED but were instead caught earlier, leading to a 78% reduction in late-stage cases. The model also showed that with MCED testing, detecting cancers at an earlier stage could reduce the overall cancer mortality by 21% (Hubbell et al., 2021). The authors therefore suggest that by potentially detecting cancer at any site and at earlier stages, MCED testing, when combined with usual screening practices, can reduce the burden of late-stage cancer as well as overall cancer mortality (Hubbell et al., 2021).

There is a drastic increase in the cost of treating patients diagnosed with stage III/ IV cancer as opposed to treatment at stage I/II cancer. The annual average medical cost of treating cancer in end-of-life (EOL), continuing, and initial phase is \$105,500, \$41,800, and \$5,300 respectively. (Mariotto et al., 2020). Therefore, detecting cancer at earlier stages can reduce the final burden as treatment in later stages is much more expensive. A study demonstrated that annual implementation of MCED testing for individuals between 50 and 70 years could reduce the cost per cancer treatment by USD 5421 (Tafazzoli et al., 2022). Hackshaw et al. also projected that incorporating MCED testing into current screening practices could reduce the diagnostic cost per confirmed cancer diagnosis from USD 89,054 (with current screening practices only) to USD 32,461 (Hackshaw et al., 2021b).

In summary, MCED tests show significant potential to enhance current screening practices by improving early detection, particularly for cancers without existing screening options. With high specificity and reduced false positives, MCED could complement

traditional methods, lower healthcare costs, and reduce late-stage cancer diagnoses. While they hold great promise, careful consideration is needed before implementation to ensure success, which is why understanding experts' attitudes and concerns is crucial.

2.6 Stakeholder Perceptions towards MCED Testing

A recent qualitative study was also done to understand perceptions of primary care physicians and laypersons towards the benefits, harms, and general acceptability of MCED testing. Primary care physicians stressed that benefits included convenience of use, ability to improve cancer morbidity and mortality by detecting it earlier, as well as the ability to detect cancers for which current screening does not exist. When discussing potential harms, they brought up false positives and their psychological impact on patients, cost of MCED testing leading to unequal access, risk to patient privacy, skepticism regarding the additional value they bring, as well as MCED testing and necessary diagnostic follow-ups being denied by insurance agencies (Samimi et al., 2024). Primary care physicians also had general negative views on the acceptability of MCED testing, owing to skepticism about the clinical utility of MCED testing, as well as lack of proper guidelines regarding who to test, how to interpret results, and how to conduct diagnostic follow ups (Samimi et al., 2024).

On the other hand, another recent survey-based study, which was conducted to draw insights from healthcare providers, payers, and patients to understand the anticipated challenges in the implementation of MCED testing, showed that experts, particularly healthcare providers, were in favor of MCED testing and widely acknowledged its value proposition (Schroll et al., 2024). Another study also showed that primary care providers had generally high receptivity towards the use of MCED testing in clinical practice. (C. V. Chambers et al., 2023). The PATHFINDER study found that patients generally had positive perceptions of MCED testing and were likely to adhere to health-care providers' future cancer screening recommendations (Nadauld et al., 2025). Another study showed that experts generally perceived that, when complemented with current cancer screening practices, MCED testing can enhance screening specificity and reduce the strain on healthcare systems by decreasing false positives (IJzerman, 2024.; de With, 2023).

The study by Scroll et al., additionally showed that healthcare providers and patients identified out of pocket costs affiliated with MCED testing was the biggest concern in its

adoption, followed by test performance and patient compliance (Schroll et al., 2024). Another study exploring the perceptions of primary care providers towards MCED testing also echoed this concern, as 70% expressed overwhelming concern about MCED tests being covered by insurance companies for patients (Hallman et al., 2023). Additionally, for payers, limited evidence-based research supporting the accuracy of MCED tests was the most important reason for MCED testing not being included in insurance coverage (Schroll et al., 2024).

Brito-Rocha et al., also conducted a study where they addressed the important question of “What is stopping MCED tests from moving into clinical application?” and some of the factors they noted were lack of guidelines in cases of false positives and negatives test results, more research needed to assess the diagnostic capabilities of MCED tests, confusion regarding when, how, and to whom to provide a MCED test, adequate medical communication and public understanding, cost-benefit analysis, and lack of standardization (Brito-Rocha et al., 2023).

Another study stresses the importance of addressing healthcare inequities when implementing MCED testing, and provides comprehensive recommendations to address it which include having representation in clinical trials, ensuring equitable insurance coverage for MCED tests and diagnostic follow-up, as well as education the public about MCED testing (Miller et al., 2024). This concern was also reflected in an interview-based cross-sectional study conducted to understand public perspectives on MCED testing as participants expressed concern that the benefits of MCED testing would not reach people equitably (Crossnohere et al., 2024).

Overall, experts’ perspectives show varying levels of acceptability and favor towards MCED testing. Even among healthcare providers and physicians, there are contrasting perceptions of receptivity towards MCED testing. This underscores the need for further research into experts’ attitudes towards MCED testing, including physicians' attitudes. Moreover, given that FDA approval and clinical guidelines for MCED testing are not yet in place, it is essential to address the challenges associated with its potential implementation now, rather than waiting until they escalate into more significant obstacles in the future

2.7 Ambiguity Aversion and Risk Perception in Medical Decision-Making

Ambiguity refers to uncertainty about how reliable, credible, or sufficient information is, and aversion to ambiguity can play a role in impacting judgements and medical decision-making, particularly in situations where there is conflicting information regarding the potential harms and benefits of a medical intervention (Han et al., 2009). The impact of ambiguity aversion in cancer is highlighted by a study that shows that perceived ambiguity about cancer prevention recommendations is inversely related with prevention-related perceptions as well as uptake of interventions (Han et al., 2006).

Perceived ambiguity has also been found to be positively related to perceived cancer risk, and it was suggested that it could be due to several reasons; ambiguity regarding cancer prevention recommendations could increase perceptions of cancer risk or ambiguity could reduce belief in cancer preventability, thereby increasing cancer risk perceptions (Han et al., 2006). The study further showed that perceived cancer risk acted as a partial mediator between perceived ambiguity and worry (Han et al., 2006).

In an NIH genome sequencing study, it was found that participants who had higher perceived ambiguity about genome sequencing results had a diminished intention to learn about their results, therefore showing that ambiguity can influence learning intentions about genetic testing (Taber et al., 2015). Another study shows that ambiguity aversion can evoke irrational behavior in patients using direct-to-consumer genetic tests, which can lead them to seek unnecessary testing or avoid genetic testing altogether (Felder & Sevim, 2024). These studies suggest that ambiguity aversion can drive perceptions and behaviors that do not align with optimal medical decision-making.

As MCED testing is an emerging technology, expansive discussions are being held about its potential value. At American Society of Clinical Oncology's session held on Jun 04, 2024 to discuss the experiences of researchers, physicians and oncologists with MCED testing, these experts stressed that regardless of the potential of MCED testing in revolutionizing early cancer detection, currently there is more uncertainty than certainty about how MCED testing can and should be incorporated into patient care, highlighting the ambiguity that currently exists regarding the scope of usage of MCED testing (*Oncologists Contend With Practice Implications of Emerging Multi-Cancer Detection Tests*, 2024).

Recently, a focus group finding also draws attention to the skepticism among primary care physicians regarding MCD tests. Physicians expressed concerns about the lack of systematic evaluation, guidelines for clinical application, and the ambiguity surrounding the tests' accuracy and utility in saving lives (Samimi et al., 2024). These uncertainties around MCED testing may contribute to how primary care physicians perceive MCED testing.

MCED tests may identify early-stage cancers with underlying micro-metastatic disease, where curative treatments like surgery may not improve survival but could still subject patients to unnecessary interventions. This uncertainty about whether detected cases will genuinely benefit from treatment can complicate decision-making for physicians, increasing hesitation about the widespread adoption of MCED tests (Fagery et al., 2024).

Currently, the relationship between ambiguity aversion and MCED testing remains unexplored. Given the absence of FDA approval and established guidelines for MCED testing, investigating this association could shed light on experts' concerns and decision-making processes. Additionally, examining how ambiguity aversion and cancer risk perception shape experts' attitudes may uncover critical psychological and decision-making barriers, offering valuable insights to support the successful acceptance and implementation of MCED testing in clinical practice.

2.8 Physicians' Perceived Competence

A study exploring the receptivity of primary care providers towards MCED testing found that primary care providers generally feel confident in their competencies to educate and guide their patients about MCED testing, as well as explain results. The study further found that primary care providers who had higher perceived competence in their ability to educate, explain and guide their patients about MCED testing had high likelihood to order an MCED test as well, the highest levels of which were found in physicians with the most years of experience in clinical practice (Chambers et al., 2023).

Another study, which found that primary care providers generally had negative views regarding the acceptability of MCED tests, showed that primary care providers felt that there was a need for better understanding about which patients are eligible, how often MCED test should be administered, how to interpret the results, and do diagnostic follow-

ups (Samimi et al., 2024). These are factors which can impact the confidence physicians feel in educating and guiding their patients about MCED testing and explaining results.

At American Society of Clinical Oncology (ASCO)'s session held on Jun 04, 2024 expert researchers, physicians and oncologists emphasized that due to current lack of clinical trials and conclusive research, it is challenging for physicians to participate in shared decision-making for the patient regarding prescribing MCED tests and analyzing results (*Oncologists Contend With Practice Implications of Emerging Multi-Cancer Detection Tests*, 2024). This suggests that lack of comprehensive research implicitly impacts the competencies of physicians and oncologists.

Currently, few studies have explored physicians' perceived competencies related to MCEDs and many have focused on exploring the perceptions and receptivity of physicians towards MCED testing, which has led to varied findings. Given this gap, it is important to investigate the relationship between physicians' confidence in educating and guiding patients about MCED testing and their attitudes toward its implementation. This exploration could provide insights into how perceived competencies might influence physicians' attitudes towards the future implementation of MCED testing and help address any barriers or concerns before its widespread use.

Chapter 3:

RESEARCH METHODOLOGY

3.1 *Research Design*

This study uses a mixed-method, survey-based approach to examine experts' attitudes, ambiguity aversion, cancer risk perception, and physicians' perceived competence regarding the implementation of Multi-Cancer Early Detection (MCED) testing. The research involves a cross-sectional survey that captures both quantitative data and qualitative insights, offering a comprehensive understanding of the topic.

The process is conducted in two stages. First, a pilot phase was carried out to refine the survey instrument based on expert feedback, ensuring clarity and relevance. Following this, the main study was launched, gathering responses from a diverse group of experts, including physicians, researchers, academicians, and healthcare professionals.

The survey covers participants' awareness of MCED testing, their attitudes toward its future implementation, their implementation related preferences, and their perceptions of cancer risk and ambiguity. An additional section focuses on physicians' perceived competencies in the context of MCED testing. By combining quantitative analysis with qualitative responses, the study provides both statistical trends and in-depth insights.

Ethical guidelines were strictly followed, and the study received approval from the Koç University Ethics Committee (Approval Number: 2024.162.IRB3.069). Participants' privacy and autonomy were prioritized throughout the research.

3.2 *Population and Sampling*

The target population for this study primarily consists of experts from the healthcare sector, including physicians from different specialties, academics working in related areas, researchers, and other healthcare professionals.

For the inclusion criteria, participants had to be at least 18 years old and proficient in English to ensure full understanding of the survey. Those who did not provide informed consent were not allowed to proceed with the survey. Additionally, participants who had never heard or read about MCED testing were excluded from continuing past the awareness section, ensuring that only individuals with a baseline understanding of MCED

testing were included. Duplicate responses were also excluded to maintain the integrity of the data.

To select participants, a combination of snowball, convenience, and purposive sampling methods was employed. Snowball sampling helped identify additional participants through referrals, while convenience and purposive sampling was employed to ensure the inclusion of participants with substantial knowledge and experience in cancer detection and healthcare innovation. Participants were identified through professional networks, LinkedIn communities, academic collaborations as well as through Koç University networks, including the Koç University Research Center for Translational Medicine (KUTTAM).

3.3 Data Collection Methods

The data for this study were collected through an online survey administered using the Qualtrics platform. Participants were invited to participate through individualized links or email invitations. The invitation email included essential details about the study, encouraging participants to share their valuable input. The survey invitation email was shared with the following:

- [Koç University Research Center for Translational Medicine](#) (KUTTAM), including KUTTAM faculty members, postdoctoral members, graduate students, and medical graduates, making a pool of ~ 560 individuals.
- LinkedIn Groups:
 - Systems Biology for Medical Research (SBMR)
 - Harvard T.H. Chan School of Public Health Alumni Network
 - Global Public Health - Health Systems and Policy
 - CHOIR - Center for Healthcare Operations Improvement and Research - University of Twente
 - MIT Sloan Healthcare Executives
 - HBS Health Care
 - Digital Health
 - Health Systems Global
- [Erasmus Medical Centre Oncology](#)
- [Stanford Cancer Institute](#)

- Staff at [Health Technology Assessment](#) (HTA) research group at [Erasmus School of Health Policy & Management](#) (ESHPM) of Erasmus University of Rotterdam
- Staff at [Institute for Medical Technology Assessment](#) (IMTA)
- [Hacettepe University](#) – Department of Medical Oncology, Department of Preventive Oncology, Department of Radiation Oncology, Department of Pediatric Oncology, and Department of Basic Oncology.
- [Istanbul University](#) – Department of Medical Genetics, Department of Radiology, Department of Radiation Oncology, Department of General Surgery, Department of Thoracic Surgery, Department of Heart Vascular Surgery, and Department of Urology
- [National University of Medical Sciences \(NUML\)](#) – Department of Biological Sciences and Department of Public Health

3.4 Survey Development

The development of the survey was a rigorous and iterative process, designed to ensure clarity, comprehensiveness, and relevance to the study's objectives. The survey was initially drafted based on a review of existing literature on Multi-Cancer Early Detection (MCED) testing and the research goals outlined for this study. Validated scales measuring attitudes, ambiguity aversion, cancer risk perception, and physicians' perceived competence were found in literature (Chambers et al., 2023; Han et al., 2009; Harper et al., 2021.; Horrow et al., 2021). The final survey instrument can be found in the appendix (Appendix A:Survey Instrument).

Table 3-1: Breakdown of survey sections and how they were developed

Survey Section	Section Content	References and Scales Used
Section 1	Informed Consent	From Koç University Ethics Committee
Section 2	Awareness about Genetic Testing and MCED Testing	Based on awareness related questions (Powell et al., 2012)

Section 3,4,5 or 6 (randomized sections to remove order effects bias)	Attitudes towards MCED testing	Based on the Genomic Orientation (GO) scale (Horrow et al., 2021)
Section 3,4,5 or 6 (randomized sections to remove order effects bias)	Ambiguity Aversion	Based on the Ambiguity Aversion (AA) scale (Han et al., 2009)
Section 3,4,5 or 6 (randomized sections to remove order effects bias)	Cancer Risk Perception	Based on the Cancer Risk Perception Scale (Harper et al., 2021.)
Section 3,4,5 or 6 (randomized sections to remove order effects bias)	Implementation Preferences	Based on literature review and our research questions
Section 7	Open-Ended Questions	Based on literature review and our research questions
Section 8	Demographic Questions	Based on literature review and our research questions
Section 9	Physician's Perceived Competencies	Based on Physician's Perceived Competency Scale (Chambers et al., 2023)
Section 10	Physicians' Demographic Questions	Based on literature review and our research questions
Section 11	Requesting Email Address	~60% of the respondents shared email address

The Genomic Orientation (GO) scale, which was initially developed to assess the optimistic and pessimistic attitudes of people towards the future implementation of genomic medicine, was slightly adjusted to assess the attitudes towards MCED testing in particular. Two items in this 26-item scale were revised to increase alignment with our research questions; the statement “help prevent common **diseases**” was changed to “help prevent late detection of common **cancers**” and the statement “help doctors diagnose rare

diseases earlier” was changed to “help doctors diagnose rare **cancers** earlier”. Rest of the scales were kept the same.

3.5 Pilot Study

A pilot phase was conducted to refine the survey and ensure it met the research objectives. Feedback was sought from academicians, researchers, and physicians with expertise relevant to MCED testing. To facilitate focused feedback, questions were temporarily numbered during the pilot phase. Insights were gathered both through the survey platform and via email correspondence with pilot participants. Their suggestions and constructive criticism led to continuous revisions, helping to clarify ambiguous questions, address gaps, and optimize the survey for the target audience. This iterative process involved six experts and took approximately eight weeks.

During the pilot, key revisions included refining the phrasing of questions and reordering sections for better flow. Sections covering attitudes, ambiguity aversion, cancer risk perception, and implementation-related questions were randomized to prevent sequence and priming bias. Demographic questions were moved to the end to avoid potential bias, such as social desirability and priming. Additionally, the Cancer Risk Perception scale was updated from a 4-point to a 5-point Likert scale to match the other scales. The estimated completion time for the survey was adjusted from 10 to 15 minutes, based on feedback. The title was also modified to remove “ambiguity aversion,” ensuring participants were less likely to adjust their responses based on the study's focus. Moreover, the “force response” requirement was either removed or shifted to “request response” for most of the survey items.

The final version of the survey was carefully refined through these revisions, resulting in improvements in overall survey quality and experience, and also enhancing its accuracy, coherence, and alignment with the research objectives.

3.6 Informed Consent Process

The informed consent process adhered to ethical guidelines to ensure transparency and voluntary participation. Participants were provided with a detailed informed consent form at the beginning of the survey. This document outlined the study's purpose, objectives, procedures, as well as the identities of the researchers involved in the study.

The form emphasized that participation was entirely voluntary and that participants could withdraw at any point without repercussions. It also assured confidentiality, stating that personal data would not be collected, and all responses would remain anonymous and used solely for research purposes.

Before proceeding with the survey, participants were required to indicate their consent by selecting the “I Agree” option. Those who did not wish to participate could select “I Do Not Agree,” which would terminate the survey.

The informed consent form included contact information for the research team, allowing participants to reach out with any questions or concerns. Additionally, it noted the study’s ethical approval details, including the approval from Koç University's Ethics Committee (Approval Number: 2024.162.IRB3.069), providing credibility and transparency to the process.

3.7 Key Variables and Measurements

3.7.1 Main Outcome Variable

Attitudes: The primary outcome variable of the study is the “attitudes of experts towards the future implementation of Multi-Cancer Early Detection (MCED) testing”, which will be referred to as the “attitude score of experts”, or just the “attitude score”, for the rest of this thesis. This is a variable which is the sum of the responses to all 26 questions on the scale, potentially ranging between -52 and +52.

To measure this, a previously validated 26-item Genomic Orientation (GO) scale was used from the medical literature, which explores both optimistic and pessimistic attitudes of public (Horrow et al., 2021). The GO scale, developed in previous literature to assess attitudes towards genomic medicine, includes items categorized into six domains: 1) medical benefit or harm, 2) impact on patient experience, 3) health disparities and access, 4) progress toward implementation, 5) personal impact, and 6) the overall evaluation (Horrow et al., 2021). Specifically, the scale includes 10 items designed to capture optimistic attitudes and 16 items focusing on pessimistic attitudes, offering a comprehensive assessment of experts' views on MCED tests.

Multi-Cancer Early Detection (MCED) assays are blood-based tests designed to detect multiple cancers at early stages by identifying tumor-derived biomarkers from a single sample of blood (also known as liquid biopsies).

Within the next 5 years, how likely or unlikely is it that MCED testing will:

	Very Unlikely	Unlikely	Neither Unlikely Nor Likely	Likely	Very Likely
Help doctors choose the best drugs for patients	☐	☐	☐	☐	☐
Increase the number of unnecessary tests	☐	☐	☐	☐	☐
Help prevent late detection of common cancers	☐	☐	☐	☐	☐
Detract from disease prevention efforts we know work well	☐	☐	☐	☐	☐
Help doctors diagnose rare cancers earlier	☐	☐	☐	☐	☐
Distract doctors from looking for non-genetic causes of disease	☐	☐	☐	☐	☐
Help people live longer	☐	☐	☐	☐	☐
Divert healthcare resources that could be better used for other purposes	☐	☐	☐	☐	☐
Give patients more control over their health	☐	☐	☐	☐	☐
Create a burden of worry where there wasn't one before	☐	☐	☐	☐	☐
Be difficult for many patients to understand	☐	☐	☐	☐	☐
Help doctors focus on the unique needs and goals of each patient	☐	☐	☐	☐	☐
Make it harder for doctors to engage each patient as a person	☐	☐	☐	☐	☐
Increase the cost of healthcare	☐	☐	☐	☐	☐
Increase the cost of prescription drugs	☐	☐	☐	☐	☐
Increase inequality in healthcare	☐	☐	☐	☐	☐
Create new forms of discrimination	☐	☐	☐	☐	☐
Be too expensive for most people	☐	☐	☐	☐	☐
Make it more difficult for patients to receive medical care they need	☐	☐	☐	☐	☐
Be a standard part of general medical checkups	☐	☐	☐	☐	☐
Not be available in most hospitals and clinics	☐	☐	☐	☐	☐
Benefit nearly all aspects of medicine	☐	☐	☐	☐	☐
Be beneficial to you	☐	☐	☐	☐	☐
Cause you harm	☐	☐	☐	☐	☐
Do a lot of good	☐	☐	☐	☐	☐
Create many problems	☐	☐	☐	☐	☐

Figure 3-1: The Genomic Orientation (GO) Scale

Only two items out of this 26-item scale were revised to increase alignment with our research questions; by changing the term “diseases” to “cancers”. Accordingly, the statement on item 3 “help prevent common **diseases**” was changed to “help prevent late detection of common **cancers**” and the statement “help doctors diagnose rare **diseases** earlier” was changed to “help doctors diagnose rare **cancers** earlier”. The rest of the statements were kept the same.

To measure the overall attitude score, each item on the 26-item Genomic Orientation (GO) scale was rated on a 5-point Likert scale, ranging from "Very Unlikely" to "Very Likely." These responses were assigned values of -2, -1, 0, 1, and 2, respectively. Out of the 26 items, there were 16 hypothesized pessimism items, which were carefully reverse coded so that higher scores consistently reflected a more optimistic attitude. This ensured that all items contributed uniformly to the overall attitude score. The sum of all these values across the 26 items was calculated to derive the overall attitude score. By calculating the attitude scores across the 26 statements, the potential range of the overall attitude scores was determined to range from a minimum of -52 to a maximum of +52, with a negative score indicating a pessimistic attitude and a positive score reflecting an optimistic attitude. Scores around zero represent a neutral stance.

3.7.2 Independent Variables

The main independent variables or constructs being investigated in the key research questions of this study include:

- **Ambiguity Aversion:** Ambiguity aversion was assessed using a six-item Ambiguity Aversion (AA) scale, a validated scale from the medical literature, which captures cognitive, affective, and behavioral responses to uncertainty. It was developed to measure ambiguity aversion in the healthcare context, specifically regarding medical tests and treatments (Han et al., 2009). Each item was measured on a five-point Likert scale ranging from 1 ("Strongly Disagree") to 5 ("Strongly Agree").

Below are a series of statements that assess your attitudes towards conflicting opinions among medical experts regarding tests or treatments.

Please indicate the extent to which you agree or disagree with each statement.

	Strongly Disagree	Disagree	Neither Disagree nor Agree	Agree	Strongly Agree
Conflicting expert opinions about a medical test or treatment would lower my trust in the experts.	☐	☐	☐	☐	☐
I would not have confidence in a medical test or treatment if experts had conflicting opinions about it.	☐	☐	☐	☐	☐
Conflicting expert opinions about a medical test or treatment would make me upset.	☐	☐	☐	☐	☐
I would not be afraid of trying a medical test or treatment even if experts had conflicting opinions about it.	☐	☐	☐	☐	☐
If experts had conflicting opinions about a medical test or treatment, I would still be willing to try it.	☐	☐	☐	☐	☐
I would avoid making a decision about a medical test or treatment if experts had conflicting opinions about it.	☐	☐	☐	☐	☐

Figure 3-2: Ambiguity Aversion Scale

For data analysis, two statements—Statement 4 (“I would not be afraid of trying a medical test or treatment even if experts had conflicting opinions about it.”) and Statement 5 (“If experts had conflicting opinions about a medical test or treatment, I would still be willing to try it.”)—were reverse coded to ensure consistency in interpreting the scores. The other four statements were coded directly as 1, 2, 3, 4, and 5.

An overall “Ambiguity Aversion Score” was computed by summing the responses to all six items. Scores could potentially range from 6 to 30, with higher scores indicating greater ambiguity aversion. This computed score was used in subsequent analyses to explore its relationship with experts' attitudes toward MCED testing.

- Cancer Risk Perception:** Participants' perceptions of cancer risk were assessed using a six-item questionnaire adapted from the Health Information National Trends Survey (HINTS) (Harper et al., 2021). Each item was initially rated on a four-point Likert scale but was converted to a five-point Likert scale to maintain consistency with other scales in the survey. The response options ranged from "Strongly Disagree" to "Strongly Agree," and were assigned values from 1 to 5.

We are interested in understanding your perceptions regarding the risk of cancer.

Please indicate your level of agreement with the following statements

	Strongly Disagree	Disagree	Neither Disagree nor Agree	Agree	Strongly Agree
Cancer is most often caused by a person's behavior or lifestyle	☐	☐	☐	☐	☐
It seems like everything causes cancer	☐	☐	☐	☐	☐
I'd rather not know my chance of getting cancer	☐	☐	☐	☐	☐
There's not much you can do to lower your chances of getting cancer	☐	☐	☐	☐	☐
There are so many recommendations about cancer prevention, it's hard to know which ones to follow	☐	☐	☐	☐	☐
When I think about cancer, I automatically think about death	☐	☐	☐	☐	☐

Figure 3-3: Cancer Risk Perception Scale

An overall cancer risk perception score was computed by summing the responses to all six items. Scores could range from 6 to 30, with higher scores indicating greater perceptions of cancer risk. This score was used in subsequent analyses to examine its relationship with experts' attitudes toward MCED testing.

- Perceived Physician Competence:** Perceived physician competence was assessed using a five-item scale adapted from the Physicians' Perceived Competence Scale (Chambers et al., 2023). This scale measures participants' perceptions of how confident and competent physicians are in utilizing MCED tests. Each item was rated on a five-point Likert scale, ranging from "Strongly Disagree" to "Strongly Agree," with values assigned from 1 to 5.

This section is specifically for physicians, and we appreciate your participation. We aim to gauge your confidence in various aspects of Multi-Cancer Early Detection (MCED) testing for cancer screening.

Please indicate your level of confidence in educating, informing, and engaging patients about MCED testing, as well as your ability to explain and guide patients through different scenarios related to MCED blood test results.

	Strongly Disagree	Disagree	Neither Disagree nor Agree	Agree	Strongly Agree
I would be confident in my ability to educate patients about MCED testing for cancer screening.	☐	☐	☐	☐	☐
I would be confident in my capacity to explain false positive MCED blood test results to patients (e.g., a positive MCED blood test result that is not confirmed upon further diagnostic testing).	☐	☐	☐	☐	☐
I would be confident in my ability to engage patients in shared decision making about MCED blood testing.	☐	☐	☐	☐	☐
I would be confident in my capacity to explain false negative MCED blood test results to patients (e.g., a negative MCED blood test result followed by a cancer diagnosis upon further diagnostic testing).	☐	☐	☐	☐	☐
I would be confident in my ability to guide patients with an abnormal MCED blood test result through follow-up diagnostic testing.	☐	☐	☐	☐	☐

Figure 3-4: Perceived Physicians' Competence Scale

A total perceived physician competency score was computed by summing the responses to all five items. Scores could range from 5 to 25, with higher

scores indicating greater confidence in physicians' ability to effectively educate patients, explain test results, and guide them through the MCED testing process.

Table 3-2: Scales used to measure main outcome and independent variables

Scale	Based on Previous scale	Previously Validated	Reference
<i>Attitudes</i>	Genomic Orientation (GO) Scale	Yes, validated	(Horrow et al., 2021)
<i>Ambiguity Aversion</i>	AA-Med Scale	Yes, validated	(Han et al., 2009)
<i>Cancer Risk Perception</i>	Health Information National Trends Survey (HINTS)	Yes, validated	(Harper et al., 2021)
<i>Perceived Physicians' Competence</i>	Physicians' Perceived Competence Scale	Yes, validated	(Chambers et al., 2023)

3.7.3 Control Variables

Control variables include demographic and contextual factors that could influence the outcome but are not the primary focus of the research. These variables were controlled during multiple linear regression analysis to ensure that the relationships observed between the independent and outcome variables are not confounded by other factors. The control variables included:

- **Age:** Participants were asked about their age in the demographic section of the survey.
- **Sex:** Participants were asked to identify their sex in the demographic section.
- **Education:** Respondents were asked about their highest level of education, with options ranging from college/university attendance to doctoral degrees (PhD, MD).

- **Years of Professional Experience:** Participants provided the number of years they have worked in their respective fields.
- **Primary Field of Occupation:** Participants selected their primary field of occupation, including five categories such as Physician, Researcher/Academic, Industry (Pharmaceutical Industry, Health Insurance), Healthcare Professional or Other (with an option for specifying the "Other" category).
- **Application of Genetic Knowledge in Professional Capacity:** This was assessed with two items: whether participants apply their genetic knowledge professionally (yes or no?) and in which areas (e.g., clinical practice, academic/research environments, or policy environments, etc.).

Data Analysis

3.7.4 Data Cleaning

After the data was exported to SPSS, a thorough data cleaning process was done to enhance the reliability and accuracy of the dataset. First, responses with less than 90% progress were excluded to ensure that only complete data were analyzed. To identify and remove potentially fraudulent responses, Qualtrics' Relevant ID Fraud Score was utilized; any response with a score of 30 or higher, which indicates a high likelihood of bot activity, was eliminated.

Duplicate responses were also addressed using Qualtrics' Duplicate Score, where responses with scores of 75 or higher were flagged for review. In cases of duplication, each response was carefully examined. For instance, one participant initially indicated no awareness of MCED testing but later returned to complete the survey. In such cases, the first incomplete response was removed, and the second, more comprehensive submission was retained.

Additionally, for participants who reported awareness of MCED testing, responses completed in less than five minutes were excluded to ensure data quality and reduce the likelihood of inattentive or rushed answers.

For any remaining incomplete data, missing values were addressed using the mean imputation method, where the average of the available data for a given item was

calculated and used to replace the missing values. This approach helps maintain consistency across the dataset without significantly altering its statistical properties. For statements assessing Cancer Risk Perception, 0.6% of the data was missing, for statements assessing Ambiguity Aversion, 1.4% of the data was missing, and for statements assessing Physicians' Perceived Competencies, 3.2% of the data was missing. This missing data was added to the dataset using mean imputation method.

3.7.5 *Descriptive Frequencies*

Descriptive statistics were calculated and reported for all study variables using SPSS. For categorical variables (such as scales, education, field of occupation etc.), frequencies and percentages were calculated, while for continuous variables (such as age, years of professional experience, overall computed scores etc.), measures such as mean, median, and range (minimum and maximum) were reported.

Key variables, including attitude scores, ambiguity aversion, cancer risk perception, and perceived physician competencies, were summarized to examine data distribution and identify trends or patterns within the sample.

3.7.6 *Quantitative Data Analysis*

For quantitative analysis, the scores for attitudes, ambiguity aversion, cancer risk perception and perceived physician competencies were computed as mentioned previously. All quantitative analysis was done in SPSS.

Correlation analysis was conducted to assess the relationships between key variables. Pearson's correlation coefficients were calculated to examine the strength and direction of the linear relationships between attitudes toward MCED testing and main independent variables. Linear regression analysis was then used to explore these relationships further and test the influence of independent variables on the outcome variable (attitudes). Multiple linear regression was applied to determine how independent variables predict attitudes toward MCED testing when other variables are controlled.

Table 3-3: Table showing quantitative tests and sample size for each hypothesis

Hypotheses	Quantitative Tests Used	Control Variables	N (Sample Size)
Hypothesis 1: Ambiguity aversion predicts attitudes of experts.	Correlation, Linear Regression, and Multiple Linear Regression Analysis	Age, Gender, Education, and the application of genetic testing knowledge.	99
Hypothesis 2: Cancer risk perception is inversely associated with attitudes.	Correlation Analysis	-	99
Hypothesis 3: Physicians' Perceived Competence is positively associated with attitudes	Correlation Analysis	-	25 (physician subgroup)

3.7.7 Qualitative Data Analysis

For the open-ended questions in the survey, thematic analysis was used to analyze participants' qualitative responses. The qualitative questions were:

- As a stakeholder/expert from your field, how do you think policymakers should address potential issues with Multi-Cancer Early Detection (MCED) testing?
- Any other comments/opinions?

The responses from the qualitative questions were extracted and organized in separate tables in a Google Document (Appendix B: Organization and Open Coding of the Qualitative Data), along with associated age, years of working experience, highest/current education, and field of occupation data.

The responses were read thoroughly to get an overall sense of the data, followed by Open Coding to highlight and tag sections of data, identifying recurring concepts, key phrases, and initial codes for later categorization. Then, Miro was used for Axial Coding

in which codes were clustered into broader themes. Then, codes were nested into categories and subcategories, which was followed by establishing relationships between codes, and visualizing connections (Appendix B: Miro Showing Emerging Themes, Subcategories, and Connections). Then, Selective Coding was done to connect categories and subcategories into higher-level themes. After theme development, an In-Depth Analysis was done by returning to the data to deepen each theme, identifying patterns, contrasts, and nuanced perspectives.

This mixed-methods approach ensured a comprehensive analysis of the data, combining statistical insights with a deep understanding of the participants' views on how potential issues implementation of MCED testing can be addressed.



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Chapter 4:

RESULTS

4.1 *Descriptive Statistics*

After removal of carefully assessed duplicated responses, 138 healthcare expert responses remained. Of these, 27.5% (38) respondents had never heard or read anything about MCED testing and were therefore excluded from further data analysis.

From the remaining 100 respondents who had MCED awareness, responses that were completed in less than three minutes were removed. This resulted in a final sample of 99 experts, whose responses were analyzed for descriptive frequencies and all subsequent data analyses.

Initially, we aimed for a sample size of 385, based on standard sample size calculations for a target population of unknown size with unknown prevalence. However, due to time constraints and challenges in reaching enough participants, the final number of valid responses included in the analysis was 99.

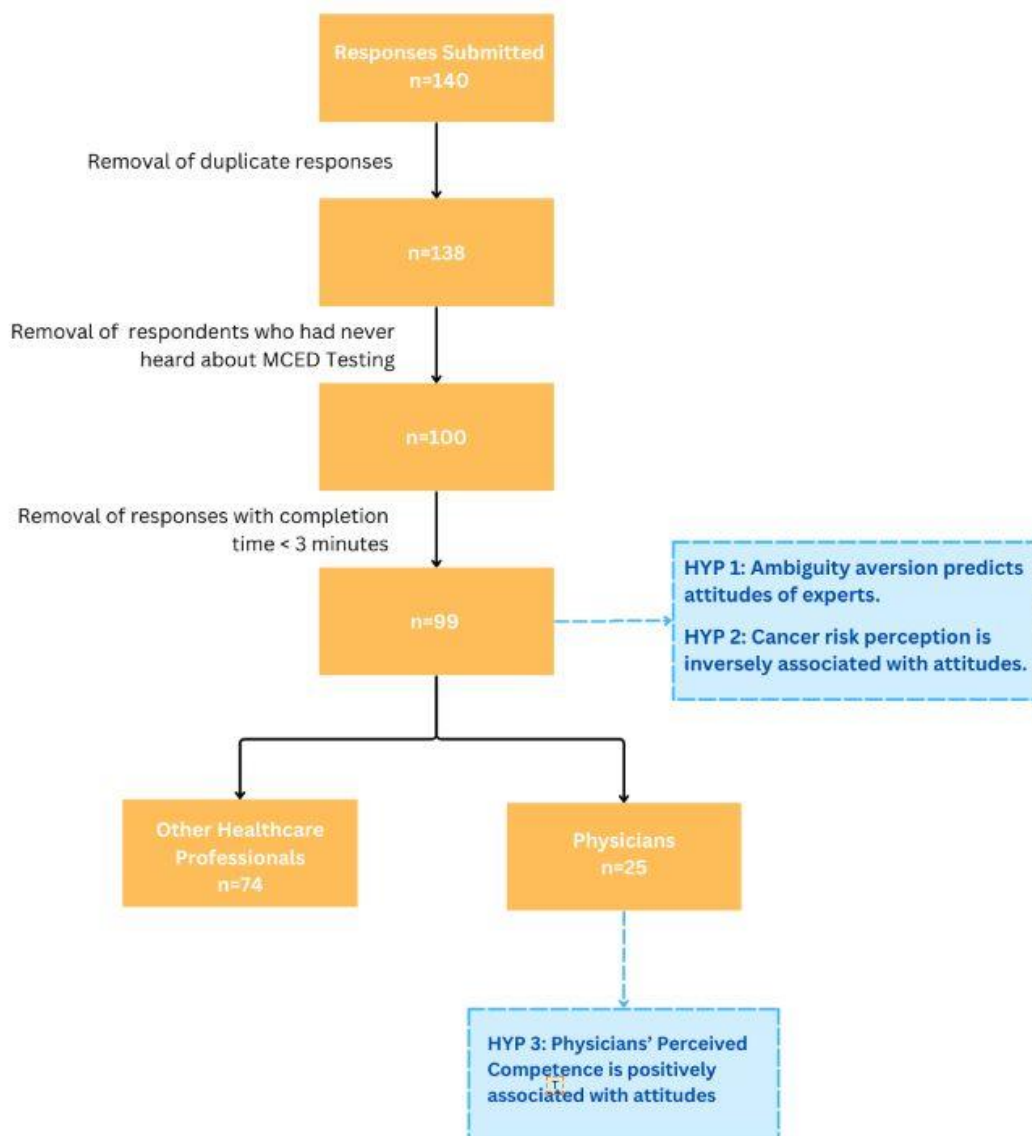


Figure 4-1: Flowchart of the study population

4.1.1 Overall Demographic Statistics

The average age of participants was 37.2 years, with a range from 19 to 75. A majority, 58.8% (58), were female. Regarding educational background, 48.5% (48) held a Doctoral degree (PhD or professional doctorate such as MD), 28.3% (28) had a Master's degree, 18.2% (18) possessed a Bachelor's degree, and 3.0% (3) had attended College/University. An additional 2.0% (2) selected "other," specifying they were either medical students/intern doctors or held multiple degrees, including an MPH and MBA. Additionally, the mean years of professional experience across all participants was 12 years, with a range from 0 to 45 years, and a median of 6 years.

Table 4-1: Frequency Distribution of Demographic Variables

Variable	Descriptive Statistics / Scale and frequencies				N
Age	Mean	SD	Min	Max	99
	37.2	13.9	19.0	75.0	
Gender	Male	Female		Other	99
	58	39		2	
Highest/Current Education Level	Attended College/University	Bachelor's Degree	Master's Degree	Professional Doctorate (PhD, MD etc)	97
	3	18	28	48	
Years of Professional Experience	Mean	SD	Min	Max	99
	12.1	12.2	0.0	45.0	

Regarding personal cancer experiences, 49.5% (49) reported having family members with cancer, 29.3% (29) had acquaintances in their social circle who had cancer, and 5.1% (5) had personally experienced cancer.

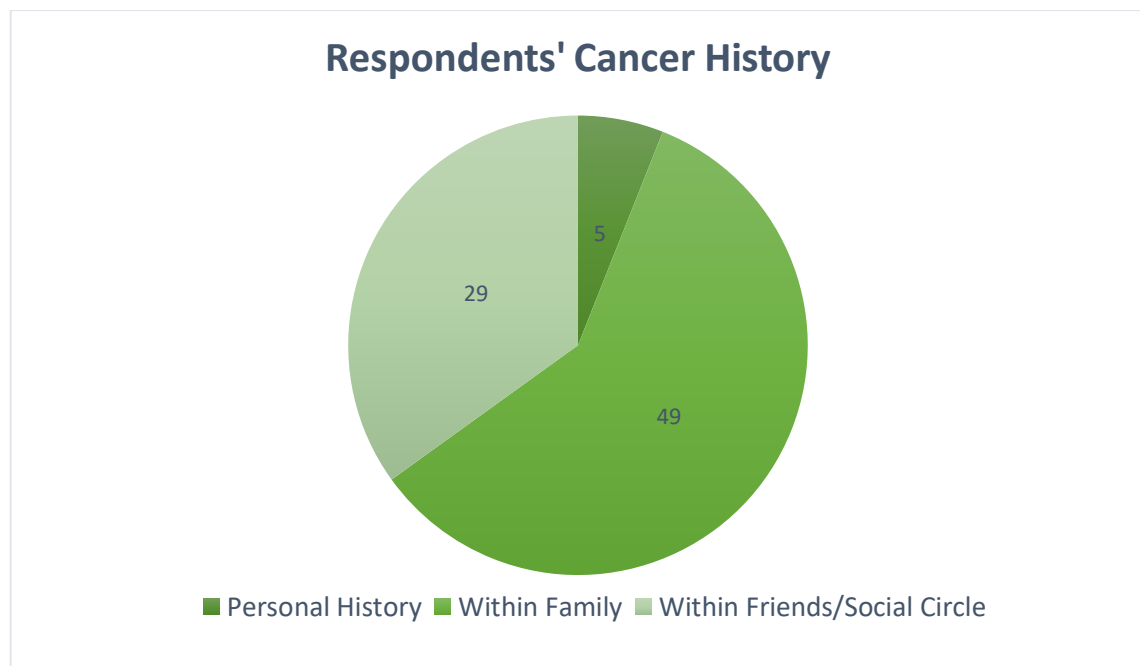


Figure 4-2: Pie chart showing number of respondents with cancer history (personal, within family, and within social circle (n=99)

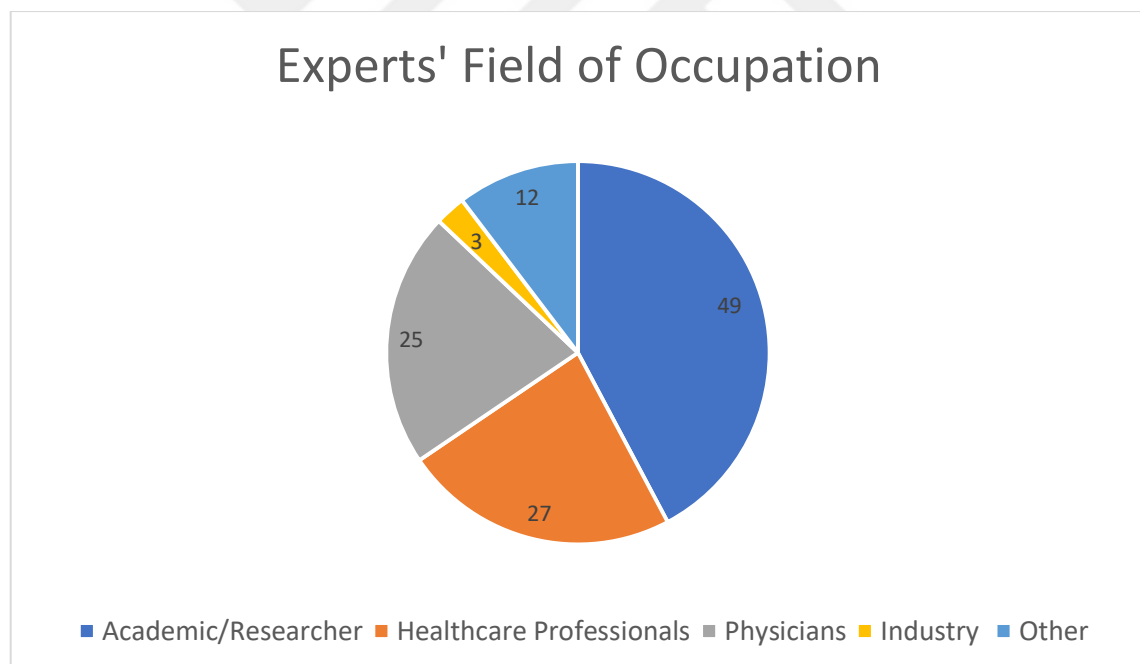


Figure 4-3: Pie chart showing distribution of experts' fields of occupation (n=99)

In terms of professional roles, 49.5% (49) were academicians/researchers, 27.3% (27) were healthcare professionals, 25.3% (25) were physicians, and 3.0% (3) worked in industries such as pharmaceuticals or health insurance. Moreover, 12% (12) selected “other” as their occupation, including roles in biotechnology, education technology, civil

services, biomedical sciences, engineering, and public health. Physicians' Demographic Statistics

Overall, the sample has 25 physicians. Their mean age was 42.3 years and mean years spent practicing as a physician was 14.7 years.

Table 4-2. Frequency Distribution of Physicians' Demographic Variables

Variables	Descriptive Statistics / Scale and frequencies				N
Age	Mean	SD	Min	Max	25
	42.3	24.0	75.0	16.1	
Gender	Male		Female		25
	12		13		
Years of Practice	Mean	SD	Min	Max	25
	14.7	15.2	0.0	45	

Among the physicians, 5 specialized in Surgery (General, Gynecological, Chest, etc.), 4 in Family Medicine, 5 in Internal Medicine, 1 in Pediatrics, and 2 in Oncology. Others specialized in fields such as Urology, Radiology, Anesthesiology, Algology, Community Health and Nutrition, and Molecular Cancer Biology. Majority of the physicians were from surgical, clinical, and basic sciences.

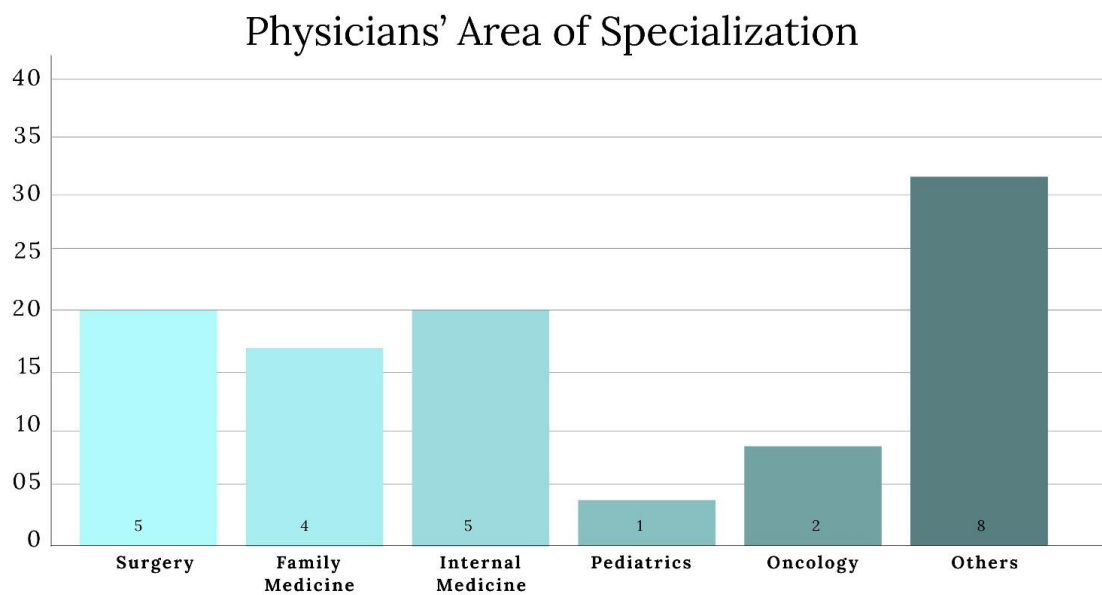


Figure 4-4: Bar graph showing frequencies of physicians' area of specialization (n=25)

In terms of work setting, 52.0% (13) of physicians worked in academic medical schools, 20.0% (5) were employed at non-university medical centers, 20.0% (5) worked in community hospitals, 16.0% (4) had private practices, and 16.0% (4) worked with government and non-governmental health authorities. The mean number of years practicing medicine was 14.8 years, with a range from 0 to 45 years, and a median of 8.5 years.

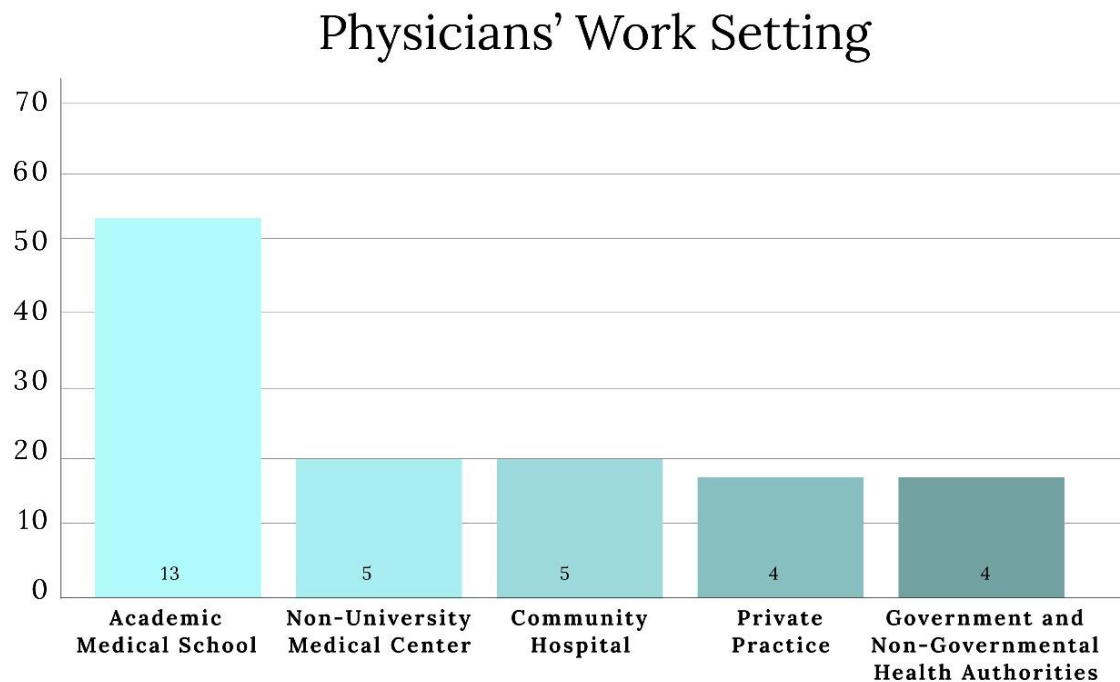


Figure 4-5: Bar graph depicting frequencies of physicians' work settings (n=25)

4.1.2 Awareness and Application of Genetic Tests

In response to the question “From which of the following sources did you hear or read anything about genetic tests that scan a person’s entire genetic makeup for potential health risks (e.g. tests marketed direct to consumers such as 23andMe, deCODEme, Navigenics)?”, 53.5% (53) responded Professional Communities (professional organization, professional or scientific meeting, medical or scientific journal etc.), 47.5% (47) responded Media Sources (television, internet, magazine article, newspaper article, radio etc.), 39.4% (39) responded Healthcare Sources (health professional, patients etc.), 9.1% (9) responded Directly from a company selling DTC genetic tests, and 3.0% (3) responded from other sources, which included online communities, family members, and undergraduate university courses.

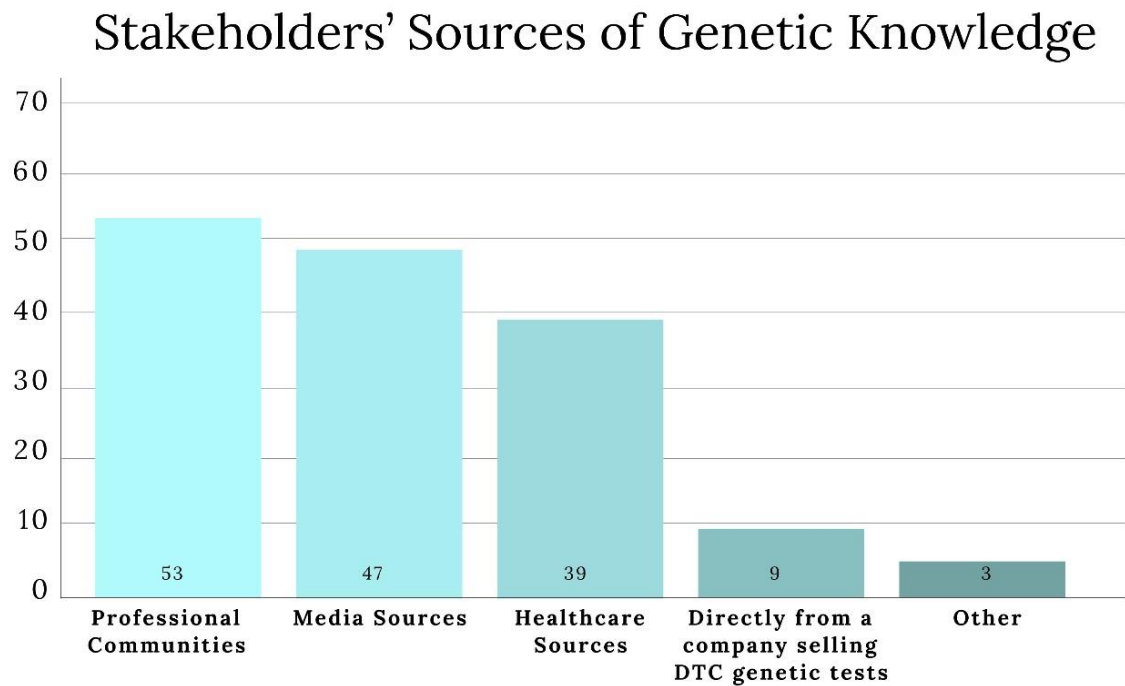


Figure 4-6: Bar graph showing experts' source of genetic knowledge (n=99)

For the question “Do you apply your knowledge of genetic tests in any professional capacity?”, 49.5% (49) responded Yes while 46.5% (46) responded No. For those who responded Yes, they were asked where they applied their knowledge of genetic testing. 73.4% (36) responded Academic/Research Environment, 42.8% (21) responded Clinical Practice, 28.6% (14) responded Public Education and Engagement, 16.5% (8) responded Biotechnology/Pharmaceutical Industry, and 6.1% (3) responded Policy Development.

Stakeholders' Application Area of Genetic Knowledge

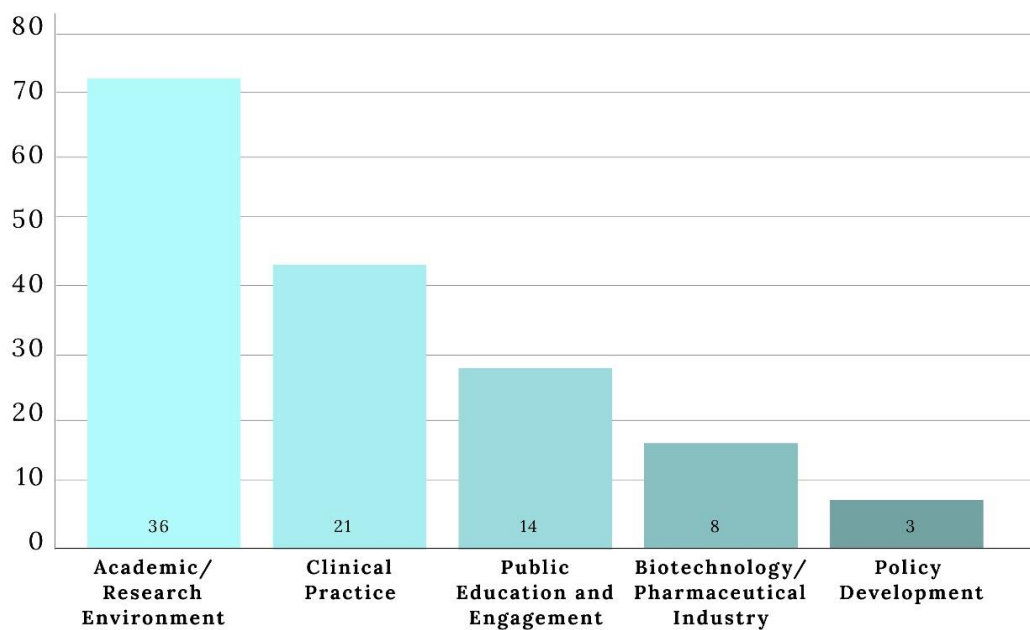


Figure 4-7: Bar graph showing the areas where experts apply their knowledge of genetic testing (n=99)

4.1.3 Implementation-related Preferences

In response to the question "In your opinion, where should MCED testing be implemented?", most participants expressed support for implementation in the hospital context, with 67.7% (67) favoring its use as a diagnostic test for patients under investigation by a specialist. A close 65.6% (62) supported its application in primary and preventive care, as a diagnostic tool for primary care physicians. Additionally, 45.5% (45) advocated for its use in population screening, either to replace or complement current cancer screening practices, while 16.2% (16) suggested that MCED testing could be made available over-the-counter, for purchase by individuals without a prescription.

Stakeholders' Implementation Setting Preferences

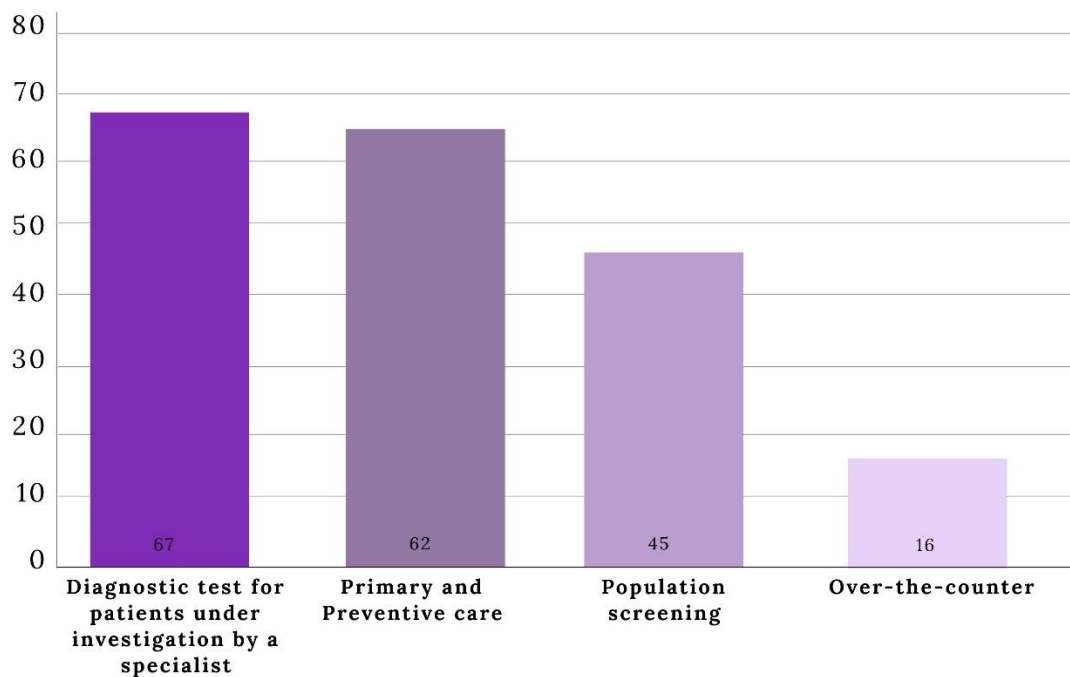


Figure 4-8: Bar graph showing experts' implementation setting preferences of MCED testing (n=99)

When asked "Whom should MCED testing be done for?", 78.8% (78) believed it should be offered to individuals with cancer risk factors. About half, 50.5% (50), supported its use for symptomatic patients, while 39.4% (39) agreed it should be available upon patient request. Furthermore, 31.3% (31) indicated it should be used for specific age groups, and 22.2% (22) believed it should be universally available.

Stakeholders' Perspectives on Eligibility of MCED Testing

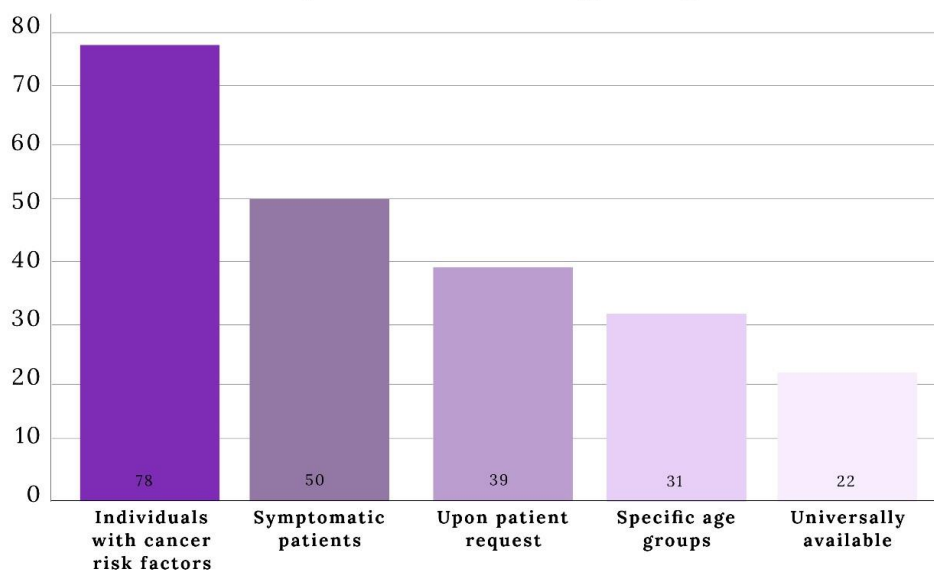


Figure 4-9: Bar graph showing experts' preferences on who should MCED testing be done for (n=99)

When asked "What policy factors are most important when applying MCED testing on a larger scale?", 85.9% (85) emphasized the importance of affordability, while 73.7% (73) highlighted accessibility. Other key factors included public awareness and communication (62.6%, 62), healthcare equity (61.6%, 61), and research and development (54.5%, 54). Data protection and storage were also seen as important by 46.5% (46), with privacy and security (43.4%, 43), health system capacity (40.4%, 40), personnel training (33.3%, 33), and global collaboration (31.3%, 31) following closely.

What policy factors are most important when applying MCED testing on a larger scale?

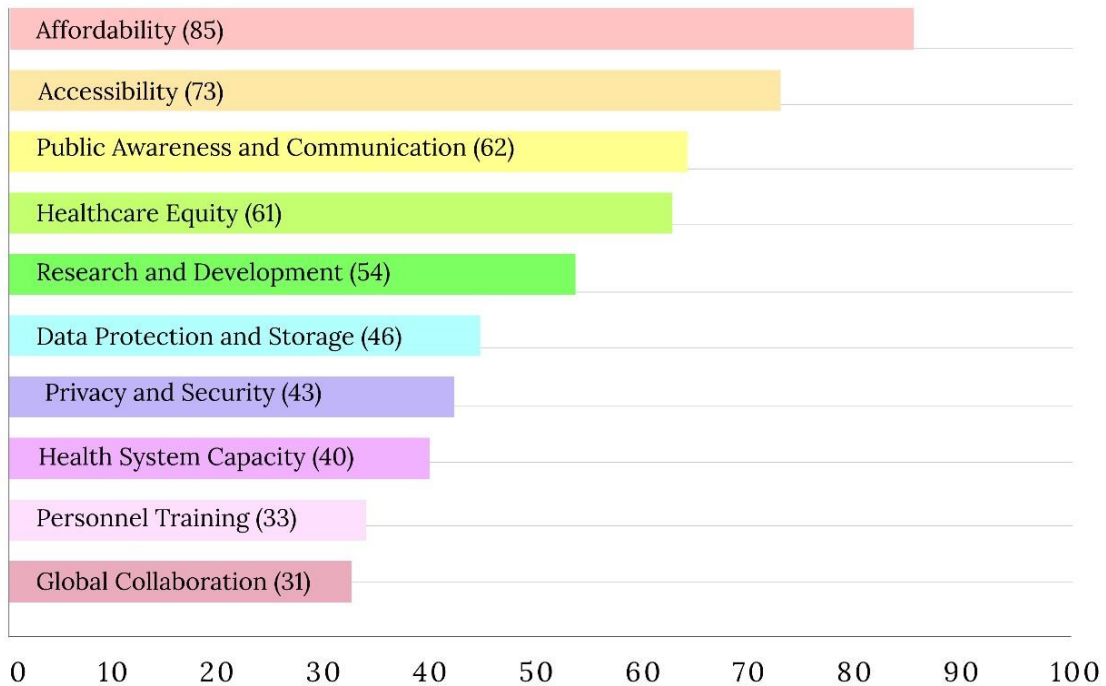


Figure 4-10: Most important policy factors to consider when implementing MCED testing according to experts (n=99)

Regarding health insurance coverage, 87.9% (87) of participants believed that MCED tests should be covered by health insurance policies for eligible individuals, and 62.6% (62) supported government involvement in promoting the use of MCED tests. Finally, when asked whether MCED testing would increase practice variation in healthcare, 65.3% (65) agreed.

4.1.4 Attitudes

Table 4-3: Frequency distribution of items in the Attitude scale

Statement	Very Unlikely	Unlikely	Neither Unlikely Nor Likely	Likely	Very Likely
1. Help doctors choose the best	3.0% (3)	10.1% (10)	5.1% (5)	56.6% (56)	25.3% (25)

drugs for patients					
2. Increase the number of unnecessary tests	4.0% (4)	37.4% (37)	12.1% (12)	34.3% (34)	12.1% (12)
3. Help prevent late detection of common cancers	2.0% (2)	4.0% (4)	7.1% (7)	54.5% (54)	32.3% (32)
4. Distract from disease prevention efforts we know work well	5.1% (5)	27.3% (27)	30.3% (30)	30.3% (30)	7.1% (7)
5. Help doctors diagnose rare cancers earlier	1.0% (1)	9.1% (9)	10.1% (10)	52.5% (52)	27.3% (27)
6. Distract doctors from looking for non-genetic causes of disease	7.1% (7)	37.4% (37)	25.3% (25)	28.3% (28)	2.0% (2)
7. Help people live longer	2.0% (2)	12.1% (12)	25.3% (25)	45.5% (45)	15.2% (15)
8. Divert healthcare resources that could be better	2.0% (2)	27.3% (27)	20.2% (20)	41.4% (41)	9.1% (9)

used for other purposes					
9. Give patients more control over their health	4.0% (4)	8.1% (8)	22.2% (22)	56.6% (56)	10.1% (10)
10. Create a burden of worry where there wasn't one before	4.0% (4)	27.3% (27)	14.1% (14)	46.5% (46)	8.1% (8)
11. Be difficult for many patients to understand	2.0% (2)	22.2% (22)	18.2% (18)	38.4% (38)	19.2% (19)
12. Help doctors focus on the unique needs and goals of each patient	1.0% (1)	9.1% (9)	9.1% (9)	65.7% (67)	15.2% (15)
13. Make it harder for doctors to engage each patient as a person	8.1% (8)	51.5% (51)	17.2% (17)	15.2% (15)	8.1% (8)
14. Increase the cost of healthcare	3.0% (3)	11.1% (11)	15.2% (15)	48.5% (48)	22.2% (22)
15. Increase the cost of prescription drugs	4.0% (4)	32.3% (32)	20.2% (20)	30.3% (30)	13.1% (13)

16. Increase inequality in healthcare	6.1% (6)	23.2% (23)	20.2% (20)	34.3% (34)	16.2% (16)
17. Create new forms of discrimination	5.1% (5)	31.3% (31)	18.2% (18)	31.3% (31)	14.1% (14)
18. Be too expensive for most people	0% (0)	9.1% (9)	14.1% (14)	51.5% (51)	25.3% (25)
19. Make it more difficult for patients to receive medical care they need	7.1% (7)	46.5% (46)	19.2% (19)	20.2% (20)	7.1% (7)
20. Be a standard part of general medical checkups	12.1% (12)	24.2% (24)	10.1% (10)	42.4% (42)	11.1% (11)
21. Not be available in most hospitals and clinics	3.0% (3)	11.1% (11)	17.2% (17)	51.5% (51)	17.2% (17)
22. Benefit nearly all aspects of medicine	4.0% (4)	15.2% (15)	20.2% (20)	47.5% (47)	13.1% (13)
23. Be beneficial to you	2.0% (2)	10.1% (10)	18.2% (18)	49.5% (49)	20.2% (20)
24. Cause you harm	27.3% (27)	41.4% (41)	23.2% (23)	7.1% (7)	1.0% (1)
25. Do a lot of good	4.0% (4)	3.0% (3)	19.2% (19)	51.5% (51)	22.2% (22)

26. Create many problems	14.1% (14)	40.0% (40)	23.2% (23)	19.2% (19)	3.0% (3)
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Items were divided into 6 domains: Medical benefit or harm (items 1-8), impact on patient experience (items 9-13), health disparities and access (items 14-19), progress toward implementation (items 20-22), personal impact (items 23-24), and overall evaluation (items 25-26).

Medical Benefit or Harm (Items 1-8):

Participants generally perceived MCED testing as beneficial in improving cancer outcomes. 81.9% (81) found it likely or very likely to help doctors choose the best drugs for patients. Similarly, 86.8% (86) agreed it would help prevent late detection of common cancers, and 79.8% (79) believed it would aid in diagnosing rare cancers earlier. However, concerns about potential drawbacks were noted, with 37.4% finding it likely to increase unnecessary tests and 41.4% believing it might likely divert healthcare resources, highlighting a tension between anticipated benefits and potential risks.

Impact on Patient Experience (Items 9-13):

MCED testing was seen as empowering for patients, with 66.7% (66) agreeing it would give patients more control over their health. Additionally, 80.9% (80) believed it would help doctors focus on the unique needs and goals of each patient. A notable portion, 54.6% (54), expressed worries about the potential burden of increased anxiety, and 57.6% (57) highlighted difficulties in understanding the test, emphasizing the need for clear communication to address these concerns.

Health Disparities and Access (Items 14-19):

Participants recognized the potential financial and social implications of MCED testing. Majority (73.7%, 73) agreed it might be too expensive for most people, and 50.5% (50) felt it could increase healthcare costs. Concerns about increasing inequalities (50.5%, 50) and creating new forms of discrimination (45.4%, 45) were also noted, though fewer participants (27.3%, 27) believed it would make it harder for patients to receive necessary care.

Progress Toward Implementation (Items 20-22):

While 53.5% (53) considered it likely or very likely that MCED testing would become a standard part of general checkups, 68.7% (68) felt it might not be widely

available in hospitals and clinics. Still, 60.6% (60) agreed it would benefit nearly all aspects of medicine.

Personal Impact (Items 23-24):

Participants were optimistic about the personal benefits of MCED testing, with 69.7% (69) finding it likely or very likely to be personally beneficial. Conversely, 68.7% (68) disagreed that it would cause them harm.

Overall Evaluation (Items 25-26):

Overall, 73.7% (73) believed MCED testing would do a lot of good, whereas 54.1% (54) disagreed it would create many problems. This reflects an overall positive outlook on the potential of MCED testing despite some reservations.

Afterwards, statements from the GO scale were recoded to compute Attitude Score. The 10 optimism statements were coded normally (-2,-1,0,1,2), while the 16 pessimism statements were reverse coded (2,1,0,-1,-2). The attitude score could range between -52 to 52, with more positive score depicting more optimistic attitudes and the more negative scores depicting more negative attitudes. The descriptive statistics are reported below:

Table 4-4: Descriptive statistics of Attitude Score

Statistics

Attitude_Score

N	Valid	99
	Missing	0
Mean		5.1212
Median		6.0000
Std. Deviation		13.04801
Range		60.00
Minimum		-29.00
Maximum		31.00

Table 4-5: Mean attitude scores based on gender.

Report

Attitude Score

Gender_recoded	Mean	N	Std. Deviation
Male	3.2308	39	13.63328
Female	6.5345	58	12.17593
Total	5.2062	97	12.81596

Table 4-6: Distribution of Attitude Scores based on education

Report			
Attitude Score			
Highest/Current Academic Degree or Level of Education Completed			
	Mean	N	Std. Deviation
Bachelor's degree	12.4444	18	12.91248
Master's degree	3.9286	28	12.90687
Doctoral degree (PhD, professional doctorate like MD etc.)	2.6458	48	12.80872
Attended College/University	7.0000	3	6.24500
Other	12.5000	2	12.02082
Total	5.1212	99	13.04801

Table 4-7: Descriptive statistics of attitude scores based on the application of genetic test knowledge in a professional capacity.

Group Statistics					
Do you apply your knowledge of genetic tests in any professional capacity?		N	Mean	Std. Deviation	Std. Error Mean
Attitude Score	Yes	49	5.6327	13.88749	1.98393
	No	46	4.2174	12.13977	1.78991

Table 4-8: Descriptive statistics of attitude scores based on history of cancer (personal/within family/within friends)

Group Statistics					
History of Cancer (Personal/Family/Friend)		N	Mean	Std. Deviation	Std. Error Mean
Attitude Score	Yes	65	4.7077	13.28500	1.64780
	No	34	5.9118	12.74070	2.18501

The Attitude Score had a mean of 5.1, median of 6, and ranged between -29 and 31. Female participants, on average, had higher attitude scores (6.53) than male participants (3.23). The attitude scores for both groups varied considerably, with male

participants having more variation in their scores ($SD = 13.63$) compared to female participants ($SD = 12.18$). Attitude scores also varied across educational levels, with individuals holding a Bachelor's degree having the highest mean (12.44), followed by those with a Master's (3.93) and Doctoral degrees (2.65). The mean attitude score was higher for those who apply their knowledge of genetic tests ($M = 5.63$) compared to those who do not ($M = 4.22$). The mean attitude score was also higher for people who did not have any history of personal, or family/friends related history of cancer (5.91) as opposed to those who did (4.70).

A reliability analysis was conducted to assess the internal consistency of the Attitude scale. The results showed a high level of reliability (Cronbach's $\alpha = .872$), indicating strong consistency among the 26 items.

Table 4-9: Reliability analysis of the Attitude Scale

Reliability Statistics		
Cronbach's Alpha	Cronbach's Alpha Based on Standardized Items	N of Items
.872	.874	26

4.1.5 Ambiguity Aversion

Table 4-10: Frequency distribution of items in the Ambiguity Aversion Scale

Statement	Strongly Disagree	Disagree	Neither Disagree nor Agree	Agree	Strongly Agree
Conflicting expert opinions about a medical test or treatment would lower my trust in the experts.	5.1% (5)	36.4% (36)	21.2.0% (21)	29.3% (29)	8.1% (8)
I would not have confidence in a	4% (4)	20.2% (20)	21.2% (21)	46.5% (46)	8.1% (8)

medical test or treatment if experts had conflicting opinions about it.					
Conflicting expert opinions about a medical test or treatment would make me upset.	1.0% (1)	25.3% (25)	29.3% (29)	37.4% (37)	7.1% (7)
I would not be afraid of trying a medical test or treatment even if experts had conflicting opinions about it.	7.1% (7)	23.2% (23)	24.2% (24)	42.4% (42)	3.0% (3)
If experts had conflicting opinions about a medical test or treatment, I would still be willing to try it.	6.1% (6)	15.2% (15)	24.2% (24)	51.5% (51)	3.0% (3)
I would avoid making a decision about a medical test or treatment if experts had conflicting opinions about it.	1.0% (1)	34.3% (34)	25.3% (25)	31.3% (31)	8.1% (8)

The descriptive frequencies for the ambiguity aversion statements reveal that a notable proportion of participants, 46.5% (46), agreed that they would lack confidence in a medical test or treatment if experts held conflicting opinions, with an additional 8.1% (8) strongly agreeing. Similarly, 37.4% (37) agreed that conflicting expert opinions would make them upset, though fewer participants, 7.1% (7), strongly agreed with this sentiment.

Interestingly, while trust and confidence appeared to be impacted by conflicting opinions, a significant proportion of participants expressed willingness to proceed with a medical test despite such conflicts. Over half, 51.5% (51), agreed they would still be willing to try a test under these circumstances, and only 6.1% (6) strongly disagreed. Furthermore, 42.4% (42) agreed that they would not be afraid of trying a test even with conflicting expert opinions, indicating a nuanced attitude where willingness to act persists despite potential concerns.

Lastly, responses to avoidance in decision-making showed mixed tendencies: 31.3% (31) agreed they would avoid making a decision if experts had conflicting opinions, but a notable 34.3% (34) disagreed with this statement. Similarly, 29.3% (29) agreed that conflicting expert opinions about a medical test or treatment would lower their trust in the experts while 35.4% (35) disagreed with this statement. These findings highlight the complexity of attitudes toward ambiguity, with some participants demonstrating hesitation while others exhibit resilience in the face of conflicting information.

After reporting frequencies, the statements from the Ambiguity Aversion (AA) scale were re-coded, while paying particular attention to reverse code statements 4 and 5. The Ambiguity Aversion (AA) Score was then computed in SPSS which could range between 6 and 30, with a higher score showing greater levels of ambiguity aversion. The descriptive statistics for the AA score are reported below:

Table 4-11: Descriptive statistics for the Ambiguity Aversion Scale

Item Statistics			
	Mean	Std. Deviation	N
Statement 1	2.9899	1.09260	99
Statement 2	3.3434	1.02182	99
Statement 3	3.2424	.94859	99
Statement 4 (Reverse-coded)	2.8889	1.02906	99
Statement 5 (Reverse-coded)	2.6970	.97368	99
Statement 6	3.1111	1.00903	99

Table 4-12: Descriptive Statistics of Ambiguity Aversion Score

Statistics

AA_Score

N	Valid	99
	Missing	0
Mean		18.2727
Median		18.0000
Std. Deviation		3.70278
Range		20.00
Minimum		10.00
Maximum		30.00

The mean AA score was 18.3, and the median score was 18.0, with the AA score fluctuating between 10 and 30. Male participants had a mean ambiguity aversion score of 17.62, while female participants had a mean score of 18.72.

Table 4-13: Mean ambiguity aversion scores by gender.

Report

Ambiguity Aversion Score

Gender_recoded	Mean	N	Std. Deviation
Male	17.6154	39	3.94445
Female	18.7241	58	3.55801
Total	18.2784	97	3.73815

The Cronbach's Alpha for the ambiguity aversion scale was 0.661, suggesting moderate internal consistency.

Table 4-14: Reliability statistics for the Ambiguity Aversion Scale

Reliability Statistics

Cronbach's Alpha	Cronbach's Alpha Based on Standardized Items	N of Items
.661	.662	6

4.1.6 Cancer Risk Perception

Table 4-15: Frequency distribution of items in Cancer Risk Perception Scale

Statement	Strongly Disagree	Disagree	Neither Disagree nor Agree	Agree	Strongly Agree
Cancer is most often caused by a person's behavior or lifestyle	6.1% (6)	28.3% (28)	23.2% (23)	39.4% (39)	3.0% (3)
It seems like everything causes cancer	12.1% (12)	45.5% (45)	23.2% (23)	16.2% (16)	3.0% (3)
I'd rather not know my chance of getting cancer	18.2% (18)	34.3% (34)	16.2% (16)	24.2% (24)	7.1% (7)
There's not much you can do to lower your chances of getting cancer	23.2% (23)	51.5% (51)	9.1% (9)	14.1% (14)	2.0% (2)
There are so many recommendations about cancer prevention, it's hard to know which ones to follow	11.1% (11)	28.3% (28)	16.2% (16)	38.4% (38)	6.1% (6)
When I think about cancer, I automatically think about death	8.1% (8)	32.3% (32)	15.2% (15)	33.3% (33)	11.1% (9)

The descriptive frequencies for the cancer risk perception statements reveal varying levels of agreement and disagreement among participants. A notable proportion, 39.4% (39), agreed that cancer is most often caused by a person's behavior or lifestyle, while 28.3% (28) disagreed, showing diverse beliefs about the role of lifestyle in cancer causation. Similarly, while 45.5% (45) disagreed with the statement "It seems like everything causes cancer," a smaller group (16.2%, 16) agreed, reflecting contrasting perceptions. Moreover, 34.3% (34) disagreed with the statement "I'd rather not know my chance of getting cancer," but a notable 24.2% (24) agreed, indicating that a subset of participants may prefer to avoid this type of knowledge.

Participants largely rejected the notion that there is little one can do to lower cancer risk, with 51.5% (51) disagreeing and only 14.1% (14) agreeing. However, 38.4% (38) agreed that the abundance of cancer prevention recommendations can make it difficult to know which to follow, reflecting potential confusion or information overload.

Lastly, when considering the emotional impact of cancer, 33.3% (33) agreed that they automatically think about death when considering cancer, while 32.3% (32) disagreed, showcasing contrasting emotional associations with the disease. These findings illustrate the complex and multifaceted perceptions participants hold about cancer risk and prevention.

Afterwards, the statements were recoded in SPSS to compute a score for Cancer Risk Perception, which could be between 6 and 30, with a higher score showing greater levels of cancer risk perception. The descriptive statistics are shown below:

Table 4-16: Descriptive statistics of Cancer Risk Perception Scale

Item Statistics			
	Mean	Std. Deviation	N
Cancer is most often caused by a person's behavior or lifestyle	3.09	1.221	99
It seems like everything causes cancer	2.80	1.370	99
I'd rather not know my chance of getting cancer	2.69	1.307	99
There's not much you can do to lower your chances of getting cancer	2.22	1.112	99

it's hard to know which ones to follow	2.88	1.198	99
When I think about cancer, I automatically think about death	2.93	1.172	99

Table 4-17: Descriptive statistics of Cancer Risk Perception Score

Statistics

Cancer Risk Perception Score

N	Valid	99
	Missing	0
Mean		16.5253
Median		16.0000
Std. Deviation		3.55236
Range		16.00
Minimum		8.00
Maximum		24.00

The Cancer Risk Perception score had a mean of 16.5, median of 16, and it fluctuated between 8 and 24.

The reliability of the Cancer Risk Perception scale was assessed using Cronbach's alpha, which resulted in a value of 0.463, indicating relatively low internal consistency. This suggests that the scale may require further refinement to improve its reliability.

Table 4-18: Reliability statistics for Cancer Risk Perception Scale

Reliability Statistics

Cronbach's Alpha	Cronbach's Alpha Based on Standardized Items	N of Items
.463	.463	6

Upon examining the item-total correlations, it was found that some items displayed weak correlations with the overall scale. Specifically, the items "Cancer is most often caused by a person's behavior or lifestyle" (corrected item-total correlation = 0.163) and "When I think about cancer, I automatically think about death" (corrected item-total correlation = 0.110) had the weakest associations.

Only two statements showed stronger correlations: "There are so many recommendations about cancer prevention, it's hard to know which ones to follow" (corrected item-total correlation = 0.405) and "I'd rather not know my chance of getting cancer" (corrected item-total correlation = 0.301), contributing more effectively to the scale.

Table 4-19: Item-total Statistics for Cancer Risk Perception Scale

Item-Total Statistics					
	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Squared Multiple Correlation	Cronbach's Alpha if Item Deleted
Cancer is most often caused by a person's behavior or lifestyle	13.52	11.987	.163	.079	.455
It seems like everything causes cancer	13.81	11.157	.199	.123	.439
I'd rather not know my chance of getting cancer	13.92	10.585	.301	.118	.375
There's not much you can do to lower your chances of getting cancer	14.38	11.933	.219	.120	.424
There are so many recommendations about cancer prevention, it's hard to know which ones to follow	13.73	10.302	.405	.172	.318
When I think about cancer, I automatically think about death	13.68	12.568	.110	.062	.480

4.1.7 Physicians' Perceived Competence

Table 4-20: Frequency distribution of items in Physicians' Perceived Competence Scale

Statement	Strongly Disagree	Disagree	Neither Disagree nor Agree	Agree	Strongly Agree

I would be confident in my ability to educate patients about MCED testing for cancer screening.	4.0% (1)	8.0% (2)	8.0% (2)	48.0% (12)	32.0% (8)
I would be confident in my capacity to explain false positive MCED blood test results to patients.	0% (0)	8.0% (2)	12.0% (3)	68.0% (17)	12.0% (3)
I would be confident in my ability to engage patients in shared decision making about MCED blood testing.	0% (0)	16.0% (4)	12.0% (3)	60.0% (15)	12.0% (3)
I would be confident in my capacity to explain false negative MCED blood test results to patients.	0% (0)	8.0% (2)	24.0% (6)	56.0% (14)	12.0% (3)
I would be confident in my ability to guide patients with an abnormal MCED blood test result through follow-up diagnostic testing.	0% (0)	12.0% (3)	12.0% (3)	56.0% (14)	20.0% (5)

The descriptive analysis of physicians' perceived competence regarding MCED testing revealed generally high levels of confidence among participants. Most physicians, 48.0% (12), agreed, and 32.0% (8) strongly agreed that they could effectively educate

patients about MCED testing for cancer screening, with only 12.0% (3) expressing disagreement or neutrality.

Confidence was high in explaining false positive and false negative MCED test results. 68.0% (17) agreed and 12.0% (3) strongly agreed that they felt confident in their capacity to explain false positive results while 56.0% (14) agreed, and 12.0% (3) strongly agreed they felt capable of explaining false negative results to patients.

Guiding patients through follow-up diagnostic testing after abnormal MCED results also garnered substantial confidence, with 56.0% (14) agreeing and 20.0% (5) strongly agreeing. Similarly, 60.0% (15) agreed, and 12.0% (3) strongly agreed that they could engage patients in shared decision-making about MCED testing.

Overall, these findings indicate that physicians generally feel confident in their competencies related to MCED testing, though some variability exists in engaging patients in shared decision making about MCED testing.

For computation of Physicians' Perceived Competencies score, all the statements were recoded and summed. The PPC score could range between 5 and 30, with higher scores showing higher confidence of physicians in their competencies. The descriptive statistics are reported below:

Table 4-21: Descriptive statistics for Physicians' Perceived Competence Scale Items

Item Statistics			
	Mean	Std. Deviation	N
Statement_1	3.9600	1.05987	25
Statement_2	3.8400	.74610	25
Statement_3	3.6800	.90000	25
Statement_4	3.7200	.79162	25
Statement_5	3.8400	.89815	25

Table 4-22: Descriptive statistics of Physicians' Perceived Competence Score

Statistics

Physicians' Perceived Competencies Score		
N	Valid	25
	Missing	0
Mean		19.0400
Median		20.0000
Std. Deviation		3.62261

Range	15.00
Minimum	10.00
Maximum	25.00

Table 4-23: Mean Physicians' Perceived Competence Score by gender.

Report

Physicians' Perceived Competencies Score

Gender_recoded	Mean	N	Std. Deviation
Male	19.1667	12	3.29830
Female	18.9231	13	4.03033
Total	19.0400	25	3.62261

The mean PPC Score was 19.0, median was 20.0, and the scores fluctuated between 10 and 25. The score for males is 19.17 (SD = 3.30), while for females it is 18.92 (SD = 4.03). Overall, results show that physicians seem to have high confidence in their abilities to engage with their patients to guide them about MCED tests and explain results.

A reliability test was conducted to assess the internal consistency of the scale, and we observed a Cronbach's alpha of .876 (.885 based on standardized items) across 5 items, indicating good reliability. This was reflected in the inter-item correlation matrix as well.

Table 4-24: Reliability analysis of the Physicians' Perceived Competence Scale

Reliability Statistics

Cronbach's Alpha	Cronbach's Alpha Based on Standardized Items	N of Items
.876	.885	5

Table 4-25: Inter-item correlation matrix for the Physicians' Perceived Competence Scale

Inter-Item Correlation Matrix

	Statement_1	Statement_2	Statement_3	Statement_4	Statement_5
Statement_1	1.000	.571	.772	.483	.387
Statement_2	.571	1.000	.665	.838	.520
Statement_3	.772	.665	1.000	.629	.553
Statement_4	.483	.838	.629	1.000	.638
Statement_5	.387	.520	.553	.638	1.000

4.2 Quantitative Analysis

4.2.1 Overview

The quantitative analysis revealed several key findings. First, ambiguity aversion was negatively correlated with attitude scores, as shown by the correlation analysis. Linear regression and multiple regression analysis further confirmed that ambiguity aversion significantly predicted attitude scores, supporting our hypothesis that higher ambiguity aversion is associated with less optimistic attitudes toward Multi-Cancer Early Detection (MCED) testing.

In contrast, we hypothesized that higher cancer risk perception would be associated with less optimistic attitudes, but this relationship was not supported by the data.

Consistent with our expectations, we found that physicians' perceived competence was positively associated with more optimistic attitudes in the correlation analysis. Additional regression analysis revealed that perceived physician competence independently predicted attitude scores, even though this was not initially hypothesized. This unexpected finding provides a valuable avenue for future research.

Overall, the results highlight the significant role of ambiguity aversion and perceived physician competencies in shaping attitudes toward MCED testing, while also pointing to areas where our hypotheses did not hold true, offering insights for further investigation.

Table 4-26: Overview of the quantitative results

Hypothesis	N	Result
Hyp 1: Ambiguity aversion predicts attitudes of experts.	99	We accept this hypothesis as the linear multiple regression analysis, ambiguity aversion still significantly predicted attitude scores ($B = -1.028$, $p = 0.005$).
Hyp 2: Cancer risk perception is inversely associated with attitudes.	99	We fail to accept this hypothesis as Pearson's correlation analysis did not yield statistically significant results.

Hyp 3: Physicians' Perceived Competence is positively associated with attitudes	25	We accept this hypothesis as one tailed Spearman's rank correlation analysis showed moderate positive correlation ($r=0.411$, $p=0.021$) with statistical significance.
Additional Hypothesis: Physicians' Perceived Competence predicts attitudes	25	This was an additional test we performed. Linear regression analysis showed that physicians' perceived competence significantly predicted attitude scores ($B=1.488$, $p = 0.035$).

4.2.2 Hypothesis 1

Hypothesis 1: Ambiguity aversion predicts attitudes of experts.

A test of normality was conducted to determine whether the variables met the assumptions for Pearson's correlation. The Shapiro-Wilk test indicated that Ambiguity Aversion Score was not normally distributed ($p=0.024$), while Attitude Score was normally distributed ($p=0.592$). Given the non-normal distribution of ambiguity aversion, Spearman's correlation was used to assess the relationship.

The results showed a weak to moderate negative correlation ($r=-0.324$, $p<0.001$), suggesting that higher ambiguity aversion is associated with less positive attitudes. This relationship was statistically significant, indicating a meaningful inverse association between the two variables.

Table 4-27: Spearman's Correlation Analysis between Ambiguity Aversion and Attitudes

Correlations

			Ambiguity Aversion Score	Attitude Score
Spearman's rho	Ambiguity	Correlation Coefficient	1.000	-.324**
	Aversion Score	Sig. (1-tailed)	.	<.001

	N	99	99
Attitude Score	Correlation Coefficient	-.324**	1.000
	Sig. (1-tailed)	<.001	.
	N	99	99

** . Correlation is significant at the 0.01 level (1-tailed).

Next, to investigate whether ambiguity aversion predicts attitude scores, a simple linear regression analysis was conducted.

The results revealed that ambiguity aversion was a significant predictor of attitudes ($R^2 = 0.073$). The model summary explained 7.3% of the variance in attitude scores. This indicates that while ambiguity aversion is a statistically significant predictor, it explains only a small proportion of the variance in attitude scores, suggesting other factors may also play a substantial role.

Table 4-28: Model Summary: Regression Analysis between Ambiguity Aversion and Attitudes

Model Summary

Model	R	R Square	Adjusted Square	R	Std. Error of the Estimate
1	.270 ^a	.073	.063		12.62887

a. Predictors: (Constant), Ambiguity Aversion Score

The analysis of variance (ANOVA) revealed that the regression model was statistically significant ($p = 0.007$), indicating that ambiguity aversion significantly predicts attitudes.

Table 4-29: ANOVA: Regression Analysis between Ambiguity Aversion and Attitudes

ANOVA^a

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	1214.187	1	1214.187	7.613	.007 ^b
	Residual	15470.359	97	159.488		
	Total	16684.545	98			

a. Dependent Variable: Attitude Score

b. Predictors: (Constant), Ambiguity Aversion Score

The regression analysis further shows that ambiguity aversion significantly predicts attitude scores ($B=-0.951$, $p=0.007$). For each one-unit increase in ambiguity aversion, the attitude score decreases by 0.951 units. This indicates a significant negative relationship between the two variables.

Table 4-30: Coefficients Table: Regression Analysis between Ambiguity Aversion and Attitudes

Coefficients^a

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
		B	Std. Error	Beta			Lower Bound	Upper Bound
1	(Constant)	22.491	6.422		3.502	<.001	9.745	35.238
	Ambiguity Aversion Score	-.951	.345	-.270	-2.759	.007	-1.634	-.267

a. Dependent Variable: Attitude Score

This confirms our hypothesis that ambiguity aversion predicts the attitudes towards MCED testing.

Next, a multiple regression analysis was conducted to examine the extent to which ambiguity aversion predicts the attitudes toward Multi-Cancer Early Detection (MCED) testing, while controlling for other variables such as age, gender, highest/current academic degree, and the application of genetic test knowledge.

The overall model was statistically significant ($p = .031$), meaning the predictors together had a meaningful impact on attitude scores. After accounting for the number of predictors, the model explained about 8.3% of the variation in attitudes.

Table 4-31: Model Summary: Multiple Regression Analysis between Ambiguity Aversion and Attitudes

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
					R Square Change	F Change	df1	df2	Sig. F Change

1	.366 ^a	.134	.083	12.48636	.134	2.604	5	84	.031
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a. Predictors: (Constant), Age, Gender, Do you apply your knowledge of genetic tests in any professional capacity?, Ambiguity Aversion Score, Highest/Current Academic Degree or Level of Education Completed

After controlling for other variables, ambiguity aversion still significantly predicted attitude scores ($B = -1.028$, $p = .005$). This indicates that for every one-unit increase in ambiguity aversion, attitude scores decrease by approximately 1.03 units, suggesting a negative relationship between ambiguity aversion and attitudes toward MCED testing.

Table 4-32: Coefficients Table: Multiple Regression Analysis between Ambiguity Aversion and Attitudes

Coefficients^a

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B		Collinearity Statistics	
		B	Std. Error				Lower Bound	Upper Bound	Tolerance	VIF
1	(Constant)	6.203	13.560		.457	.649	-20.762	33.168		
	Ambiguity Aversion Score	-1.028	.360	-.300	-2.853	.005	-1.745	-.311	.932	1.073
	Do you apply your knowledge of genetic tests in any professional capacity?	-.630	2.668	-.024	-.236	.814	-5.936	4.676	.975	1.025
	Gender	4.982	2.428	.211	2.052	.043	.153	9.811	.974	1.027
	Highest/Current Academic Degree or Level of Education Completed	.622	1.037	.063	.599	.551	-1.441	2.685	.920	1.086
	Age	-.158	.095	-.170	-1.657	.101	-.348	.032	.982	1.018

a. Dependent Variable: Attitude Score

In summary, ambiguity aversion significantly predicts attitude scores toward MCED testing, even after controlling for other variables, supporting our hypothesis that ambiguity aversion influences these attitudes.

4.2.3 Hypothesis 2

Hypothesis 2: Cancer risk perception is inversely associated with attitudes.

A Pearson's correlation was conducted to assess the relationship between cancer risk perception and attitudes. The results revealed a very weak negative correlation ($r=-0.080$), which was not statistically significant ($p=0.215$). This suggests that there is no meaningful relationship between cancer risk perception and attitudes in this sample.

Table 4-33: Pearson's Correlation between Cancer Risk Perception and Attitudes

Correlations

			Attitude Score	Cancer Risk Perception Score
Attitude Score	Pearson Correlation		1	-.080
	Sig. (1-tailed)			.215
	N		99	99
Cancer Risk Perception Score	Pearson Correlation		-.080	1
	Sig. (1-tailed)		.215	
	N		99	99

This rejects our hypotheses that people who have high cancer risk perception have less optimistic attitudes.

4.2.4 Hypothesis 3

Hypothesis 3: Physicians' Perceived Competence is positively associated with attitudes

For the physician specific subset, a normality test was conducted using the Shapiro-Wilk test, which indicated that the Physicians' Perceived Competencies (PPC) Score deviated significantly from a normal distribution ($p<0.05$), while the other variables were

normally distributed. As a result, one-tailed Spearman's rank correlation was used to assess the relationship between physicians' perceived competencies and attitudes.

Table 4-34: Tests of normality in the physician data subset

Tests of Normality

	Kolmogorov-Smirnov ^a			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Attitude Score	.091	25	.200*	.983	25	.944
Physicians' Perceived Competencies Score	.244	25	<.001	.908	25	.028
Cancer Risk Perception Score	.110	25	.200*	.976	25	.802
Ambiguity Aversion Score	.099	25	.200*	.967	25	.568

*. This is a lower bound of the true significance.

a. Lilliefors Significance Correction

The results indicated a moderate positive correlation ($r=0.411$, $p=0.021$), which was statistically significant, suggesting that higher perceived competencies are associated with more positive attitudes toward MCED testing.

Table 4-35: Spearman's Correlation Analysis Physicians' Perceived Competencies and Attitudes

Correlations

			Physicians' Perceived Competencies Score	Attitude Score
Spearman's rho	Physicians' Perceived Competencies Score	Correlation Coefficient	1.000	.411*
		Sig. (1-tailed)	.	.021
		N	25	25
	Attitude Score	Correlation Coefficient	.411*	1.000
		Sig. (1-tailed)	.021	.
		N	25	25

*. Correlation is significant at the 0.05 level (1-tailed).

Therefore, we can accept our hypothesis that physicians who have greater perceived competency have more optimistic attitudes.

Additionally, after observing a positive and significant association between PPC Score and Attitude Score, a regression analysis was conducted to further explore whether

these competencies can predict attitudes. The results from the regression analysis show that a physicians' perceived competencies can significantly predict attitudes, explaining approximately 18% of the variance in attitudes.

Table 4-36: Model Summary: Regression Analysis between Physicians' Perceived Competencies and Attitudes

Model Summary

Model	R	R Square	Adjusted Square	R	Std. Error of the Estimate
1	.423 ^a	.179	.143		11.80054

a. Predictors: (Constant), Physicians' Perceived Competencies Score

The ANOVA results show that the model is statistically significant ($p = 0.035$), meaning physicians' perceived competencies are a significant predictor of attitudes.

Table 4-37: ANOVA: Regression Analysis between Physicians' Perceived Competencies and Attitudes

ANOVA^a

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	697.187	1	697.187	5.007	.035 ^b
	Residual	3202.813	23	139.253		
	Total	3900.000	24			

a. Dependent Variable: Attitude Score

b. Predictors: (Constant), Physicians' Perceived Competencies Score

The results suggest that physicians' perceived competencies can significantly predict attitude score. Specifically, for each one-unit increase in physicians' perceived competencies, there is an expected increase of 1.488 units in the attitude score, and this relationship is statistically significant ($p = 0.035$).

Table 4-38: Coefficients Table: Regression Analysis between Physicians' Perceived Competencies and Attitudes

Coefficients^a

Model		Unstandardized Coefficients B	Std. Error	Standardized Coefficients Beta	t	Sig.
1	(Constant)	-27.928	12.878		-2.169	.041

Physicians' Perceived Competencies Score	1.488	.665	.423	2.238	.035
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a. Dependent Variable: Attitude Score

Next, a multiple regression analysis was conducted to examine the extent to which physicians' perceived competencies predict their attitudes toward Multi-Cancer Early Detection (MCED) testing, while controlling for other variables such as application of genetic test knowledge, age, gender, and highest/current academic degree. However, the model did not reach statistical significance. This could be because the current sample size in the physician subset was not sufficient to detect these effects.

Table 4-39: Results of the ANOVA for the multiple linear regression model predicting Attitude Score.

ANOVA ^a						
Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	1088.134	5	217.627	1.827	.164 ^b
	Residual	1906.230	16	119.139		
	Total	2994.364	21			

a. Dependent Variable: Attitude Score

b. Predictors: (Constant), Highest/Current Academic Degree or Level of Education Completed, Do you apply your knowledge of genetic tests in any professional capacity?, Physicians' Perceived Competencies Score, Gender, Age

4.3 Qualitative Analysis

4.3.1 Overview

Among the respondents, 35.3% (35) provided answers to one or both of the qualitative survey questions. The mean age of these participants was 39.3 years, with a median of 32.5 years.

In terms of educational background, 54.3% (54) held a doctoral degree (PhD or professional doctorate such as MD), 40% (31) held a master's degree, and 14.3% (14) had a bachelor's degree. One participant additionally noted having earned MPH and MBA degrees.

Regarding professional roles, 60% (21) of the respondents were academicians or researchers, 39.4% (14) were physicians, 25.7% (9) were healthcare professionals, and 2.9% (1) worked in major industries such as health insurance or pharmaceuticals. The mean professional experience among respondents was 14.6 years, with a median of 10 years.

The physician respondents represented diverse specialties, including Surgery (General, Gynecological, Chest, etc.), Internal Medicine, Family Medicine, Oncology, Anesthesiology, Algology, Pediatrics, Urology, Community Health and Medicine, and Molecular Cancer Biology.

Thematic analysis of the qualitative responses revealed five key themes: Public Awareness and Communication, Research and Development, Healthcare Equity, Ethical Considerations, and Diagnostic Procedures and Guidelines. These themes encapsulated the primary challenges and areas of focus identified by respondents.

Table 4-40: Emerging themes and subcategories from qualitative data analysis

Emerging Themes	Subcategories
Public Awareness and Communication	Cancer Education and Information <i>"Challenges can be addressed through information about types of cancer as well as new tools and methods for early detection of cancer." - Academic with a doctoral degree and 11 years of experience.</i>
	Awareness Campaigns and Outreach <i>"I think the most important thing is considering the population's education level. Because what is worse than not knowing is knowing partially." - Researcher with Master's degree</i>

	Addressing Cancer Stigma <i>“Policymakers should work on the cancer stigma, and help the public to understand cancer better.” - Academic with 20 years of experience and a doctoral degree.</i>
Research and Development	Understanding Value and Cost-Effectiveness <i>“Widespread implementation will be difficult as MCED implementation will initially be seen as a burden on the health system. However, since such preventive interventions will reduce the burden and budget of subsequent drug applications, such an expenditure beforehand may lead to better economic management in cancer treatment.” - Physician specializing in Molecular Medicine and Oncology</i>
	Improving Test Sensitivity and Reliability <i>“They should ensure that there is sufficient data backing their claims, so doctors are confident when prescribing these tests and when carrying out treatments.” - Physician specializing in Pediatrics and Internal Medicine</i>
	Communication of research <i>“Thorough research and effective communication is required to face the challenges in the</i>

	<i>implementation of MCED.” - Academic with a doctoral degree and 20 years of experience</i>
Healthcare Equity	• Access and Affordability <i>“It should be subsidized by governments to make it easier for the public to access. If the treatment is expensive, it will not be available to the general public; therefore, the scope of its use and its development will be limited.” - Health insurance industry professional</i>
	• Role of Insurance and Policy <i>“It should be emphasized as part of the standard of care for patients that have needs that could be met by their insurance companies and healthcare providers.” - Physician with MD, MPH, and MBA</i>
	• Risks of Financial Exploitation <i>“This is basically the future of medicine, and multinational industries will kill the people by squeezing their resources instead of (killing) cancer.”- Physician specializing in Urology and Surgery</i>
Ethical Considerations	• Patient Autonomy and Informed Consent

	<i>“Upon promotion of the tests, everyone deserves to know the ups and downs of the testing, and the decision still should be made by the patient after all.” - Surgeon with 20 years of experience</i>
	• Data Privacy and Trust <i>“Even with the current genetic testing approaches, there have been many concerns of data privacy. People are not convinced that their samples are only used for the testing and come up with plenty of conspiracy theories.” - Researcher with Master’s degree</i>
Diagnostic Procedures and Guidelines	• Addressing Diagnostic Challenges <i>“The test is a significant innovation in early diagnosis, but it also comes with certain challenges. False positive results can lead to unnecessary medical interventions and anxiety for patients. These issues can be addressed through confirmatory diagnostic methods and by providing psychological support.” - Oncologist with 12 years of experience</i>
	• Guideline Development and Implementation <i>“Policymakers must adopt a cautious yet forward-thinking approach to MCED testing. While its potential to revolutionize cancer detection is significant, careful attention must be paid to ensuring clinical efficacy, equity, affordability, and</i>

	<i>integration with existing healthcare systems.” - Physician with 30 years of experience</i>
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4.3.2 Public Awareness and Communication

Cancer Education and Information

One of the key points raised by respondents is the need for better public education about cancer and methods for early detection, especially with the introduction of new technologies like MCED testing. These are specialized and relatively new areas, making it essential to integrate them into educational systems to raise awareness and understanding. One respondent suggested that education about MCED testing should be included in high school curriculum.

"Challenges can be addressed through information about types of cancer as well as new tools and methods for early detection of cancer," noted an academician with a doctoral degree and 11 years of experience. This highlights the existing gap in public understanding of early cancer detection technologies, which causes challenges in its widespread implementation and acceptance, underscoring the need for comprehensive cancer education and accessible information.

Developing a better understanding of MCED testing can reduce ambiguity around this emerging topic, prompting people to make informed decisions about their health, as well as impacting their attitudes toward emerging technologies like MCED testing.

Awareness Campaigns and Outreach

Respondents emphasized the importance of conducting public awareness campaigns to educate the public about MCED testing and the potential of early cancer detection technologies. These campaigns can play a vital role in disseminating knowledge and addressing existing gaps in understanding. However, respondents also cautioned that the information shared during these efforts must be evidence-based and transparent to avoid the risks of misinformation.

A young researcher with a Master's degree highlighted this concern, stating, *"I think the most important thing is considering the population's education level. Because what is*

worse than not knowing is knowing partially". This is critical as inaccurate or incomplete information could foster ambiguity, public distrust, and negative perceptions of MCED testing.

This underscores the critical need for policymakers to adopt a cautious and strategic approach when designing such campaigns, ensuring they are both comprehensive and scientifically grounded. Evidence-based awareness initiatives can help build public trust and promote informed decision-making, enabling individuals to shape their own perceptions of MCED testing without undue influence or misunderstanding.

Addressing Cancer Stigma

Cancer stigma occurs when negative attitudes and misconceptions about cancer cause significant delays in seeking timely diagnosis, thereby hindering early detection efforts and delaying treatment (Scott et al., 2015). By constraining discussions about cancer, stigma can cause immense psychological distress for patients and negatively impact their well-being and quality of life (S. K. Chambers et al., 2015).

"Policymakers should work on the cancer stigma, and help the public to understand cancer better", notes a 41 year old academician with 20 years of experience and a doctoral degree. This highlights the current gap in the understanding of cancer by the public, which may discourage people from openly discussing these topics and fostering stigma.

Therefore, policymakers should ensure that public awareness campaigns not only provide information about cancer and its early detection but also aim to tackle stigma by encouraging patients to seek help. This can allow the public to engage in more open and informed discussions about cancer and emerging technologies like MCED testing, which may, in turn, promotes a cultural shift toward acceptance and proactive health behavior.

4.3.3 *Research and Development*

Understanding Value and Cost-Effectiveness

Respondents emphasized the importance of research to evaluate the additional benefits of MCED testing when compared to existing screening practices that are in place. Understanding this is important for determining the real potential of MCED testing in improving early cancer detection outcomes, when compared to current screening practices. They also mentioned that comprehensive cost-benefit analysis must be

conducted rigorously in research to understand the short-term and long-term cost related benefits and disadvantages of MCED testing.

A young researcher illustrates this, *"They should take into account the cost-reducing effect of early detection via MCED testing by decreasing the amount of radio, chemo, and systemic therapies"*. This observation underscores the economic implications of early detection. By identifying cancer at an earlier stage, the burden of costs incurred due to late diagnosis and treatments can be relieved.

This perspective also reinforced by another 60 years old researcher with a PhD degree in Molecular Medicine specializing in Oncology: *"Widespread implementation will be difficult as MCED implementation will initially be seen as a burden on the health system. However, since such preventive interventions will reduce the burden and budget of subsequent drug applications, such an expenditure beforehand may lead to better economic management in cancer treatment"*. This further stresses that while the initial costs of implementing MCED testing might pose challenges for healthcare systems, the long-term economic benefits—through reduced treatment costs and improved cancer prevention—make it a worthwhile investment.

Therefore, for real-world implementation of MCED testing, understanding the value that it brings in terms of cost and in comparison, with current screening practices is essential. Research can produce evidence-based insights that can impact the public attitudes towards accepting MCED testing.

Improving Test Sensitivity and Reliability

Respondents emphasized that there is a critical need for research to focus on enhancing the sensitivity and reliability of MCED tests as this can have a huge impact on their adoption. One physician specializing in Pediatrics and Internal Medicine underscored this by stating, *"They should ensure that there is sufficient data backing their claims, so doctors are confident when prescribing these tests and when carrying out treatments"*.

This insight illustrates the dual impact of improving test sensitivity and reliability: not only can it build public trust and acceptance of MCED testing, but it can also increase the perceived competencies of physicians. If physicians believe the tests to be reliable and accurate, they will be more confident in prescribing MCED tests and interpreting results effectively to ensure the best outcome for their patients. By focusing research

efforts on these areas, policymakers can improve attitudes of both physicians and patients towards MCED testing, thereby facilitating smoother integration into healthcare systems.

Communication of Research

As MCED testing is a relatively new and rapidly evolving technology, there is ambiguity surrounding its implementation and effectiveness. Respondents emphasized that research alone is not sufficient to address these challenges; effective communication of research findings is just as important. A 61 year old academician with a doctoral degree and 20 years of experience highlighted this: *“Thorough research and effective communication is required to face the challenges in the implementation of MCED”*.

Effective communication can be achieved through public awareness campaigns and cancer education initiatives, as previously highlighted. By sharing evidence-based research with the public, policymakers can tackle ambiguity, rebuke misconceptions, and foster increased trust in MCED testing.

4.3.4 Healthcare Equity

Access and Affordability

Respondents highlighted significant concerns regarding access and affordability in the implementation of MCED testing. While MCED testing can generate benefits in terms of early detection, it also has enormous potential to create or worsen inequities. A 41 years old researcher with 20 years of experience and a doctoral degree noted, *“This type of test has the risk of creating inequalities of access; therefore, health systems should orient themselves towards making them accessible and affordable to everyone”*. This emphasizes the need for caution when adopting MCED testing into healthcare systems to ensure that it benefits all segments of the population, irrespective of socioeconomic status.

Another respondent from the health insurance industry suggested that government subsidies could play a pivotal role in reducing inequality: *“It should be subsidized by governments to make it easier for the public to access. If the treatment is expensive, it will not be available to the general public; therefore, the scope of its use and its development will be limited”*. This further highlights that if MCED testing is not affordable and accessible to the general public, its potential impact on early cancer detection and overall public health may be significantly diminished. Therefore,

governments need to recognize their role in making MCED testing affordable and accessible to all.

Moreover, the importance of integrating MCED testing into a more personalized approach to healthcare was also mentioned: *“This testing should be considered as a part of the ‘individualising’ approach to healthcare in general”*, urges a 75 year old physician specializing in anesthesiology and algology and with 45 years of experience. This underscores the importance of taking into account individual needs, preferences and circumstances of patients. Additionally, according to the respondents, inequities in accessibility and affordability in the context of MCED testing can also be achieved by making the tests available to the entire public on request and by implementing regular screenings to minimize missed detections.

While MCED testing lends the hope of transforming the future of early cancer detection, at every step, it is important to consider how it can be integrated equitably as well. An academician with a doctoral degree summarizes this well “MCED can become a game changer, but it is important how they are going to be integrated into the lives of ordinary people”. This sums up the need for ensuring that the benefits of MCED testing are accessible to all.

Role of Insurance and Policy

Respondents pointed out that insurance companies are vital experts in the implementation of MCED testing, as their involvement can help bridge gaps in access and affordability. They emphasized that policies should aim to make MCED testing a standard part of care, and there should be collaboration between private and public experts to ensure equitable access to MCED testing. For instance, collaboration between government and insurance companies to subsidize the cost of MCED testing.

A 29 year old researcher with a Master’s degree explained the importance of integrating MCED testing into standard patient care: *“It should be emphasized as part of the standard of care for patients that have needs that could be met by their insurance companies and healthcare providers.”* This highlights the necessity of making MCED testing accessible through insurance, which can facilitate its integration into routine healthcare practices.

A physician with a MD, MPH, and MBA degrees noted, *“Equitable access must be prioritized by addressing disparities, subsidizing costs, and including MCED in public*

and private insurance coverage.” This further underscores the role of insurance industry as a major stakeholder in diminishing healthcare inequities through insurance coverage.

Furthermore, respondents raised concerns about potential discriminatory practices by insurance companies and healthcare providers. *“Policymakers should pay attention to any discrimination practices that might arise with insurance companies and healthcare providers, as the benefits of genetic testing far outweigh the toll of late diagnoses or life-threatening illnesses that could be prevented with early measures,”* noted one 29 year old researcher. This suggests that policymakers need to ensure that regulatory measures are in place to monitor discrimination practices that can occur in major industries as this not only has the potential to widen inequities but also disrupt early detection efforts.

In summary, ensuring the involvement of insurance companies, establishing MCED testing as a standard of care, and implementing policies to address discrimination are key steps toward reducing disparities in cancer detection.

Risks of Financial Exploitation

Respondents expressed concerns about the potential for MCED testing to exacerbate socioeconomic disparities if not implemented carefully. They caution against the danger of this technology becoming a means of financial gain for corporations rather than serving as a tool to improve public health.

One respondent, a 60 years old physician specializing in Family Medicine with 36 years of experience, emphasized the importance of having protective policies to ensure equitable access: *“Depending on the financial status of patients, policymakers should make the criteria so to benefit low socioeconomic people.”* This statement underscores the need for targeted financial policies to ensure equitable access for all, regardless of economic status.

Another respondent, a 59 years old physician specializing in Urology and Surgery with 33 years of experience, expressed a more critical view, warning of the potential for corporate exploitation: *“This is basically the future of medicine, and multinational industries will kill the people by squeezing their resources instead of (killing) cancer.”* This highlights the fear that, without appropriate policies in place, the commercialization of MCED testing could prioritize profit over patient welfare, thereby leaving the most vulnerable populations at risk of being exploited.

These insights emphasize the importance of implementing policies that prevent financial exploitation, ensuring that the implementation of MCED testing focuses on improving public health rather than maximizing corporate profit.

4.3.5 Ethical Considerations

Patient Autonomy and Informed Consent

Respondents emphasized the importance of respecting patients' rights to make informed decisions about their healthcare. As MCED testing is a relatively new technology, there should be transparent communication about its benefits and risks, allowing individuals to make decisions aligned with their personal values and circumstances.

A 50 years old surgeon with 20 years of experience, highlighted this by stating: *“Upon promotion of the tests, everyone deserves to know the ups and downs of the testing, and the decision still should be made by the patient after all.”* This underscores the need for patients to be given comprehensive information about potential benefits and risks of MCED testing and allowing them to make informed decisions about their health.

Another healthcare professional with expertise in public health added a broader perspective, emphasizing the multifaceted ethical responsibilities associated with MCED testing: *“Ethical considerations like informed consent, data privacy, and psychosocial support must be prioritized, alongside public awareness campaigns.”* This iterates that ethical consideration is not limited to informed consent but must also ensure that there are policies in place to ensure confidentiality and provide psychosocial support services to those who might require it while undergoing MCED testing, for example, in the case of false positives.

This also connects with earlier themes of public awareness campaigns and cancer education as these efforts should not only focus on spreading awareness about MCED testing but should also educate the public on their rights to decision-making and informed consent.

Data Privacy and Trust

As a relatively new technology, MCED testing raises legitimate concerns about how personal and genetic data are managed. Given this, respondents emphasized the

importance of safeguarding patient information to build trust in the adoption of MCED testing.

Another researcher with a Master's highlighted this sentiment by stating: *"Even with the current genetic testing approaches, there have been many concerns of data privacy. People are not convinced that their samples are only used for the testing and come up with plenty of conspiracy theories."* This underscores the skepticism that arises when individuals cannot trust that their sensitive data is being handled with confidentiality and protected accordingly. Misinformation can also exacerbate these concerns.

To address these concerns, policy makers should ensure that there is continuous monitoring and strict data protection protocols are in place to ensure that patient information is not being misused or shared without their consent. Doing so can diminish potential pessimistic attitudes towards MCED testing, ensuring that data concerns do not become a barrier to its acceptance and integration into healthcare systems.

4.3.6 Diagnostic Procedures and Guidelines

Addressing Diagnostic Challenges

Many respondents highlighted concerns about false positives and negatives, which could lead to unnecessary medical interventions, delays in detection, and increased psychological distress for patients. There was a consensus on the need for clear guidelines and support systems to manage these challenges.

An oncologist with 12 years of experience, noted, *"The test is a significant innovation in early diagnosis, but it also comes with certain challenges. False positive results can lead to unnecessary medical interventions and anxiety for patients. These issues can be addressed through confirmatory diagnostic methods and by providing psychological support."* This highlights the importance of having clear guidelines including confirmatory testing in place for managing false positives effectively, as they can lead to unnecessary treatments and emotional strain for patients.

On the other hand, to deal with false negative results, respondents stress on the importance of improving test sensitivity and ensuring the careful interpretation of results, thereby highlighting the need for ongoing improvement in MCED testing to minimize missed detections.

A physician with 36 years of experience further emphasized the dual impact of MCED testing, stating: *“Implementing Multi-Cancer Early Detection (MCED) testing has the potential to profoundly impact an individual's life, both positively and negatively. MCED testing can potentially improve lives by enabling early cancer detection, better treatment options, and proactive healthcare decisions. However, it also carries risks of psychological distress, financial strain, and unnecessary interventions.”* This quote reinforces that while MCED testing has great benefits to offer, one cannot ignore that it has the potential to be expensive and generate false negatives, which can cause psychological distress and delayed diagnosis for the patient.

Another researcher with a Master's degree reiterated these negative effects of false positives: *“The diagnostic kits can give false positive / negative results which may upset the patient. One may trust the kit's positive result (which is false positive) and dismiss the check-ups, ultimately delaying the time of detection”*. This underscores the importance of research needed to improve the reliability of MCED testing as well as the need for providing psychological support in case of false positives.

Overall, these insights suggest that to fully realize the benefits of MCED testing, more research on improving the tests, clear diagnostic guidelines and effective support systems are required, especially in the case of false positive and false negative results. This is essential to address diagnostic challenges.

Guideline Development and Implementation

Respondents emphasized the need for clear and evidence-based guidelines for MCED testing. A physician with 36 years of experience, stated, *“Policymakers must adopt a cautious yet forward-thinking approach to MCED testing. While its potential to revolutionize cancer detection is significant, careful attention must be paid to ensuring clinical efficacy, equity, affordability, and integration with existing healthcare systems.”* This quote stresses that a cautious approach must be adopted by policymakers to ensure that the test is both effective, accessible, and well-integrated into the healthcare systems.

A healthcare professional further stressed the need for standardized implementation: *“In my opinion, policymakers should ensure MCED testing is validated, standardized across all labs, and integrated into healthcare systems with equitable access for all.”* This highlights the need for policymakers to not only ensure the scientific validity of

MCED testing but also to guarantee that it is equitably integrated across healthcare institutions.

Another physician with an MBA and MPH degrees further reiterated the need for clear and reliable guidelines, stating: *“Policymakers should establish clear guidelines and ensure regulatory oversight for MCED testing to guarantee its accuracy, reliability, and safety.”* This quote emphasizes that implementation of MCED testing must be done under a well-structured regulatory framework to ensure that the tests meet the necessary standards for accuracy and equity.

Another perspective by a surgeon with a Master’s degree in Healthcare Management brought into focus the role of a rigorous review process to ensure that the issue of MCED implementation is approached from a holistic perspective. They stated, *“Carefully review applicability across different system aspects—such as system capacity, test performance in various risk groups and situations, costs, health outcomes, and the ability to inform patients effectively about risks—before moving forward with implementation”*. This insight underscores the importance of a comprehensive evaluation that includes operational feasibility, cost-effectiveness, and patient education to mitigate risks associated with the test.

Overall, these insights stress the critical role that policymakers need to play in guiding the safe and effective implementation of MCED testing. Clear, evidence-based guidelines, along with regulatory oversight and international standards, will be essential to ensure that MCED testing can be integrated effectively into existing healthcare systems and provide equitable access to all. Policymakers must also consider system-wide implications, including infrastructure capacity, cost, and patient communication, to achieve equitable and impactful implementation.

Chapter 5: **DISCUSSION**

5.1 Interpretation of Findings

Our findings reveal generally optimistic attitudes toward Multi-Cancer Early Detection (MCED) testing among experts. This is a significant observation, particularly as existing literature presents conflicting results regarding experts' perceptions and receptivity toward MCED testing (Chambers et al., 2023; Samimi et al., 2024; Schroll et al., 2024). Notably, our study shows that mean attitudes vary in distribution across education levels, with experts holding Bachelor's degrees displaying the highest optimism, followed by a reduction in optimism among experts with Master's degrees, and an even further decline in optimism observed among experts with PhDs. Additionally, attitude scores differ based on personal or familial history of cancer; those with such experiences tend to be less optimistic.

These findings suggest that education level and history of cancer may play a role in shaping perceptions of MCED testing and the rationale behind this should be explored further. This is important because positive perceptions, as identified in the literature, are crucial for the successful adoption of MCED testing (Roybal et al., 2024).

Our results indicate that participants generally have moderate levels of ambiguity aversion. Ambiguity aversion towards MCED testing also has a negative correlation with the attitudes of respondents. Additionally, as aversion to ambiguity increases, it can cause a significant decrease in optimistic attitudes in domains of medical harms and benefits of MCED testing, its impact on patient experience, how it contributes to health disparities, as well as progress towards its implementation. This effect is seen even after controlling for other variables such as age, gender, highest/current academic degree, and the application of genetic test knowledge of respondents.

This finding is particularly important because Multi-Cancer Early Detection (MCED) testing is an emerging technology, and as highlighted by experts in their qualitative responses, it still lacks sufficient FDA approval, established diagnostic guidelines, comprehensive clinical trials, and robust research. This uncertainty can create ambiguity regarding its reliability and the balance of its potential benefits and harms. The psychological phenomenon of ambiguity aversion, where individuals are reluctant to make decisions in the face of uncertain information, could therefore significantly

influence how MCED testing is received by key experts. This, in turn, could shape the development of policies surrounding its adoption and implementation.

Currently, there are few clinical trials in place to assess the benefits of MCED testing and understand the added utility it brings when complemented with the current cancer screening practices in place. One such trial being conducted to assess whether MCED testing can reduce late-stage cancer (III and IV) incidence is the NHS-Galleri trial, which is a randomized controlled trial with 140,000 individuals based in England (Neal et al., 2022). However, due to the small number of trials and the time required for their completion, research on this front is still developing. Moreover, 47.5% of the respondents mentioned that they got their knowledge of genetic testing from media sources (such as television, internet, magazine article, newspaper article, radio etc.), which may not always report evidence-based MCED information.

Given this context, it is crucial to monitor the quality of ongoing research and, equally important, to consider how and where new developments in MCED testing are communicated to experts. Qualitative expert insights from our research also emphasize the need for improved cancer knowledge dissemination and awareness campaigns. Such communication can influence experts' perceptions, particularly by impacting their levels of ambiguity aversion.

Future research can also focus specifically on what causes ambiguity aversion, particularly in the context of MCED testing to understand if improvements in clinical trials research and communication of findings can impact skepticism about experts' attitudes towards it.

Our findings also reveal that physicians generally have moderate to high levels of perceived competencies. Additionally, we found that an increase of physicians' confidence in their abilities to educate and guide their patients about MCED testing causes more optimistic attitudes towards MCED testing. This is particularly important, as experts, including physicians, stressed the need for clear, evidence-based guidelines to address the diagnostic challenges associated with MCED testing. Concerns about false positives and negatives are significant, as they can impact the way MCED testing is perceived and ultimately adopted.

Physicians are major experts in the implementation of MCED testing and play a critical role in educating, prescribing, and guiding their patients about these tests. According to a recent study, patients preferred to hear about MCEDs from their medical

providers which highlighted the importance of medical providers proactively and equitably discussing and recommending MCEDs (Roybal et al., 2024). Therefore, their confidence in their abilities to carry out these roles is integral, especially since it shapes their receptivity and optimism towards MCED testing. This is an important finding because successful and equitable implementation of MCED testing requires substantial involvement of physicians and could impact their practice considerably in the future. According to a recent study, healthcare providers were willing to incorporate MCED tests into practice if they are supported by clinical data and are screening for a cancer type with high unmet need (Schroll et al., 2024). This demonstrates the potential of evidence-based clinical research in impacting the perceptions and behaviors of physicians,

Therefore, there is a need for deliberate development of evidence-based educational and training programs for physicians as these may enhance their confidence regarding how, when and to whom MCED tests should be prescribed, as well as diagnostic follow ups, which will in turn, foster more optimistic attitudes towards MCED testing.

Future research can also focus on understanding what factors impact the competencies of physicians, particularly in the context of MCED testing, and whether this can affect their clinical practice as well. This might shed further light on different ways in which professional competencies of physicians can be enhanced so that physicians feel more confident in prescribing MCED testing and guiding their patients through them, especially in complex cases of false positives and false negatives.

It is also important to note that ambiguity aversion and physicians' perceived competencies explain 8.3% and 18% of the variability in attitudes towards MCED testing, which shows that even though they predict attitudes significantly, there may be other, more important predictors of MCED attitudes that have not yet been explored. Future studies can also focus on other potential predictors MCED attitudes to gain a more comprehensive understanding of what shapes their levels of optimism and pessimism regarding this emerging technology.

Interestingly, our study also found that although participants have moderate levels of cancer risk perception, they are not significantly associated with attitudes towards MCED testing, which is contrary to our hypothesis. To elaborate, heightened feelings of risk around cancer i.e. feeling like everything causes cancer, that it is hard to know which cancer recommendations to follow as there are an abundance of them etc., does not associate with or impact attitudes towards MCED testing. It is possible that this

association does not exist in our target population particularly, which consists of major experts including academicians, researchers, physicians and healthcare professionals. Therefore, it would be interesting to re-evaluate this relationship within a different target population. For example, future research can focus on exploring the relationships between perceived cancer risk and attitudes towards MCED testing in a laypersons group or a particular age group.

The findings from our qualitative analysis reiterate the concerns well-documented in literature that need to be addressed before widespread implementation of MCED testing, such as lack of information and knowledge about screening and financial inaccessibility (Roybal et al., 2024). Experts stress on concerns regarding the need for comprehensive cancer education and information, improvements in the sensitivity and reliability of the tests, understanding the additional value it adds, patient autonomy and informed consent, as well as general guidelines to address diagnostic challenges and successfully implement MCED testing (Brito-Rocha et al., 2023; Chambers et al., 2023; Crossnohere et al., 2024; Hallman et al., 2023; Samimi et al., 2024).

Experts also emphasize the importance of ensuring that MCED testing is implemented equitably, by highlighting the need for accessibility and affordability, as well as the role of insurance and policy in this regard. In our study, an overwhelming 87.9% of experts believed that MCED tests should be covered by health insurance policies for eligible individuals. The concern about healthcare equity has also been emphasized heavily in literature related to MCED testing. For example, a recent study provides nine equity considerations and associated recommendations for MCEDs and stress on the importance to implementing these before rather than after implementation of MCEDs to reduce health disparities (Miller et al., 2024).

In the qualitative responses, experts raised concerns about the risks of financial exploitation in the commercialization of MCED testing. Without appropriate guidelines, there is a potential for certain groups to prioritize profit over patient welfare, which could exacerbate healthcare inequities, particularly among vulnerable populations. This underscores the need for regulatory frameworks that ensure the ethical implementation of MCED testing and protect patients from exploitation. Additionally, participants stressed the importance of addressing cancer stigma, highlighting that awareness campaigns could foster public discussions about emerging technologies like MCED testing, which has the

potential to detect cancer early. Reducing stigma could enhance public acceptance and engagement with MCED testing, ultimately facilitating its broader adoption.

Respondents also emphasized the necessity of evaluating the current capacity of health systems to integrate MCED testing without diverting resources from other essential healthcare services. Given the varied levels of support for MCED testing across different healthcare settings (67.7% of respondents favored its use as a diagnostic tool for specialist-referred patients, 65.6% supported its use in primary and preventive care, and 45.5% advocated for population screening), understanding how MCED testing can be seamlessly incorporated into existing health systems is vital. This is critical not only for the efficient delivery of care but also for ensuring that MCED testing does not strain already overstretched healthcare resources. Addressing these challenges can help ensure that the implementation of MCED testing maximizes its benefits while minimizing potential risks, ultimately improving healthcare outcomes for patients.

These insights show that there are many concerns, some highlighted in literature already, and some additional concerns such as the possible commercial exploitation of MCED testing and need for capacity evaluation of healthcare systems. These concerns underscore the importance of adopting holistic thinking to understand the challenges that need to be addressed before MCED testing can be implemented widely across healthcare settings.

5.2 Limitations of the Study

This study has several limitations that must be acknowledged. First, the sample was drawn primarily from convenience and purposive sampling strategies, which may limit the generalizability of the findings. Additionally, focusing on academics, researchers, physicians, and healthcare professionals provides valuable insights, excluding other stakeholder groups (e.g. patients, policymakers, or payers) might limit a comprehensive understanding of attitudes and perceptions.

It is also important to note that, while we were able to achieve statistically significant correlations and regressions, the sample size of the physician subset was small, and therefore the results must be interpreted with caution when generalizing. Moreover, the internal validity of the cancer risk perception scale was lower than desired, which may affect the reliability of the results regarding cancer risk assessment.

The survey responses also had missing values in the data set (which was 0.6% for responses assessing cancer risk perception scale, 1.4% for responses assessing ambiguity aversion, and 3.2% for responses assessing physicians' perceived competencies). We replaced the missing data by using mean imputation method. Although missing data was minimal, there is a possibility that this may have slightly impacted the results.

Finally, the length of the survey may have contributed to participant fatigue, which could have affected the quality of responses, particularly for the open-ended questions.



Chapter 6:

CONCLUSION

This study highlights two significant factors, ambiguity aversion and physicians' perceived competencies, that shape attitudes toward Multi-Cancer Early Detection (MCED) testing, thereby highlighting the need to address uncertainties around MCED testing and to support physicians with the tools and training they need to confidently guide their patients.

Reducing ambiguity around MCED testing will require evidence-based research, robust clinical trials, and effective communication strategies. Empowering physicians through targeted education and training programs will not only enhance their confidence but also foster more positive perceptions of this emerging technology. Additionally, policy guidelines must focus on ensuring equitable access to MCED testing by addressing the potential risks of commercialization and the capacity of health systems to integrate MCED testing without compromising other critical services.

Future research should explore what drives ambiguity aversion in the context of MCED testing as these findings can generate actionable insights into improving the receptivity of this emerging technology. Long-term studies are also needed to track changes in attitudes as more evidence about MCED testing becomes available. Conducting research to include other stakeholder groups, such as patients, policymakers, and insurers etc., can provide a broader understanding of the challenges and opportunities surrounding MCED testing. It would also be valuable to revisit the role of cancer risk perception in shaping attitudes, perhaps with different scales and particularly in different populations, such as laypeople or specific age groups.

In summary, addressing these knowledge gaps and proactively tackling challenges will be essential for successfully integrating MCED testing into healthcare systems.

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APPENDIX A: SURVEY INSTRUMENT

6.1 [*Survey Instrument*](#)

(The survey instrument can also be requested by contacting the researcher at:
musman21@ku.edu.tr)



APPENDIX B: QUALITATIVE DATA ANALYSIS

6.2 [Organization and Open Coding of the Qualitative Data](#)

6.3 [Miro Showing Emerging Themes, Sub-categories, and Connections](#)

