GENETIC COUNSELING AROUND THE GLOBE: PRENATAL SCREENING PRACTICES DURING THE FIRST TRIMESTER

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Abstract

Keywords: prenatal screening; genetic counseling; referral practices; carrier testing; international practice; genetics testing; reimbursement; guidelines; recommendations.

The global state of prenatal screening during the first trimester of pregnancy by genetics professionals has not yet been extensively studied. The current study explored whether carrier screening, biochemical marker screening, ultrasounds with nuchal translucency measurements, and non-invasive prenatal screening (NIPS) were offered as standard of care. It also examined whether the presence of established practice guidelines impacted their decision to offer testing as standard of care and screening reimbursement methods. Prenatal genetics providers, primarily genetic counselors, from 11 countries spanning 4 continents, were surveyed about the screening tests offered to the patients. Of the first trimester screening tests, NIPS was not found to be standard of care globally with the exception of the United States. Government reimbursement was reported by providers to be a major form of reimbursement for all four types of screening tests. Patient out-of-pocket was reported to be an equally popular form of reimbursement for NIPS and respondents expressed reimbursement challenges as potential barriers for offering NIPS as standard of care. Governments were more likely to reimburse well-established tests despite the greater accuracy of NIPS. These findings lay the groundwork for a deeper exploration of the continually evolving prenatal genetic counseling field on a global scale.

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Introduction

Prenatal screening provides information about genetic risks and is utilized as one predictor of pregnancy outcomes. Methods of screening may include carrier screening, biochemical markers, ultrasound with nuchal translucency (NT) measurements, and/or non-invasive prenatal screening (NIPS) (also referred to as non-invasive prenatal testing (NIPT)). Prenatal genetic counseling involves genetics professionals working with individuals, couples, or families before or during a pregnancy to determine the risks for genetic conditions or birth defects. While there have been investigations of international implementation of screening tests such as reproductive carrier screening (Delatycki et al. 2019) and non-invasive prenatal testing (Minear et al. 2015), there remains limited information about the global state of prenatal screening and genetic testing offered during the first trimester of pregnancy. This international study explored provider practices, a majority of whom were genetic counselors, the utilization of practice guidelines, and service reimbursement methods.

Based on data gathered from the 2016 Transnational Alliance of Genetic Counseling (TAGC) and the 2017 World Congress of Genetic Counselling in the UK, the authors report that as of 2018, there are approximately 7,000 genetic counselors and that the profession is either established or developing in at least 28 countries. The growing need for testing necessitates the inclusion of different providers, such as obstetricians and midwives, to offer prenatal genetic counseling (Minkoff & Berkowitz. 2014). The varied approaches prenatal providers take may potentially impact patient care and a need has been proposed to streamline and standardize access to genetic counseling services for prenatal populations (Minkoff & Berkowitz. 2014). For

instance, aneuploidy screening and testing decisions are heavily patient value-driven and individuals choosing to undergo screening or testing should receive guideline-based counseling on the risks, benefits, and limitations from a health care provider or genetic counselor (Carlson & Vora. 2017).

The types of screening tests and the time at which they are offered during the first trimester are both aspects of practice that vary not only between countries but within countries. For instance, divergent approaches in NIPS offerings have been noted in countries like India and Germany (Verma et al. 2017; Kozlowski et al. 2019). Differences in practice were similarly noted for biochemical marker screening with and without NT measurements. In France, alpha-fetoprotein (AFP), human chorionic gonadotropin (HCG), and NT measurement, along with maternal age are taken into consideration in screening for trisomy 21 (Royere et al. 2016). In Germany, biochemical marker screening includes the additional assessment of placental growth factor (PlGF) (Kozlowski et al. 2019). These studies show variation in geographical and financial access to screening, as well as the gestational time point at which screening is offered. Policies and barriers that exist within these regions contextualize prenatal offerings and elucidate whether screening practices may be comparable to other countries.

While data exists regarding reimbursement of prenatal genetic services within countries, reimbursement across countries has not yet been widely defined. The integration of prenatal first trimester genetic screening services into a country's healthcare system can help provide insight into accessibility and availability of services. For example, Brazil's Unified Health System (Sistema Unico de Saude) is one of the largest publicly funded health systems in the world, but

only some genetic services receive funding. As of 2013, it was noted this lack of funding was due to the inability of the Unified Health System to recognize the clinical genetic specialty. However, mandated insurance coverage exists for specific tests depending on established guidelines (Horovitz et al. 2013).

Practice guidelines and recommendations vary globally in their content and often exist alongside other region-specific guidelines. For instance in Europe, guidelines and recommendations exist for preconception and prenatal testing of women at elevated risk for having a child with a genetic condition (Skirton et al. 2014). Country specific guidelines have also been established: Netherlands' implementation of genome-wide non-invasive prenatal testing (van der Meij et al. 2019), prenatal fetal anomaly screening and Down syndrome screening in France (Ferrier et al. 2019), and sickle cell anemia screening in Cuba (Roblejo et al. 2017), are such examples.

NIPS is a screening test that has been implemented widely across the world over the last decade. Past variation in NIPS testing and services found between the United States, Canada, and Australia may have been attributed to an absence of established practice guidelines (Suskin et al. 2016). Such findings were also seen upon global assessment of NIPS implementation where providers revealed variability in testing protocols and provider perspectives on appropriate candidates for testing (Minear et al. 2015). In the Minear study, providers expressed a desire for clinical practice guidelines. Our study aimed to examine the global NIPS offerings given the guidelines that have since been published.

This study aims to fill the gap in knowledge about international prenatal screening in the first-trimester, specifically if screening tests were standard of care, if the decision was based on presence or absence of practice guidelines by a professional association or regulatory body, and reimbursement methods. This research will allow us to better understand the practice differences that exist internationally and elucidate the context in which these practices are carried out.

Methods

This study was approved by the Institutional Review Board at Sarah Lawrence College.

Survey

The survey consisted of multiple choice and free response questions that focused on the participants' demographics, involvement in the genetic counseling process, patient referral indications during the first trimester, and referral indications warranting: carrier screening for any number of genetic conditions, biochemical marker screening including PAPP-A (pregnancy-associated plasma protein A), bhCG (beta human chorionic gonadotropin) and msAFP (maternal serum alpha-fetoprotein), ultrasounds with nuchal translucency measurements, and non-invasive prenatal screening tests (Appendix 15). Information about whether the screening tests were offered as standard of care, offered due to the presence of recommendations and guidelines from a regulatory body or professional association, as well as how the tests were reimbursed for were collected. The survey was distributed via an online survey platform, SurveyPlanet, to allow for international participation. No questions were required and no IP addresses were collected.

Recruitment

We utilized various recruitment strategies for this global survey with the goal of obtaining respondents from each continent. An initial list of international genetics provider contacts were compiled from connections made during conferences by advisors (LAE, LH), Sarah Lawrence College alumni, and public genetic counselor databases available online. Providers were not exclusively prenatal care providers. Individuals were encouraged to either personally take the survey, forward the survey to fellow prenatal colleagues, and/or to their respective professional societies. Convenience sampling was intended to increase the global participant response coverage. These contacts were emailed directly or contacted via LinkedIn. List-serve advertisements with the National Society of Genetic Counselors (NSGC)(N= 4589) and Canadian Association of Genetic Counsellors (CAGC) (N=418) were also utilized. Approximately 1 week prior to the closure of the survey, the survey was advertised on Twitter using the #GCchat hashtag via one of the advisor's accounts (LH).

Procedures

All communications utilized templates (Appendix 13). A reminder email was sent approximately 2 weeks after the initial email invite (Appendix 14). The survey was opened for a total of 4 months. The survey and survey communications were only in English. A consent form (Appendix 15) was presented in which participants had to read and accept before continuing onto survey questions (Appendix 16). Possible confounding factors included the possibility of participants taking the survey multiple times. Due to the distribution method utilized, the response rate could not be determined. Since we permitted participant anonymity, we are unable to verify the identity of the respondents and their eligibility.

Data Analysis

A total of 97 submissions were received (n = 97). Five respondents who reported seeing less than one prenatal patient weekly were excluded from the survey. Two respondents provided one gestational age week time point for a screening test outside the typical gestational age range for these tests and were also excluded from the data analyses. One respondent was excluded after indicating they did not wish to participate in the survey.

Data analysis was performed independently for each question given no questions were required to be completed. Analysis for each question was confirmed by a second member of the authorship team. For reponses to have been considered a majority, the response had to be chosen by at least 60% of respondents for that particular question.

Results

Demographics

A sum of 89 respondents was obtained from 11 countries: United States, France, Canada, South Africa, Australia, India, Switzerland, Oman, Ireland, Qatar, and Israel (Figure 1). The majority of participants were practicing genetic counselors (87/89). The majority also cited a Master's degree as their highest relevant degree (80/89) while a notable amount indicated a PhD (5/89).

Over half of respondents indicated that they worked in public hospitals (52/89), while a significant number of respondents worked in a private hospital or medical facility (31/89). Other settings included community hospital, community family practice clinic, industry setting, lab

setting, military hospital, and university-affiliated medical center. Most of the respondents stated they specialize in “Genetics” and “Prenatal” along with a variety of other specialties. Respondents from South Africa mentioned they do not specialize and practice in all specialties.

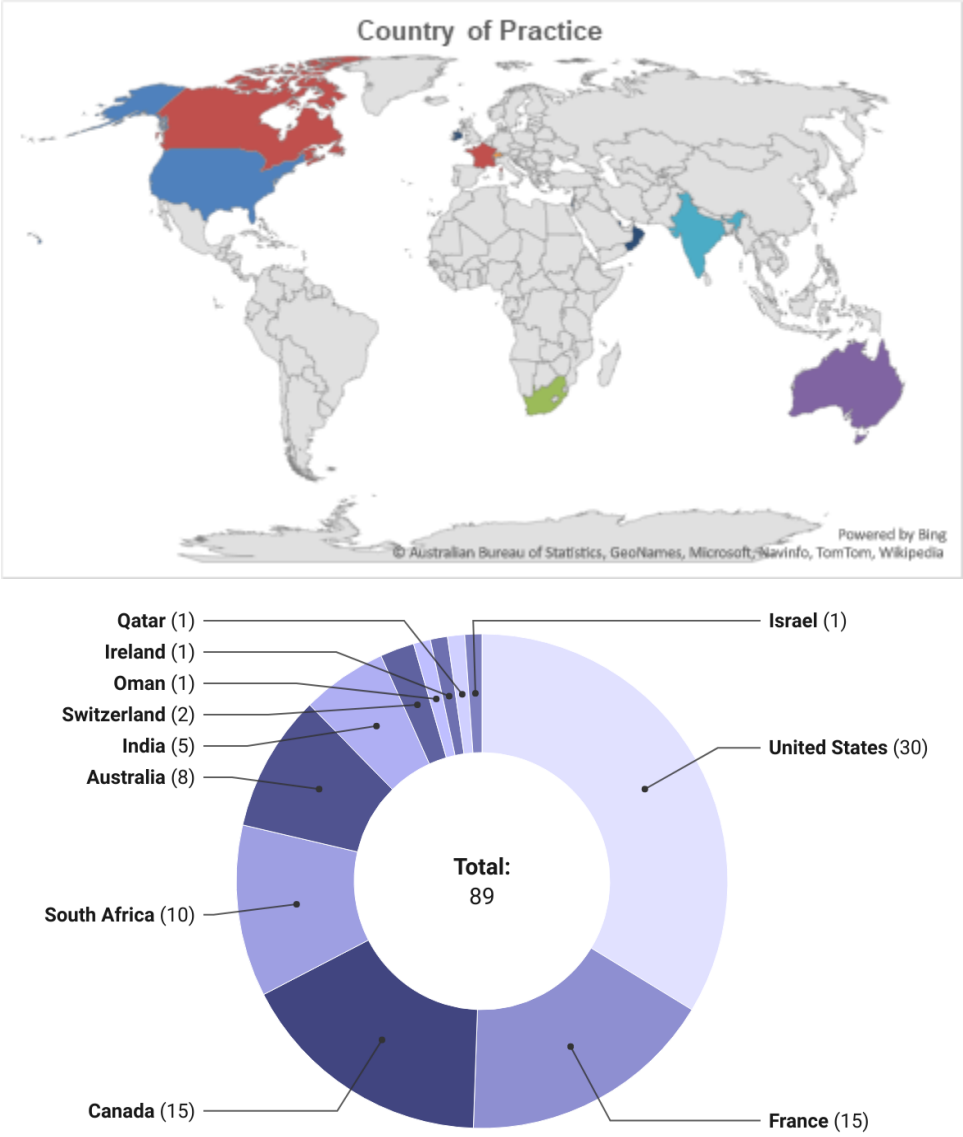

Figure 1. The countries in which the respondents practice are indicated on the map (top) and the number of respondents from each country is shown in brackets in the pie chart (bottom).

Global Trends

I. Average Prenatal Patients Seen in a Week

A majority of respondents reported seeing 1-10 patients per week (59/89) with the majority of those responses (43/59) coming from Canada (12/59), France (12/59), South Africa (10/59), and the United States (9/59), respectively. Only respondents from the United States and France reported seeing over 20 patients per week (4/89). Respondents who saw 0 patients were excluded from the survey.

II. Referral Indications

The majority of referral indications for prenatal screening during the first trimester were, “family history of a genetic condition” (77/90) “carrier/suspected carrier of a genetic condition” (75/90) and “abnormal first trimester screen (ultrasound or bloodwork)” (72/90) (Appendix 6). There were some differences in the most popular referral indications depending on the country. For Australia, in addition to the three already mentioned, “consanguinity” was also often selected (6/8). For South Africa, the most often selected indication was “advanced maternal age” (10/10), which was the second most popular for the United States (25/30). Refer to Appendix 7-10 for test-specific referral indications.

Standard of Care

I. Carrier Screening

Across the 89 prenatal care providers practicing in 11 countries, there was a split between respondents that offered carrier screening as standard of care to patients and those that did not. 51.7% (46/89) of respondents reported carrier screening of any kind was standard of care to

patients whereas 44.9% of respondents reported the test was not standard of care (Figure 2A). 3.4% (3/89) did not provide a response. Of the respondents that indicated carrier screening was offered as standard of care at their practice, a majority of respondents, 89.3% (41/46) of respondents reported that the decision was based on professional guidelines and recommendations (Figure 3).

II. Biochemical Marker Screening

Across the 89 prenatal care providers practicing in 11 countries, a majority of respondents reported screening for PAPP-A and bhCG markers as standard of care (64/89 for both) (Figure 2B). There was a split between respondents that offered msAFP screening as standard of care to patients (42/89) and those that do not (47/89). Of the respondents that indicated carrier screening was offered as standard of care at their practice, a majority of respondents reported that the decision was based on professional guidelines and recommendations (58/67) (Figure 3).

III. Ultrasound with NT measurements

A majority of respondents reported ultrasound with NT measurements are offered as standard of care at their practice (63/89) (Figure 2C). Of respondents that indicated that ultrasounds with NT measurements were standard of care, a majority (58/63) indicated the offering was due to guidelines and recommendations (Figure 3).

IV. NIPS

A majority of respondents reported NIPS was not offered as standard of care (56/89) (Figure 2D). Of individuals that indicated the screening test was standard of care, a majority, 23/30 of respondents reported it was due to guidelines or recommendations (Figure 3).

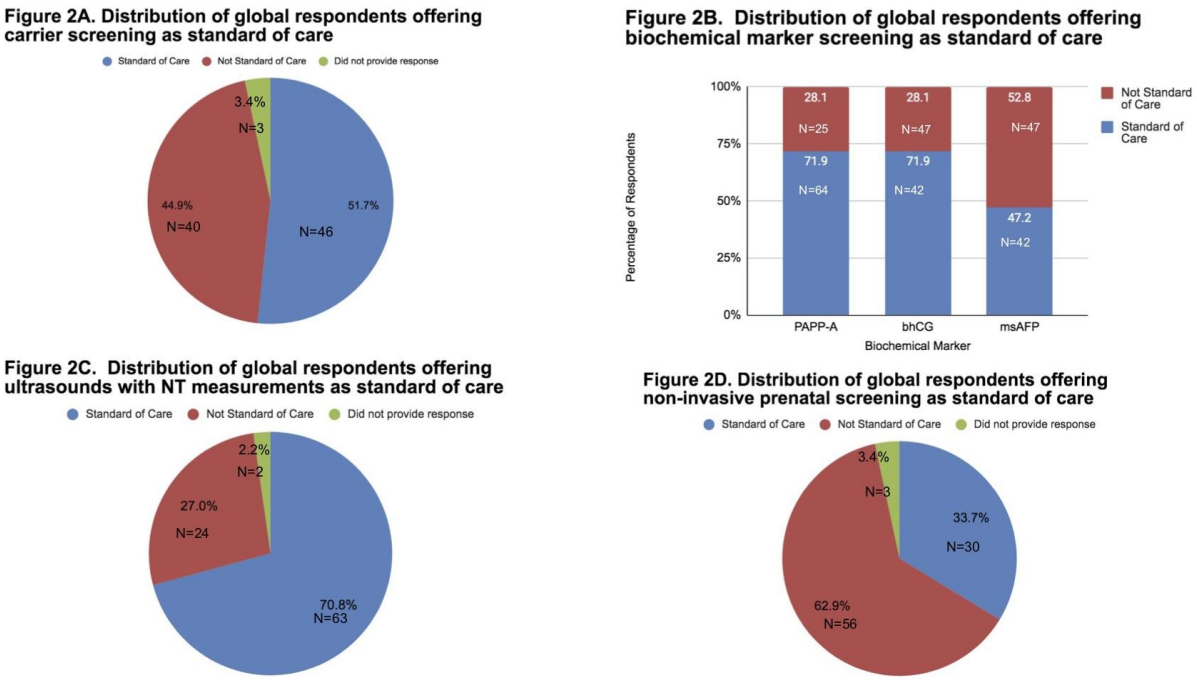

Figure 2A-D. Distribution of global respondents that reported offering A) carrier screening, B) biochemical marker screening (PAPP-A, bhCG, and msAFP), C) ultrasounds with NT measurements, and D) non-invasive prenatal screening (NIPS) as standard of care at their clinical practice.

Reimbursement

I. Carrier Screening

Surveying for reimbursement type for carrier screening showed that for the majority across all countries it was “covered by government health insurance” (59/86). Some deviations from this majority were seen in Australia (8/8), India (5/5), and South Africa (7/9) where the

reimbursement type that represented the majority was “patient out of pocket”. Country-specific reimbursement methods for each screening test can be found in Figure 4 and Appendix 12. The United States had the most diversity among respondents, with “covered by government insurance” (22/30), “covered by private health insurance” (26/30), and “patient out of pocket” (26/30) all representing a majority for the country. For those who selected “other”, respondents quoted reasons such as, “patient who select expanded carrier screening pay out of pocket”, “it depends on where patients are seen” or that “for healthy people it is up to the patient to pay”, but that it’s covered by the government “for patients with cancer”.

II. Biochemical Marker Screening

Similarly for the biochemical marker screening test, the majority of responses regardless of country selected “covered by government health insurance” as the type of reimbursement (55/71). “Patient out of pocket” represented the majority for India (4/5) and “covered by private health insurance” was the majority of responses from South Africa (4/6). Again, the United States was split with both “covered by government health insurance” (19/22) and “covered by private health insurance” (21/22) being the most popular reponses.

III. Ultrasound with NT measurement

The majority of responses across countries surveyed selected “covered by government health insurance” as the reimbursement type for ultrasounds with nuchal translucency (55/72). This again differed in India where “patient out of pocket” was the majority (4/5). South Africa and the United States had two majorities, “covered by government health insurance” (South Africa- 7/10, US- 15/21) and “covered by private health insurance” (South Africa- 6/10, US- 18/21). For the

"other" responses, some cited that it "depends on the ultrasound practice- if public or private", a "portion of them are covered by a government rebate", and that it's "covered by government health insurance provided the patient is covered/resident of [their] province".

IV. NIPS

The noninvasive prenatal screening (NIPS)/cell-free fetal DNA testing was the only test where the majority of responses from all countries was both "covered by government health insurance" (54/88) and "patient out of pocket" (61/88). Majority in Australia was solely "patient out of pocket" (7/8) as was the case for India (5/5), as well as South Africa (6/10). The United States had a three way majority again that was pretty evenly split between "covered by government health insurance" (25/30), "covered by private health insurance" (26/30), and "patient out of pocket" (24/30). A common theme among the "other" responses had to do with whether there was already an increased risk established. For example, it would be covered by the government if a previous assessment determined the risk would be between "1/2 and 1/1000", if there was a "positive integrated screen, maternal age over 40, previous T13, T18, or T21", and similarly in the case of "[previous history] T21, 18, 13".

Country	Carrier Screening	Biochemical Marker	Ultrasounds with N/T	NIPS
Australia (N=8)	**Standard of Care**			
	Yes* (5/8)	PAPP-A* (5/8), bHCG* (5/8), msAFP* (5/8), PlGF (1/8)	Yes* (6/8)	Yes* (7/8)
	Recommendations			
	Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG)	RANZCOG	RANZCOG	RANZCOG
	Australian Society of Genetic Counsellors (ASCGC)	Human Genetics Society of Australasia (HGSA)	Human Genetics Society of Australasia (HGSA)	"International guidelines"
	Human Genetics Society of Australasia (HGSA)			
Canada (N=15)	**Standard of Care**			
	No* (10/15)	PAPP-A* (13/15), bHCG*(12/15), msAFP* (11/15)	Yes* (10/15)	No*(11/15)
	Recommendations			
	Society of Obstetricians and Gynaecologists of Canada (SOGC)	Joint statement by the SOGC and CCMG	Joint statement by the SOGC and CCMG	SOGC
	Journal of Obstetrics and Gynaecology Canada (JOGC)	ACMG, JOGC, and the AMQG	ACMG, JOGC, and the AMQG	
	Canadian College of Medical Geneticists (CCMG)			
	Association of Medical Geneticists of Quebec (AMGQ)			
France (N=15)	**Standard of Care**			
	No* (9/14)	PAPP-A* (15/15), bHCG* (15/15), msAFP (5/15)	Yes* (15/15)	No* (13/15)
	Recommendations			
	French Organization of Human Genetics (Association Française de Génétique Humaine)	Haute Autorité de Santé (HAS)	Haute Autorité de Santé (HAS)	French bioethics laws
	French bioethics laws	French Biomedicine Agency	French Biomedicine Agency	
	Guidelines from a multidisciplinary Centre for Prenatal Diagnosis	French bioethics laws	French bioethics laws	
India (N=5)	**Standard of Care**			
	Yes* (3/5)	PAPP-A* (4/5), bHCG* (4/5), msAFP* (3/5), Inhibin A (2/5)	Yes* (4/5)	No*(3/5)
	Recommendations			
	Pre-Conception and Pre-Natal Diagnostic Techniques Act (PCPNDT)	Unspecified	Pre-Conception and Pre-Natal Diagnostic Techniques Act (PCPNDT)	Unspecified
Ireland (N=1)	**Standard of Care**			
	No	N/A, Other providers may	N/A, Other provider may offer	No. To be requested by patients.
	Recommendations			
	N/A	N/A	N/A	N/A

Israel (N=1)	**Standard of Care**			
	Yes	PAPP-A, bhCG	Yes	No
	Recommendations			
	Ministry of Health of Israel	Ministry of Health of Israel	Ministry of Health of Israel	
Oman (N=1)	**Standard of Care**			
	No	No	Yes	No
	Recommendations			
	N/A	N/A	Oman Obstetric and Gynecology Association	N/A
Qatar (N=1)	**Standard of Care**			
	Yes	No	Yes	No
	Recommendations			
	Based on unspecified guidelines/ recommendations	N/A	American College of Obstetricians and Gynecologists (ACOG)	N/A
South Africa (N=10)	**Standard of Care**			
	No* (8/9)	PAPP-A (2/4), bcHG (2/4), msAFP (1/4)	No* (6/10)	No* (7/7)
	Recommendations			
	ACOG	South African Society for Ultrasound in Obstetrics and Gynaecology (SASUOG)	SASUOG	N/A
	European Society of Human Genetics (ESHG)	ACOG	ACOG	
		ESHG	South African Society of Obstetricians and Gynaecologists (SASOG)	
Switzerland (N=2)	**Standard of Care**			
	No* (2/2)	PAPP-A* (2/2), bhCG* (2/2),	Yes* (2/2)	No* (2/2)
	Recommendations			
	N/A	Swiss Society of Gynecology and Obstetrics	Swiss Society of Gynecology and Obstetrics	N/A
United States (N=30)	**Standard of Care**			
	Yes* (26/30)	PAPP-A* (22/30), bhCG* (22/30), msAFP* (19/30)	Yes* (19/29)	Yes* (19/30)
	Recommendations			
	American College of Obstetricians and Gynecologists (ACOG)	ACOG	ACOG	ACOG
	American College of Medical Genetics (ACMG)	NSGC	NSGC	ACMG
	The Society for Maternal Fetal Medicine (SMFM)	SMFM	SMFM	SMFM
		California Department of Public Health- Genetic Disease Screening Program	The International Society of Ultrasound in Obstetrics & Gynecology (ISUOG)	
			The Nuchal Translucency Quality Review Program (NTQR)	

Figure 3. Country-specific responses about whether first trimester- screening tests were offered/not offered as standard of care and the cited guidelines/recommendations contributing to the decision to offer as standard of care. A count of how many respondents reporting a majority response (>60% of total responses) out of the total responses for the question is provided. Asterisks (*) denote a majority response.

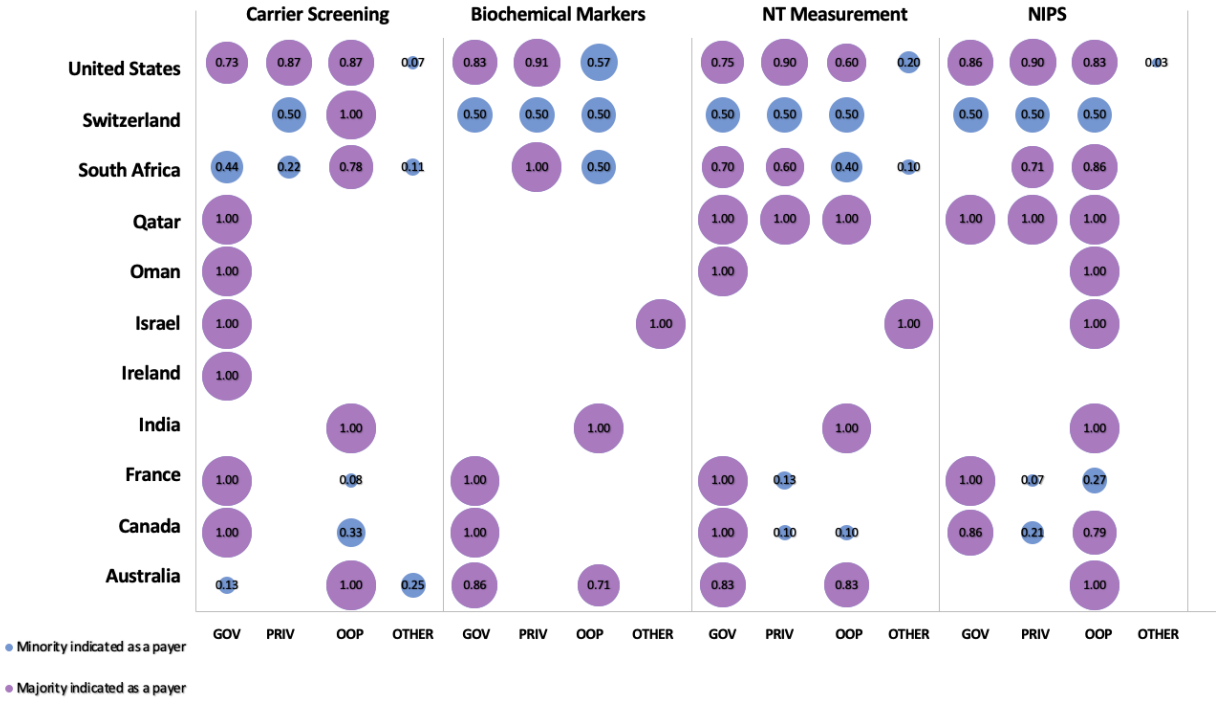

Figure 4. National reimbursement methods for each screening measure (carrier screening, biochemical markers, NT measurement, and NIPS) are indicated, along with whether a majority (60% or more) or a minority (less than 60%) of respondents indicated it as a reimbursement method. Respondents could select multiple reimbursement methods for one screening method. (GOV = government funded; PRIV = covered by private insurance; OOP = Out of pocket for patient; OTHER includes funded by lab, institution, research, etc.)

Discussion

Referral Indications

Referral indications for prenatal screening tests during the first trimester followed general trends with some exceptions. With regards to carrier screening, “family history of a genetic condition” represented the majority of responses with “carrier/suspected carrier of a genetic condition” as the second most common indication. However, India contradicted this global trend, instead citing consanguinity. Consanguinity is a well-known cause of autosomal recessive conditions; as consanguinity rates are estimated to be as high as 50% in some parts of India, its reporting as the most popular referral indication for carrier screening is understandable (Roy et al. 2020).

In a minority of countries, genetic counselors were found to play specialized roles within a prenatal care team not directly involved in the screening process. In Ireland, an obstetric consultant-led, midwife-managed service model predominates in maternity care (Begley et al. 2011). This was supported by the response that genetic counselors are not a part of the maternity unit. Conversely, genetic counselors provide consultations for indications not limited to the prenatal speciality and are not directly involved in offering biochemical marker screening, ultrasound with NT measurements, or NIPS. This is thought to explain the dearth of screening offerings by the genetic counselor respondent. In Qatar, a genetic counseling program was only recently introduced and so this, similarly, may explain the limited services provided by the genetic counselor, emphasizing the importance of the broader clinical team (Al-Dewik, 2018). The respondent from Qatar similarly reported that "being the only team of its kind in Qatar, the prenatal genetics team does not offer/ facilitate prenatal screening tests, but rather only diagnostic testing. Prenatal screening tests including NIPS are offered by obstetrics providers.”

The biochemical marker screening test was generally found to be offered to all patients on a global scale but was not found to be offered to any patients in Oman and Qatar, and as reported by half of the respondents from South Africa. Of those who did not offer biochemical marker screening, including the Omani respondent and a respondent from South Africa, the most common reason selected was that this test is not deemed as accurate as other screening tests. This is a sentiment that has been echoed in the literature: one study reports it has a detection rate of about 81% using a 5% screen positive rate, which is slightly lower than that of the first trimester screen (Carlson & Vora, 2017). Using markers such as hCG, AFP, inhibin A, and unconjugated estriol is an older test, one of the first serum screening tests that started to be offered in the 1990s, and it is starting to be phased out in the United States to make way for other more accurate prenatal testing options. Many respondents denied offering biochemical marker screening and instead offered screening methods known to be more accurate for certain indications. Apprehension towards the utility of biochemical screening may increase over time as more screening options with greater accuracy become widely available.

Ultrasounds with nuchal translucency measurement was the screening test that showed the least amount of variation in referral indications among countries. The majority of respondents reported that all patients were offered this screening test. Similar to the biochemical marker screening, this test is a mainstay among prenatal screening with ultrasound becoming increasingly prominent in the 1970's and nuchal translucency first being described in 1992 (Bardi et al. 2019). The visualization of anomalies by the ultrasound with NT measurement is beneficial at early stages of pregnancy, allowing more time to interpret the results and make

decisions for further monitoring of the pregnancy. The near-universal offering of this test speaks to the advantages of such information.

While a universal trend was observed in the standardization of ultrasound screening with NT measurement, this finding is not a true portrayal of prenatal care for all individuals. Many respondents in Canada advised that while an ultrasound with NT measurement was technically offered to all prenatal patients, it was not as accessible to individuals living in remote northern areas. The dislocation of prenatal care has been previously reported in the literature and is one of many factors involved in the inadequate prenatal care in First Nations' communities (Heaman et al. 2018; Couchie et al. 2007). While Canada boasts a universal health care system, a large disparity of care exists that is comparable to that of the United States, reinforcing the notion that adequate prenatal care is impacted by multiple factors in addition to cost (Heaman et al. 2018). This highlights the importance not only of offering prenatal screening services but also of ensuring such services are accessible to all pregnant individuals within their own community.

Referral indications for non-invasive prenatal screening (NIPS) were mixed between high risk patients and standard of care: it is posited that the recent change in professional recommendations in the United States is a contributing factor to this difference. Previously, the American College of Obstetricians and Gynecologists (ACOG) recommended this screening only for women with an elevated risk of aneuploidy (Carlson & Vora. 2017). This reflected what was found in the survey data with the "abnormal first trimester screen" referral indication representing the global majority. However, ACOG recently updated their guidelines to advise that all pregnant women should be offered this screening test regardless of age or risk (Kaimal et

al. 2020). Genetic counselors located in the United States were more likely to report offering NIPS to all patients and adhering to these recently changed guidelines. As many countries indicated following ACOG guidelines, future studies are recommended to observe whether these countries will implement these new NIPS recommendations.

Reimbursement

In general, the majority of respondents for each prenatal screening test except NIPS reported that the cost of testing was covered by government health insurance. Financial barriers were seen as a common reason NIPS was not offered to all patients and this has previously been reported in the literature (Chandrasekharan et al. 2014). Survey data found that NIPS reimbursement was split between government health insurance and at an out-of-pocket cost to the patient. The same authors also noted a regulatory gap when it comes to the content or quality of the test because of the lack of local validation studies performed (Chandrasekharan et al. 2014). As this screening test gains popularity among providers and patients, greater government regulation could be enacted to encourage an increase in government reimbursement in the future.

Countries that were found to stray from this global majority included the United States, Australia, South Africa, and India. Across all tests, the United States was the one country where responses were consistently spread across various reimbursement sources. This was anticipated as the United States' healthcare system is notorious for being more divided than the healthcare systems of other countries. The Indian healthcare system is similarly inconsistent: health care services vary depending on region and as such, contextualizes the findings that all screening methods surveyed were shown to have a private pay component.

Carrier screening reimbursement in Australia was reported as a cost to patients out of pocket whereas the majority across all countries surveyed was reported to be through government health insurance. Carrier screening has been available to the general population at their own cost for cystic fibrosis, spinal muscular atrophy, and Fragile X syndrome since Victorian Clinical Genetic Services began offering it in 2012. This program was one of the first genetic carrier screening panels available, though literature has cited a lack of awareness of this test's private availability among healthcare providers within the Australian public system (Archibald et al. 2018). Given that carrier screening is more often offered by private practitioners, this institutional discrepancy may explain why reimbursement is mostly the patient's responsibility.

While the funding of South Africa's healthcare system is a mix of private and public funding with about 57% of the population utilizing public services and 43% utilizing private facilities, patient self-pay was most often selected for carrier screening and NIPS (Kromberg et al. 2013). Prenatal diagnostic genetic testing, carrier testing, and genetic counseling services are provided at the tertiary care level and all pregnant individuals are entitled to free healthcare through public hospitals. That being said, financial support from public funds for genetic services is lacking because it is not reportedly a priority for the Department of Health (Kromberg et al. 2013). This near-even split between the private and public sectors, as well as the general lack of public funding would serve as an explanation as to why "patient out of pocket" was selected most often for carrier screening and NIPS.

This sentiment of insufficient government coverage was echoed by South African genetic counselors. Respondents further elaborated on their responses, commenting that if a patient is seen in government healthcare, the government will usually cover the cost, but testing is "very limited" and how "not all medical aids will cover the cost of even local testing". Likewise, another South African respondent advised that those with a higher income will receive a higher portion of the bill and that the hospital will cover the cost for those under a certain financial tier but that "no government insurance exists". Responses from South Africa was split between government health insurance and private health insurance as reimbursement types for ultrasounds with nuchal translucency, which is a reflection of the more evenly divided healthcare system.

Standard of Care and Presence of Professional Guidelines & Recommendations

Presumably, national guidelines set forth by professional organizations and regulatory bodies would facilitate and guide more uniform practices. In the past, recommendations and guidelines have guided and directed prenatal care practice (Lou et al. 2018; van der Meij et al. 2019; Ferrier et al. 2019; Roblejo et al. 2017). Alternatively, in the absence of established practice guidelines, there has been variation in how testing and services offered by prenatal providers (Suskin et al. 2016; Minear et al. 2015).

Variability existed in the offering of carrier screening, biochemical marker screening, and ultrasounds with NT measurements, and NIPS as standard of care during the first trimester of pregnancy both across countries and within countries. The one exception to this finding was the respondents from France uniformly reporting they offer biochemical testing of PAPP-A and

bhCG and ultrasounds with NT measurements as standards of care to prenatal patients. This uniformity may be attributable to the national health care system and clear recommendations by France's Haute Autorité de santé in 2007 for Down Syndrome (HAS, 2007). While carrier screening was consistently reported as not standard of care as per French bioethics laws, carrier screening is gaining popularity in France and may change in the future (Bonneau et al. 2021).

The limited availability of genetic counselors as well as laboratory resources in Canada are relevant factors pertaining to carrier screening offerings (SOGC-CCMG 2016). As of 2016, CCMG and SOGC in Canada recommends a discussion about the value and risk of reproductive carrier screening to all women and families during preconception, first prenatal visit, and regardless of gestational age at the time of visit (Wilson et al. 2016/ SOGC-CCMG). In particular, it is advised that carrier screening should be offered in response to an indicative family history of a condition and, in particular, notes that routine carrier screening of spinal muscular atrophy is not provided as the laboratory infrastructure and access to genetic counseling is not equally distributed throughout the country (SOGC-CCMG 2016). Some respondents noted recommendations from these associations in their offering of carrier screening as standard of care. The debate over equitable resource allocation and carrier screening is common among many countries that offer publicly funded health services.

Respondents from European countries such as France and Switzerland, similarly reported that the current practice is to offer carrier screening only to those with a family history in their or their partner’s family, even though it's not reimbursable by the mandatory public health insurance system. There is currently limited data concerning Swiss and French carrier screening practices.

Rowe and Wright (2020) suggest that countries with universal health care face the challenge of a lack of proof of efficacy regarding offering carrier testing when limited resources and equitable access to care exist.

Carrier screening was not found to be standard of care in Oman through our survey, though premarital genetic screening has been reported to be available for hemoglobinopathies in some regions of the country as of the year 2000 through The National Program for the Control of Genetic Blood Disorders (Rajab et al. 2013). It is possible that a general unwillingness of individuals to participate in premarital carrier screening in the country may be a causal factor preventing the implementation of this service as a standard of care (Al-Farsi et al. 2014). In particular, it was found that when surveyed, almost one third of adults in Oman were unwilling to personally partake in premarital carrier screening despite a large majority of respondents acknowledging its importance (Al-Farsi et al. 2014).

This contrasts with the neighbouring country of Qatar, a population with similarly high rates of consanguinity but a more drastic approach to carrier screening as a preventative health measure has been taken to improve the health of its population, which was inline with carrier screening findings from our one Qatari respondent. A National Premarital Genetic Screening program implemented in 2009 introduced the concept of carrier screening and falls in line with this overall national vision. This testing is offered by public hospitals as well as private clinics and is a necessary requirement for marriage in Qatar, a country with a high rate of consanguineous unions (Al-Dewik, 2018). The sole respondent from Qatar reported that patients with a family history of a genetic condition, suspected carriers, or those who request it are offered carrier

screening. The accessibility criteria for carrier screening are a part of their national health initiatives.

Also among these countries with lesser genetic counseling representation in our survey, the sole respondents from Ireland, Oman, and Qatar each reported biochemical marker screening as not offered as standard of care at their clinics. In Oman, it has also been noted that a lack of maternal serum screening is available and can be attributed to a lack of familiarity with the testing that existed both among patients and providers (Rajab et al. 2013). NIPS is a highly accurate form of prenatal screening and may obviate the need for a serum screen that would prompt confirmatory invasive testing in the event of a high-risk result. Its emergence as a first-tier screening tool continues to be evaluated globally (TRIDENT, 2018). All this must be understood within a context of broader religion-based laws forbidding pregnancy interruptions (Rajab et al. 2013).

Countries in which a majority of respondents reported offering carrier screening, ultrasound with NT measurements, biochemical marker screening, and NIPS as standard of care frequently noted their decision was based on guidelines and recommendations established by a regulatory body in their country of practice or cited an international guideline. There were, however, instances where responders offered tests as standard of care and did not point to particular guidelines and recommendations in influencing their offerings.

A majority of respondents from South Africa reported carrier screening, ultrasounds with NT measurements and NIPS were not offered as standard of care at their practice. A further majority of individuals did not provide responses regarding the biochemical marker screening test being

offered as standard of care. Kromberg et al. (2013) report limited preconception care and an absence of genetic services in rural areas apart from the outreach clinics provided by academic centers. Due to limited financial resources in the country, biochemical screening is limited to the private sector only and prenatal diagnostic procedures are provided at tertiary centers only (Geerts 2008; Urban et al. 2011). Similar sentiments were echoed by respondents in this study.

Practice Implications

The current study examines global prenatal first-trimester screening practices in order to critically assess the similarities and differences in care, as well as to inform future practice decisions. Respondents indicated screening tests offered are often limited to the resources and bandwidth available to each institution, which suggests a global need for genetic counselors to provide prenatal care. Additionally, it was found that while some screening tests may be standard of care, the degree of accessibility by pregnant individuals is variable. These aspects must be considered holistically when evaluating the applicability of screening methods to respective prenatal practices.

Limitations

Clinical practices of respondents are not representative of the practices of the country as a whole. There were limited respondents from some countries covered in the study. We intended to target responses from practicing genetic counselors and for countries with limited numbers of practicing genetic counselors, there were low numbers of responses. As a result, statistical comparisons could not be made. There were also limited participants from the United States considering the number of practicing genetic counselors. Furthermore, while we intended to

expand our reach to non-genetic counselor prenatal providers, the method of survey distribution may have led to a preferential bias towards sampling genetic counselors.

Data were excluded from respondents that reported single gestational age week time points that were outside the limits of screening test capabilities (e.g. offering biochemical marker screening at 4 weeks gestational age). Similarly, data were included in the analyses when different providers practicing within the same country reported offering screening at similar gestational age time points (e.g. Offering NIPS at 6 weeks and biochemical marker screening at 6 weeks GA). There was a potential for user error due to the absence of a "back" or "return" button on the survey.

Research Recommendations

Future research studies should further investigate prenatal screening practices in countries not represented in the current study. Given the majority of respondents to the study were genetic counselors, practices of non-genetic counselor prenatal service providers may allow for a more comprehensive understanding of global prenatal care practices. Importantly, the motivating factors in screening options offered as standard of care and the subsequent patient uptake of these testing options may continue to be explored in future studies.

Conclusion

Among the first trimester screening tests surveyed, non-invasive prenatal screening (NIPS) was not found to be standard of care globally with the exception of the United States. However, respondents from various countries expressed interest in offering NIPS as a standard of care at

their practice. Government reimbursement was reported by providers to be a major form of reimbursement for all four types of screening tests. NIPS was unique in that patient out of pocket was an equally popular form of reimbursement. Participants expressed reimbursement challenges to be potential barriers for offering NIPS as standard of care. Government-funded services were more likely to cover more established tests despite increasing accuracy of NIPS.

Coverage may be subject to change with the recently updated ACOG recommendations that NIPS be offered to all pregnant individuals. Even in the presence of guidelines, other factors such as reimbursement availability are more likely to be a determining factor for the offering of screening tests. Further research is needed to understand and overcome barriers to appropriate and quality prenatal care for all individuals.

Conflicts of Interest

Dharti Adhia declares that she has no conflict of interest.

Ming Bauer declares that she has no conflict of interest.

Rachel Lanning declares that she has no conflict of interest.

Jenny Zhang declares that she has no conflict of interest.

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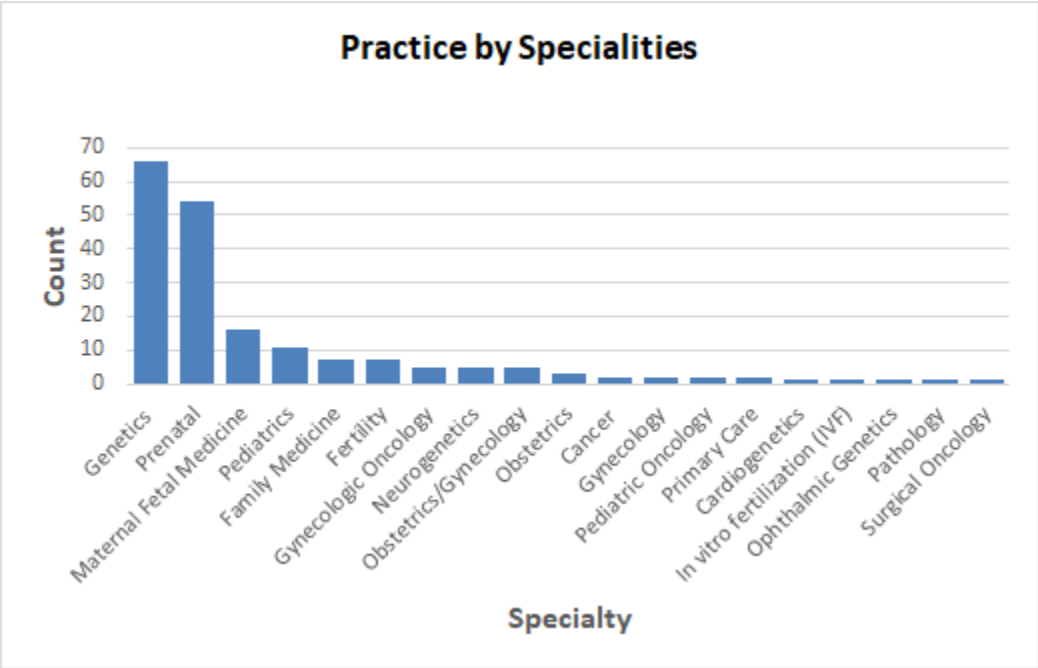
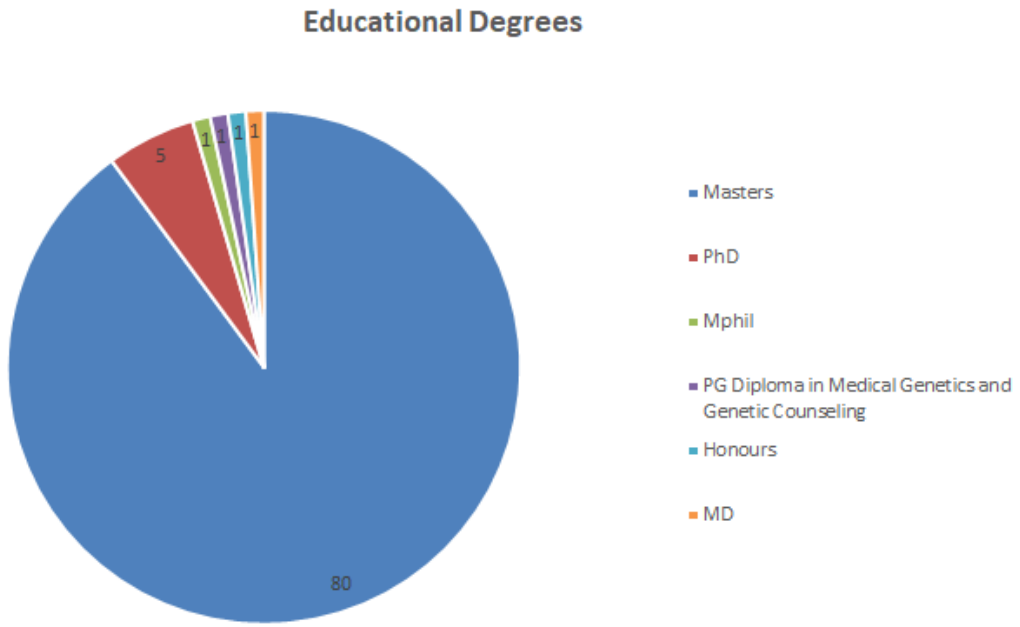
Appendix 1. Number of prenatal patients seen per week by each respondent

# of prenatal patients seen per week	Total # of respondents	Australia	Canada	France	India	Ireland	Israel	Oman	Qatar	South Africa	Switzerland	United States
1-10	60	7	12	12	3	1	1	1	1	10	2	9
11-20	25	1	3	0	2	0	0	0	0	0	0	19
More than 20	4	0	0	2	0	0	0	0	0	0	0	2

Appendix 2. Respondents' reported specialities of expertise



Appendix 3. Educational degrees held by respondents



Appendix 4. Respondent affiliated professional organizations

Country of Practice	Affiliated Professional Organization(s)
Australia	Australasian Society of Genetic Counselors American Board of Genetic Counseling
Canada:	Canadian Association of Genetic Counselors National Society of Genetic Counselors Quebec Association of Genetic Counsellors
Qatar	American Board of Genetic Counseling National Society of Genetic Counselors
Ireland	Association of Genetic Nurses and Counselors
United States of America	American Board of Genetic Counseling NSGC
France	French Association of Genetic Counselors
Switzerland	French Association of Genetic Counselors Swiss Association of Genetic counselors
South Africa	Health Professional Council of South Africa
India	Genetic Counseling Board of India
Israel	Israeli Society of Genetic Counselors
Oman	Oman Association of Medical Genetics

Appendix 5. Respondent work settings. Multiple work settings could have been selected.

Work Setting	Total # of respondents	Australia	Canada	France	India	Ireland	Israel	Oman	Qatar	South Africa	Switzerland	United States
Community hospital	3	0	2									1
Physician private practice	5	0	0	0	0	0	0	0	0	0	0	5
Private hospital/medical facility	26	1	2		2				1	5		15
Public hospital	51	7	10	15		1	1	1	1	7	2	6
Other												
Community family practice clinic	1	0	1	0	0	0	0	0	0	0	0	0
Industry	1	0	0	0	1	0	0	0	0	0	0	0
Laboratory	2	0	0	0	2	0	0	0	0	0	0	0
Military hospital	2	0	0	0	0	0	0	0	0	0	0	2
University affiliated public hospital	1	0	1	0	0	0	0	0	0	0	0	0
University medical center	2	0	0	0	0	0	0	0	0	0	0	2

Appendix 6. General referral indications for prenatal screening during the first trimester. Respondents could select multiple referral indications.

General Referral Indications	Total Responses	Australia	Canada	France	India	Ireland	Israel	Oman	Qatar	South Africa	Switzerland	United States
Advanced maternal age	47	3	4	1	2	0	0	0	1	10	0	25
Carrier/suspected carrier of a genetic condition	75	7	12	14	4	1	1	1	1	7	2	25
Personal medical history	50	3	8	7	3	0	1	1	1	6	0	19
Abnormal first trimester screen (ultrasound or bloodwork)	72	6	12	14	5	0	1	1	1	8	2	22
Pregnancy complications (either past or present)	43	3	7	8	3	0	0	1	1	5	0	14
Exposures/ Teratogen Counseling	26	0	4	0	1	0	0	0	1	5	0	15
Family history of a genetic condition	77	8	12	15	4	1	1	1	1	6	2	26
Consanguinity	47	6	8	6	4	0	1	0	1	2	0	18
All prenatal patients are referred	10	0	2	0	1	0	0	0	0	0	0	7
Other	6	0	1	0	0	0	0	0	0	0	0	5

Appendix 7. Referral indications for carrier screening. Respondents could select multiple referral indications.

Carrier Screening Referral Indications	Total Responses	Australia	Canada	France	India	Ireland	Israel	Oman	Qatar	South Africa	Switzerland	United States
Advanced maternal age	12	2	0	0	2	0	0	0	0	1	0	6
Carrier/suspected carrier of a genetic condition	49	3	11	13	4	1	0	1	1	6	2	7
Personal medical history	23	2	2	6	3	0	0	0	0	2	0	7
Abnormal first trimester screen (ultrasound or bloodwork)	24	1	3	9	4	0	0	0	0	1	0	6
Pregnancy complications (either past or present)	16	1	1	4	2	0	0	0	0	0	0	7
Exposures	5	0	0	0	0	0	0	0	0	0	0	5
Family history of a genetic condition	55	3	12	14	4	1	0	1	1	8	2	8
Consanguinity	28	2	5	4	4	0	0	0	0	4	0	8
All patients	37	4	3	0	2	0	1	0	0	1	0	26
At patient's request	21	2	3	0	1	0	0	0	1	5	0	8
No one is offered carrier screening	2	0	0	1	0	0	0	0	0	1	0	0
Other	9	1	7	0	0	1	0	0	0	0	0	1

Appendix 8. Referral indications for biochemical marker screening. Respondents could select multiple referral indications.

Biochemical Marker Screening Referral Indications	Total Responses	Australia	Canada	France	India	Ireland	Israel	Oman	Qatar	South Africa	Switzerland	United States
Advanced maternal age	5	0	0	0	1	0	0	0	0	1	0	3
Carrier/suspected carrier of a genetic condition	7	0	0	4	1	0	0	0	0	0	0	2
Personal medical history	6	0	0	3	1	0	0	0	0	0	0	1
Abnormal first trimester screen (ultrasound or bloodwork)	10	0	0	6	1	0	0	0	0	0	1	2
Pregnancy complications (either past or present)	4	0	0	3	0	0	0	0	0	0	0	1
Exposures	1	0	0	0	0	0	0	0	0	0	0	0
Family history of a genetic condition	6	0	0	4	1	0	0	0	0	0	0	1
Consanguinity	2	0	0	0	1	0	0	0	0	0	0	1
All patients	55	7	13	9	4	0	1	0	0	2	1	18
At patient's request	8	1	0	0	1	0	0	0	0	2	0	4
No one is offered the biochemical marker screening test	11	0	1	0	0	0	0	1	1	5	0	3
Other	11	0	1	0	0	0	0	0	0	3	0	7

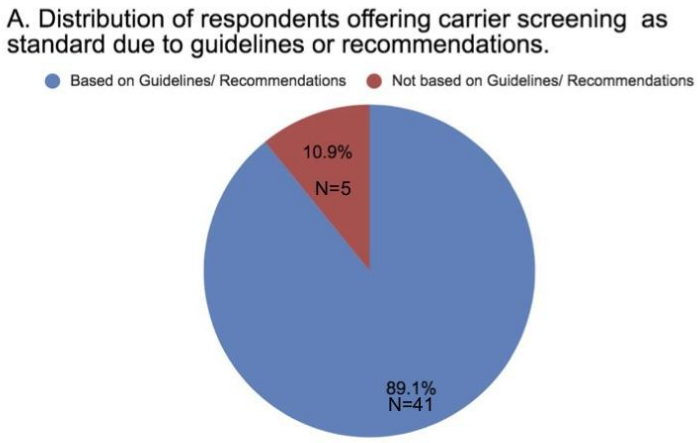
Appendix 9. Referral indications for ultrasounds with NT measurement. Respondents could select multiple referral indications.

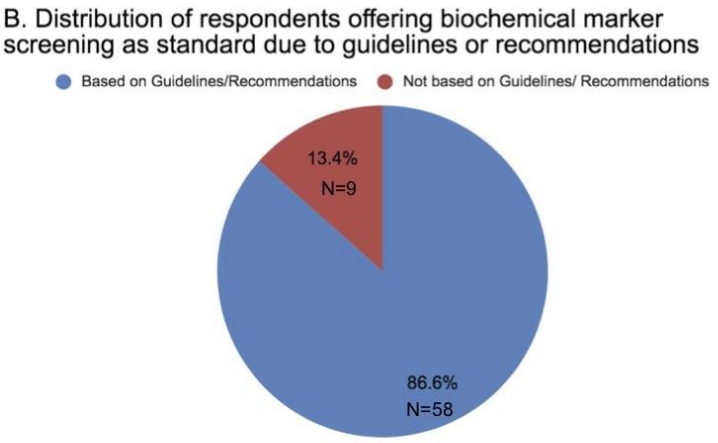
Ultrasounds with NT Measurement Referral Indications	Total Responses	Australia	Canada	France	India	Ireland	Israel	Oman	Qatar	South Africa	Switzerland	United States
Advanced maternal age	16	1	3	0	0	0	0	1	0	6	0	4
Carrier/suspected carrier of a genetic condition	5	0	2	0	0	0	0	0	0	0	0	3
Personal medical history	5	1	0	0	0	0	0	0	0	0	0	3
Abnormal first trimester screen (ultrasound or bloodwork)	9	1	2	0	0	0	0	1	0	0	0	5
Pregnancy complications (either past or present)	11	1	2	0	0	0	0	1	0	1	0	5
Exposures/Teratogen Counseling	6	1	2	0	0	0	0	0	0	0	0	3
Family history of a genetic condition	7	1	1	0	0	0	0	0	0	2	0	3
Consanguinity	4	0	1	0	0	0	0	0	0	0	0	2
All patients	67	7	10	15	5	0	1	0	1	4	2	22
At patient's request	7	0	0	0	0	0	0	0	0	0	0	6
No one is offered ultrasounds with NT measurements	2	0	1	0	0	0	0	0	0	0	0	1
Other	10	0	4	0	0	0	0	0	0	2	0	4

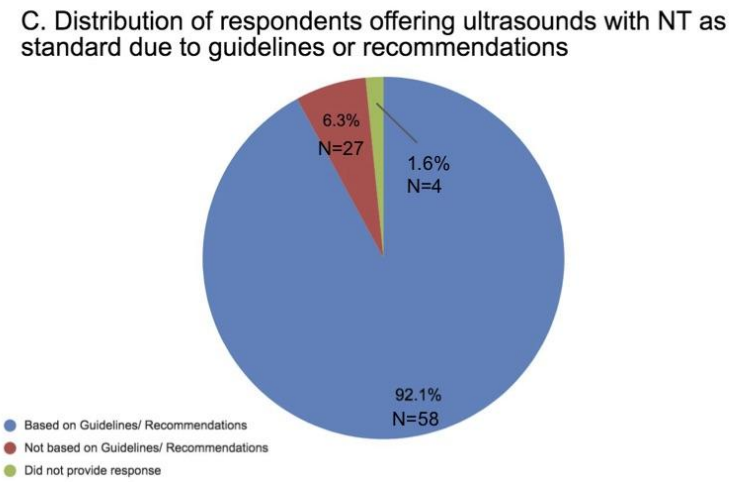
Appendix 10. Referral indications for non-invasive prenatal screening. Respondents could select multiple referral indications.

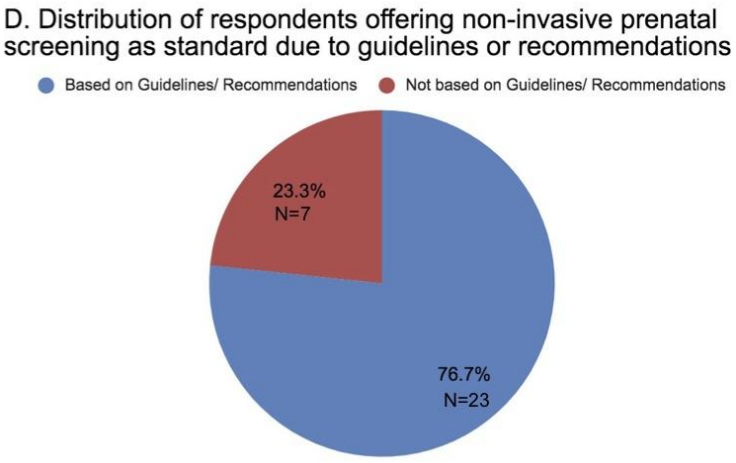
NIPS Referral Indications	Total Responses	Australia	Canada	France	India	Ireland	Israel	Oman	Qatar	South Africa	Switzerland	United States
Advanced maternal age	28	0	10	1	2	0	0	1	1	4	0	8
Carrier/suspected carrier of a genetic condition	12	0	1	6	1	0	0	0	0	0	0	3
Personal medical history	6	0	0	2	1	0	0	0	0	0	0	2
Abnormal first trimester screen (ultrasound or bloodwork)	41	0	12	11	4	0	0	0	1	4	2	7
Pregnancy complications (either past or present)	16	0	7	3	0	0	0	1	0	1	0	3
Exposures/Teratogen Counseling	2	0	0	0	0	0	0	0	0	0	0	2
Family history of a genetic condition	15	0	2	6	3	0	0	0	0	1	0	3
Consanguinity	4	0	0	0	1	0	0	0	0	0	0	2
All patients	31	7	4	0	2	0	0	0	0	0	0	18
At patient's request	16	1	3	3	3	0	0	0	0	3	0	3
No one is offered NIPS or cell-free fetal DNA testing	3	0	0	0	0	0	0	0	0	3	0	0
Other	13	0	2	3	0	1	1	0	0	4	0	2

Appendix 11A-D. Percentage of respondents reporting there were guidelines/ recommendations established by professional societies or regulatory bodies that led to their offering of screening tests (A) carrier screening, B) biochemical markers (any kind), C) ultrasounds with NT measurements, D) NIPS) as standard of care.









Appendix 12. Supplemental Results

Provider Involvement in the Genetic Counseling Process

Almost all respondents indicated "yes" to being part of the genetic counseling process (87/89). Almost all respondents also advised that they provide pretest counseling to patients as part of their practice (87/89). During pretest counseling, a majority indicated obtaining informed consent (82/89), explaining conditions that may be identified by prenatal genetic testing screening tests (87/89), providing an individualized risk assessment based on medical and/or family history (86/89), and helping patients understand the potential psychological implications of testing (88/89) was within their scope of practice. The vast majority of respondents also indicated that providing genetic screening results (86/89), providing help to adapt to the psychological implications and test results (84/89) was part of their scope of practice.

Global Trends for Referral Indications

I. Carrier Screening

The majority of responses cited "family history of a genetic condition" (55/89; 61.80%) as a reason to offer carrier screening. However, there were a couple countries where the referral indication that represented the majority was different. In Canada, "carrier/suspected carrier of a genetic condition" was another referral indication that gained a majority of responses. This was also a popular referral indication in France (13/15; 86.67), India (4/5; 80%), and South Africa (6/10; 60%). Majority of respondents from France (9/15; 60%) and India (4/5; 80%) also selected "abnormal first trimester screen (ultrasound/bloodwork)". India was the only country where the majority also chose "consanguinity" (9/15; 60%). For the United States, the majority

did not choose the global majority, but rather said that “all patients” were referred for carrier screening (26/30; 86.67%).

II. Biochemical Marker Screening

The majority of the total responses advised that “all patients” were offered biochemical marker screening (55/89; 61.80%). The sole response from Oman and the sole response from Qatar said that “no one is offered the biochemical marker screening test”. This was also selected for half of the responses from South Africa (5/10; 50%). The sole response from Switzerland selected the most popular referral indication across all responses, as well as “abnormal first trimester screen (ultrasound or blood work)”. As for reasons why this was not offered to everyone, around half of respondents indicated it was because this screening test is “not as accurate as other types of screening” (5/11; 45.45%).

III. Ultrasounds with NT Measurement

The majority of responses indicated that “all patients” were offered this screening (67/89; 75.28%). There was not much deviation from this majority apart from Oman and South Africa. The one respondent from Oman instead selected, “pregnancy complications (either past or present)”, “abnormal first trimester screen (ultrasound or bloodwork)”, and “advanced maternal age”. “Advanced maternal age” was also the indication most often selected for South Africa (6/10; 60%). Two respondents said this was not offered to patients, with one coming from the United States and the other coming from Canada. The United States respondent said they “do not have ultrasound techs with proper certifications for nuchal measurements”. The response from

Canada said their clinic was “private pay only” and that “NT ultrasounds are covered provincially” and “therefore available to everyone elsewhere”.

IV. NIPS

More variation was observed with regards to referral indications for noninvasive prenatal screening (NIPS), also called cell-free fetal DNA testing. There was no one referral indication that represented a true majority, however the indication most often selected was, “abnormal first trimester screen (ultrasound or bloodwork)” (41/87; 47.12%). For Australia, no one selected this, but instead the majority was that “all patients” were offered NIPS (7/8; 87.0%). Similarly, “all patients” was the most common indication for the United States (18/28; 64.29%).
“Reimbursement issues” and “cost” represented the majority when it came to reasons why this screening test was not offered to everyone (6/8; 75%) with half of the responses coming from the United States and the other half from South Africa. One respondent from the United States said this wasn’t offered because it is “deemed not as accurate as other types of screening for the ‘low risk’ population” and another cited “lack of provider awareness/education”.

Country-specific Practices

Australia

The majority of respondents from Australia self reported to work in a public hospital (7/8), while one works in a private hospital/medical facility. Respondents reported being members of Australasian Society of Genetic Counselors and American Board of Genetic Counseling.

Carrier screening

There was no singular referral indication for carrier screening that represented a majority. Half of the respondents reported that “all patients” were offered carrier screening (4/8; 50%) and all respondents indicated they offered carrier screening for at least one referral indication.

A majority of respondents in Australia indicated that carrier screening was offered as standard of care at their practice (5/8) a majority of respondents indicated the test was standard of care (4/5), all stated that their decision to offer carrier screening was based on recommendations or guidelines formed by Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG), the Australian Society of Genetic Counsellors, and the Human Genetics Society of Australasia (HGSA).

All respondents to this question indicated that carrier screening is reimbursed for with out of pocket pay (8/8). However, it is also possible that it may be covered under government health insurance (1/8), the providing institution/hospital (1/8) or under the guise of research (1/8). Respondents indicated that reimbursement can depend on family history such that if there is a history of a recessive condition, it is covered by public funding. If this is not the case, the patient will pay out of pocket for carrier screening. Another respondent indicated that there may be clinic funding depending on the circumstance.

Biochemical marker screening

The majority of responses indicated “all patients” as the referral reason for biochemical marker screening (7/8) while one respondent reported it was offered upon patient’s request. A majority of respondents from Australia indicated biochemical marker testing of PAPP-A (5/8) and

bHCG(5/8) were standard of care. Respondents reported Placental Growth Factor (PLGF) for preeclampsia and msAFP as additional markers screened for as standard of care at their practice. Respondents reported their decision to offer their specified biochemical markers was based on recommendations or guidelines formed by RANZCOG and The Human Genetics Society of Australasia (HGSA) (3/7). Most respondents advised that this test is offered as early as 10 weeks and onwards. The earliest reported point of this test being offered was at 8 weeks and the latest point was 12 weeks. Biochemical marker screening was indicated to be reimbursed by both the government (6/7) and at a cost out of pocket to patients (5/7) as per the respondents to this question. One respondent advised there is government rebate for both the scan and blood screening, while patients pay out of pocket for the remaining tests. Another individual advised that patients pay out of pocket during the first trimester, while the government reimburses for biochemical screening during the second trimester.

Ultrasounds with nuchal translucency measurements

The majority of respondents said that "all patients" were referred for ultrasound with NT measurement (7/8). The screening was indicated to be standard of care for a majority of respondents in Australia (6/8) and a majority of respondents reported their decision to offer the screening test was based on recommendations or guidelines formed by RANZCOG and Human Genetics Society of Australasia (HGSA) (5/6). Most respondents advised that this was offered at 11 to 12 weeks gestational age. The earliest point at which this was offered was 7 weeks and the latest was at 12 weeks gestational age.

Respondents to this question indicated that NT measurement reimbursement was possible through government health insurance (5/6) and at a cost to the patient out of pocket (5/6**)**. One respondent indicated that it can depend on whether the practice performing the ultrasound is public or private. Other individuals stated that a portion of them are covered by a government rebate while some patients can access this scan for free in a public hospital.

Non-invasive prenatal screening (NIPS)

All but one respondent indicated that “all patients” were offered NIPS (7/8). A majority of respondents indicated NIPS was not offered as standard of care at their practice (5/8). Of the individuals that indicated the screening was standard of care, a majority indicated their decision was based on guidelines and noted RANZCOG and international guidelines (2/3). All participants advised NIPS being offered from 10 weeks GA up to and including 13+ week GA. Of the respondents to this question, all advised that reimbursement of NIPS was by the patient at an out of pocket cost (7/7). Regarding NIPS, one respondent advised there was “no government or private health rebate" and that all patients pay for the test out of pocket.

Canada

The majority of respondents worked in a public hospital (11/15), while a few indicated they worked at a community hospital (2/15), private hospital/medical facility (2/15), and at a community family practice clinic (1/15). Respondents reported being members of the Canadian Association of Genetic Counselors (CAGC), the National Society of Genetic Counselors (NSGC), Québec Association of Genetic Counsellors (QAGC). There were a couple of tests other than the ones discussed in the survey that the respondents mentioned were offered during

the first trimester including an early anatomy scan and early echocardiogram for someone who has had an earlier pregnancy with an anomaly.

Carrier screening

A majority of respondents said that patients were referred for carrier screening if they were a carrier or suspected carrier (11/18) for a genetic condition or if there was a family history of a genetic condition (12/15). Respondents also emphasized offering tests for hemoglobinopathies and cystic fibrosis based on the patient's ethnic background.

A majority of respondents in Canada indicated that carrier screening of any kind was not offered as standard of care at their practice (10/15). Most respondents expressed the usefulness of having expanded carrier screening offered to all patients. One respondent stated their decision to offer carrier screening was based on recommendations or guidelines formed by the Society of Obstetricians and Gynaecologists of Canada (SOGC), the Journal of Obstetrics and Gynaecology Canada (JOGC), Canadian College of Medical Geneticists (CCMG), and the Association of Medical Geneticists of Quebec (AMGQ).

When it is offered, carrier screening was indicated by the respondents to this question to be covered by government insurance all of the time (15/15), with patient paying out of pocket being a less common method of payment (5/15). A respondent indicated that there are some targeted, carrier screening conditions covered by government health insurance depending on family history or ethnic background; however, they advised that patients could access carrier screening privately on rare occasions. Two respondents advised that they do not arrange or offer private

pay carrier screening. Another advised that patients who select expanded carrier screening pay out of pocket.

Biochemical marker screening

Almost all respondents reported that all patients are offered biochemical marker screening (13/15). One respondent elaborated by saying that it was "standard of care in Ontario for all pregnant women". Another said that it wasn't offered at their private facility but "all patients [are] offered through the provincial system". One response mentioned that "biochemical screening for aneuploidy is organized by [the patient's] OB/midwife/pregnancy care team".

A majority of respondents from Canada indicated biochemical marker testing of PAPP-A (13/15) and bHCG (12/15), and msAFP (11/15) were standard of care. Respondents reported Placental Growth Factor (PlGF) for preeclampsia, uE3, and inhibin-A as additional markers screened for as standard of care at their practice. A majority of respondents reported their decision to offer their specified biochemical markers was based on the joint statement by the SOGC and CCMG (No. 348-Joint SOGC-CCMG Guideline: Update on Prenatal Screening for Fetal Aneuploidy, Fetal Anomalies and Adverse Pregnancy Outcomes), as well as guidelines and recommendations from American College of Medical Genetics (ACMG), JOGC, and the AMQG.

Most respondents advised that this test is offered as early as 11 weeks onwards. The earliest reported point of this test being offered was at 9 weeks, and the latest point was 12 weeks. All of the respondents for this question indicated that biochemical marker screening was only paid for by government health insurance (14/14). One respondent qualified that individuals are covered

by government health insurance provided that they are a resident of that province. Otherwise, coverage would be provided by their insurance or out pocket, but this is not as common.

Ultrasounds with nuchal translucency measurement

The majority of respondents said that all patients are offered this screening test (10/15). Some respondents expanded on their selection saying that while all patients are offered this, there is limited access depending on if the patient lives in a rural area where it is not available due to lack of certified technicians.

A majority of respondents from Canada indicated ultrasounds with NT measurements were standard of care (10/15) and of these respondents, all of them reported their decision to offer their specified biochemical markers was based on the joint statement by the SOGC and CCMG, guidelines and recommendations from American College of Medical Genetics (ACMG) , JOGC, and the AMQG. Most respondents advised that this test is offered as early as 11 weeks onwards. The earliest reported point of this test being offered was at 9 weeks, and the latest point was 12 weeks. All respondents of this question indicated that the NT measurement screening by ultrasound was only indicated to be paid for only by government health insurance (10/10).

Non-invasive prenatal screening (NIPS)

There were two referral indications that received a majority of the responses which were “advanced maternal age” (10/15) and “abnormal first trimester screen (ultrasound or bloodwork)” (12/15). Other reasons mentioned included, “past affected pregnancy”, “previous child/pregnancy with aneuploidy”, or “for fetal sex if family history sex-linked condition”.

A majority of respondents from Canada indicated NIPS were not standard of care (11/15) and of these respondents that indicated NIPS was offered as standard of care reported their decision to offer their test as standard of care was based on guidelines and recommendations, noted guidelines from SOGC (2/4). Most respondents advised that this test is offered as early as 10 weeks onwards. The earliest reported point of this test being offered was at 9 weeks.

NIPS reimbursement was mostly deemed to be available through government health insurance (12/14) and at a cost to the patient out of pocket (11/14). It was more rare for private health insurance to be a method of reimbursement (3/14). One respondent advised it NIPS is only covered if there is a previous history of trisomy 21, 18, 13, a previous screening (with or without ultrasound) that was positive for trisomy 21 or 18. Another advised, "there is strict criteria for it to be covered by government health insurance (positive integrated screen, maternal age over 40, previous T13, T18 or T21); otherwise patients have to pay for it privately and private insurance sometimes covers it." A third person advised that if patients are eligible for NIPS then they would have it paid for by the government; otherwise they are able to get it privately at their own cost or through insurance coverage if it is eligible.

France

All the respondents (15/15) from France indicated working at a public hospital. Respondents reported being members of the French Association of Genetic Counselors.

Carrier screening

The majority of referral indications included “carrier/suspected carrier” (13/15), “abnormal first trimester screen (ultrasound or bloodwork)” (9/15), and “family history of a genetic condition” (14/15). One respondent said that carrier screening is not offered because genetic testing is illegal unless there is a family history of a condition or the doctor suspects the patient themselves may have a genetic condition.

A majority of respondents in France indicated that carrier screening of any kind was not offered as standard of care at their practice (9/14) and of the respondents indicating the test was standard of care, all respondents reported the decision to offer carrier screening was based on recommendations or guidelines formed by the French Organization of Human Genetics/ Association Française de Génétique Humaine (AFGC), French bioethics laws, and guidelines from a Multidisciplinary Centre for Prenatal Diagnosis.

All respondents to this question (13/13) indicated that carrier screening is covered under government health insurance with one respondent indicating the patient also has the option to pay at a cost out of pocket. One individual stated that it is situational: for example, a healthy individual will have to pay out of pocket whereas an individual with cancer would be covered by government health insurance for carrier screening. One respondent offered their opinion that cystic fibrosis carrier testing should be offered to all patients.

Biochemical marker screening

A majority of respondents said that all patients are offered this screening test (9/15). All respondents from France indicated biochemical marker testing for PAPP-A and bHCG, were

standard of care for all prenatal patients. Other respondents mentioned biochemical marker testing for msAFP as standard of care. A majority of respondents reported their decision to offer the testing was due to recommendations or guidelines formed by the Haute Autorité de Santé (HAS), French Biomedicine Agency, and according to French bioethic laws. Most respondents advised that this test is offered as early as 11 weeks onwards. The earliest reported point of this test being offered was at 9 weeks, and the latest point was 12 weeks. Maternal serum biomarker screening was only indicated to be paid for by government health insurance for all respondents (15/15). One respondent from France selected both "Yes" and "No" to the question of whether biochemical marker testing options being offered to standard of care were due to guidelines and recommendations.

Ultrasounds with nuchal translucency measurements

All respondents said that all patients are offered this screening test (15/15) and that the screening is standard of care for prenatal patients. All respondents reported their decision to offer the screening test was based on recommendations or guidelines formed by the Haute Autorité de Santé (HAS), French Biomedicine Agency, and according to bioethic laws. Most respondents advised that this test is offered as early as 11 weeks onwards. The earliest reported point of this test being offered was at 10 weeks, and the latest point was 12 weeks. All respondents (15/15) indicated that ultrasound with NT measurement was reimbursable by the government health insurance, with some coverage from private health insurance also indicated (2/15).

Non-invasive prenatal screening (NIPS)

A majority of respondents indicated NIPS was not offered as standard of care at their practice (13/15). One respondent expressed that “NIPS should be offered for all patients.” Of the individuals that indicated the screening was standard of care, respondents reported their decision to offer it as a standard of care was based on french bioethics laws (2/2).

An abnormal first trimester screen was the referral indication cited by the majority of respondents (11/15). Respondents also cited “carrier of a Robertsonian translocation with chromosome 13 and 21”, “genetic translocation which include chromosome 21, 13, or 18”, or a risk “>1/1000” as other reasons to offer NIPS as well. Most respondents advised that this test is offered as early as 10 weeks onwards. One respondent reported it was standard of care and not at a cost to patients to offer NIPS for women with a high risk of trisomy. They specified this risk would be calculated based on "maternal PAPP-A and bhCG test results, maternal age, and fetal measurements and couples with genetic risk for trisomy".

Respondents indicated reimbursement for NIPS was offered by government health insurance (15/15), with some respondents indicating patient pay out of pocket (4/15) and one individual indicated private health insurance as an option (1/15). One individual noted that NIPS is covered by government insurance if it is medically relevant. However, if it is requested by the patient, the cost is out of pocket. Another further specified that it is covered by the government when the risk assessment is between 1/2 and 1/1000; otherwise, it is at a cost to the patient.

India

The two respondents from India indicated they worked in a private hospital/medical facility, one in an ‘industrial (private) setting’, and two in a laboratory setting. Respondents reported being members of the Genetic Counseling Board of India.

Carrier screening

A majority of respondents in India indicated that carrier screening of any kind was offered as standard of care at their practice (3/5). The majority of respondents indicated that being a carrier/suspected carrier (4/5), having an abnormal first trimester screen (4/5), having a family history of a genetic condition (4/5), or consanguinity were reasons to refer for carrier screening (4/5). And of the respondents indicating the test was standard of care, a majority of respondents reported the decision to offer carrier screening was based on recommendations or guidelines in the Pre-Conception and Pre-Natal Diagnostic Techniques Act (PCPNDT) (2/3). All respondents to this question (5/5) indicated that carrier screening would be paid at an out of pocket cost to the patient. One respondent stated that they offer thalassemia carrier testing to all patients due to its high prevalence in India.

Biochemical marker screening

A majority of respondents reported that all patients are offered this screening test (4/5). A majority of respondents from India indicated biochemical marker testing for PAPP-A (4/ 5), bHCG (4/ 5), msAFP (3/ 5) were standard of care for all prenatal patients. Inhibin-A was also reported by some to be screened for as standard of care. A majority of respondents reported their decision to offer the testing was due to unspecified recommendations or guidelines (3/ 5). Most reported offering this screening starting at 11 weeks GA. The earliest reported time to offer this

was at 4 weeks, while the latest was reported as 11 weeks. Biochemical marker screening was indicated only to be paid by patients out of pocket (4/4).

Ultrasounds with nuchal translucency measurements

All respondents repeated that all patients are offered this screening test (5/5). Ultrasounds with NT measurements were indicated to be standard of care for a majority of respondents from India (4/ 5) and all of the respondents reported their decision to offer the screening test was based on recommendations or guidelines, including the Pre-Conception and Pre-Natal Diagnostic Techniques Act. Most reported offering this screening starting at 11 weeks GA. The earliest it was offered was reported to be 5 weeks while the latest was reported as 12 weeks. All respondents indicated the sole reimbursement source of NT to be at a cost to the patient out of pocket (4/4).

Non-invasive prenatal screening (NIPS)

A majority of respondents indicated NIPS was not offered as standard of care at their practice (3/ 5). One respondent expressed that "NIPS should be offered for all patients." Of the individuals that indicated the screening was standard of care, one respondent reported their decision to offer it as a standard of care was based on an unspecified guideline/recommendation (1/2). A majority of respondents said that individuals were referred for this screening test if they had an abnormal first trimester screen (ultrasound or bloodwork) (4/5). Most reported that this screening was offered starting at 10 weeks GA. The earliest NIPS was reported as being offered to patients was at 4 weeks, with the latest reported at 13 weeks. All respondents advised that NIPT was provided at a cost out of pocket to patients (5/5).

Ireland

The sole respondent from Ireland self-reported working in a public hospital and being a member of the Association of Genetic Nurses and Counselors. The respondent reported to not be a part of a maternity unit and due to their involvement in a central genetics department seeing both patients with prenatal and non-prenatal indications, they are not involved in the offering of biochemical, ultrasounds with NT measurements or NIPS. Obstetricians or midwives were reported to typically offer these screening tests. No current national standards for what screening tests should be offered were provided. It was unclear whether the respondent indicated whether testing for biochemical marker screening, ultrasounds with NT measurements, and NIPS were offered on a private basis or if genetic testing in general was offered on a private basis.

The sole response from Ireland cited both "carrier/suspected carrier for a genetic condition" and "family history of a genetic condition" as reasons for referral for carrier screening. They explained that, "we do not routinely offer routine carrier screening without a family history. We only offer carrier testing if there is a known diagnosis in the family and the risk to a pregnancy is more than 1 in 600. If it is a very rare condition, we do not offer carrier testing to partners. Couples ideally get referred to us prior to conception or get referred during a pregnancy". Carrier screening was indicated by the respondent to be paid for by government health insurance, adding that they "are a public service so there is no payment."

No response was provided regarding the reimbursement of ultrasound NT measurement.

The respondent reported that NIPS " is offered by the maternity units on a private basis, it is not routinely offered to every pregnant woman and has to be requested by the patient. As I work in a Genetics Dept we do not do screening type tests, only NIPD/invasive testing for people with a confirmed genetic risk".

Israel

The sole respondent working in Israel advised a work setting of a public hospital and reported to being a member of the Israeli Society of Genetic Counselors. They reported carrier screening, biochemical marker screening of PAPP-A and bHCG, ultrasounds with nuchal translucency measurements as being offered as standard of care at their practice and the decision to do so was based on recommendations and guidelines from the Ministry of Health of Israel. Non-invasive prenatal screening is not currently offered as a standard of care to patients.

Carrier screening is offered at 12 weeks GA and was reported to be paid for by government health insurance. Ultrasounds with nuchal translucency measurements are offered between 11 weeks GA and 12 weeks GA.

"Health organizations" were noted to be the reimbursement method for biochemical marker screening and ultrasounds with nuchal translucency measurements. It is unclear as to whether this was a reference to the public healthcare organizations that fall under the "Ministry of Health" or other types of health organization.

NIPS was reported to be offered starting from 10 weeks. Referral indications that warranted NIPS were not specified but the respondent indicated NIPS was offered at their practice. The respondent reported patients paid for the test out of pocket.

Oman

The sole respondent from Oman advised working in a public hospital setting and reported to be a member of the Oman Association of Medical Genetics. Prenatal screening is currently not reported to be a practice in national health care systems. However, it is currently provided in two governmental tertiary hospitals: these are facilities that provide highly specialized services. A majority of private centers provide prenatal screening and NIPS without genetic counselors. The respondent reported that "prenatal diagnosis services meet all recommended guidelines and include pre and post-test genetic counseling".

Carrier screening

The sole respondent from Oman reported carrier screening is not offered as standard of care for patients. The respondent selected “carrier/suspected carrier of a genetic condition” as the referral indication. This screening was indicated by the respondent to be paid for by government health insurance.

Biochemical marker screening

The sole respondent reported biochemical marker screening is not offered to any patients. They further elaborated that, “we offer chromosomal analysis if highly suspecting a syndomic fetus

with any anomalies". No information on biochemical marker screening reimbursement was provided.

Ultrasounds with nuchal translucency measurements

The sole respondent reported ultrasounds with NT measurements is offered to all patients as standard of care as per guidelines and recommendations set by the Oman Obstetric and Gynecology Association. The respondent selected "advanced maternal age", "abnormal first trimester screen (either past or present)", and "pregnancy complications (either past or present) as referral indications for this screening test. The respondent advised that this test is offered as early as 9 weeks onwards. The respondent indicated the reimbursement method for ultrasound NT measurement was through government health insurance.

Non-invasive prenatal screening (NIPS)

The respondent indicated "advanced maternal age" and "pregnancy complications (past or present)" as reasons for referral. The sole respondent reported that non-invasive prenatal screening is not offered as a standard of care to patients at their practice.The respondent advised that this test is offered as early as 9 weeks onwards.The respondent advised reimbursement of NIPS is done by the patient at an out of pocket cost.

Qatar

The only respondent from Qatar reported to work in a private hospital/medical facility and a public hospital setting. They are members of the American Board of Genetic Counseling (ABGC) and NSGC. The respondent advised, "being the only team of its kind in Qatar, the

prenatal genetics team does not offer / facilitate prenatal screening tests, but rather only diagnostic testing. Prenatal screening tests including NIPS are offered by Obstetrics providers."

Carrier screening

The sole respondent from Qatar reported that referral indications cited by this respondent include, "carrier/suspected carrier of a genetic condition", "family history of a genetic condition", and "at patient's request". The respondent from Qatar reported carrier screening of any kind is standard of care and the decision to offer the testing is based on unspecified guidelines and recommendations by an unspecified regulatory body or professional association. Carrier screening was indicated by the respondent as being paid for by government health insurance.

Biochemical marker screening

The respondent reported that no one was offered this screening test and that they were not sure as to why. No information on biochemical marker screening reimbursement was advised.

Ultrasounds with nuchal translucency measurements

The respondent reported that all patients are offered this screening test as standard of care starting by week 10 and that it was reimbursable by government health insurance, private health insurance, and at a cost to the patient out of pocket. The respondent reported the offering was potentially due to American College of Obstetricians and Gynecologists (ACOG) guidelines.

Non-invasive prenatal screening (NIPS)

The respondent cited both “advanced maternal age” and “abnormal first trimester screen (ultrasound or bloodwork) as referral indications. The NIPS screening test is not currently offered as standard of care at their practice. The respondent advised that NIPS was reimbursed by government health insurance, private health insurance, and at a cost to the patient out of pocket.

South Africa

Respondents reported to work in a private hospital/medical facility (5/10) as well as a public hospital setting (7/10). Respondents indicated they are members of the Health Professional Council of South Africa.

A majority of respondents emphasized the variation of screening tests offered based on the type of healthcare system (public vs private) as well as the location. Standards of care also differ based on where in South Africa the prenatal care takes place. In some provinces, no screening is accessible. In some, it is standard for all AMAs. Respondents expressed it would be beneficial to have NT scan, biochemical markers and NIPS offered to all patients irrespective of the healthcare system.

Carrier screening

The majority of respondents selected both “carrier/suspected carrier” (6/10) and “family history of a genetic condition” (8/10) as referral indications for carrier screening. One respondent explained that “carrier screening is not offered on the public healthcare system. It is only available to public or private patients who can pay for it”. Something similar was said by two

other respondents with one of them further explaining that “in the State/public health care, carrier screening would only be offered if a previous child is already affected or there is a clear indication to do so”. Cost was cited as a reason as to why this is not offered to everyone because the “public healthcare system cannot incur the costs”.

A majority of respondents in South Africa reported that carrier screening of any kind is not offered as standard of care at their practice (8/10). The one respondent who indicated the test was standard of care reported the decision to offer carrier screening was based on recommendations or guidelines by ACOG and the European Society of Human Genetics (ESHG). One respondent stated that they offer sickle cell carrier testing to at risk population groups.

Carrier screening was reported to be reimbursed through multiple sources, including at a cost to the patient out of pocket (7/9), government health insurance (4/9), and private health insurance (2/9). There is also a possibility of institutional/ hospital funding though this was only raised by one respondent (1/9). One respondent advised that “Limited carrier testing available for certain conditions so only applicable in certain situations/population groups. Payment dependent on financial status of payment with those with a higher income receiving all or a portion of the bill. If a patient is under a certain financial tier, the cost will be covered by the hospital. No government insurance exists.” Another respondent advised that “it depends on where the patient is seen. In government health care, they will usually cover the cost, but testing is VERY limited. In private health care it will depend on with(sic) test is requested, locally or international testing. Medical aid only pays for local testing, and not all medical aids will cover the cost of even local testing.”

Biochemical marker screening

There was no referral indication that gained the majority of responses, but it was most often selected that no patients are offered this screening test (5/10). Two responses explained saying that it's not available in "state hospitals" with one of those responses mentioning that even for those in the private sector, it's "being increasingly replaced by NIPT". One respondent selected "not as accurate as other types of screening" and "reimbursement issues" as reasons why this test isn't offered to everyone. Biochemical marker screening reimbursement was advised by all respondents as mostly private health insurance (4/4) with some instances of the patient paying out of pocket as well (2/4).

A majority of respondents from South Africa did not report whether biochemical marker testing was standard of care (8/10). Two respondents reported PAPP-A and bHCG as standard of care for all patients. MSAFP was noted as an additional marker offered as standard of care to patients (1/2). Guidelines and recommendations from South African Society for Ultrasound in Obstetrics and Gynaecology (SASUOG) , ACOG, and ESHG were cited as impacting the two providers' decision to offer it as standard of care. The earliest reported point of this test being offered was at 6 weeks, and the latest point was 12 weeks. Biochemical marker testing was reported to be offered for patients receiving testing in private settings and not for state or government settings.

Ultrasounds with nuchal translucency measurements

Majority of respondents chose "advanced maternal age" as the referral indication (6/10). One respondent reported some public hospitals perform ultrasounds with NT scans and others do not.

Ultrasounds with NT measurements were not reported to be standard of care for patients (6/10). The respondents that reported their decision to offer the screening test were based on recommendations or guidelines, noted guidelines and recommendations by the South African Society of Obstetrics and Gynecology (SASOG) and by ACOG. Most reported offering this screening starting at 11 weeks GA. Ultrasound with NT reimbursement was indicated as being through government health insurance (7/10), private health insurance (6/10), and at a cost to the patient out of pocket (4/10). One individual also specified that ultrasound NT was covered by the hospital.

Non-invasive prenatal screening (NIPS)

There was no referral indication that represented a majority of the responses, but there was an equal number of respondents that chose “advanced maternal age” (4/10) and “abnormal first trimester screen” (4/10) as referral indications for this screening test. A majority of respondents indicated NIPS was not offered as standard of care at their practice (7/10). The earliest reported point of this test being offered was at 6 weeks, and the latest point was 10 weeks. However, four respondents all said that this was only available within the private sector and not the public. Two respondents selected “reimbursement issues” to explain why this wasn’t offered to everyone. Respondents advised that NIPS reimbursement options included private health insurance (5/7) as well as at a cost to the patient out of pocket (6/7).

Switzerland

The two respondents from Switzerland both reported to be working in a public hospital setting (2/2). They reported being members of the French Association of Genetic Counselors and the Swiss Association of Genetic counselors.

Carrier screening

Both respondents reported that referral indications for this screening was for those who were carriers or suspected carriers and those who had a family history of a genetic condition. Respondents reported carrier screening of any kind is not standard of care at their practice (2/2). Respondents advised that carrier screening reimbursement is either by private health insurance (1/2) or at an out of pocket cost (2/2).

Biochemical marker screening

One respondent said that all patients are offered this screening test, while the other cited an abnormal first trimester screen as a referral reason. Biochemical marker screening for PAPP-A and bhCG are offered as standard of care by both respondents and the decision to offer the testing was noted to be based on guidelines and recommendations by the Swiss Society of Gynecology and Obstetrics. The earliest reported time to offer this screening was at 10 weeks, while the latest was reported as 12 weeks. Biochemical marker screening reimbursement was advised once each as being done by government health insurance (1/2), private health insurance (1/2), and out of pocket to the patient (1/2).

Ultrasounds with nuchal translucency measurements

Both respondents said that all patients are offered this screening test. Both respondents noted ultrasounds with NT measurements are offered as standard of care at their practice and the decision to offer it was reported to be due to guidelines and recommendations from the Swiss Society of Gynecology and Obstetrics. The earliest reported time to offer this screening was at 10 weeks, while the latest was reported as 12 weeks. Ultrasound NT reimbursement was indicated as including government health insurance (1/2), private health insurance (1/2), and at a cost to the patient out of pocket (1/2).

Non-invasive prenatal screening (NIPS)

The two respondents selected the referral indication "abnormal first trimester screen (ultrasound of bloodwork)" for this screening test. Both respondents reported NIPS was not standard of care for patients at their clinic. Both respondents reported offering this screening starting at 12 weeks GA. The respondent advised NIPS was reimbursed by government health insurance (1/2), private health insurance (1/2), and at a cost to the patient out of pocket (1/2).

United States

Approximately half of the respondents from the United States reported working in a private hospital/medical facility (15/30), with the rest reporting a work setting of public hospital (6/30), physician private practice (5/30), community hospital (1/30), university medical center (2/30), and military hospital (2/30). Respondents reported being members of ABGC and NSGC.

Respondents commented regarding other screening that is offered or screening that they would feel would be beneficial for their practice. One respondent expressed that they would like to see

sequential screening offered to all patients. Others advised they offer sequential screen, antiphospholipid antibody syndrome screening if there are 3 or more miscarriages. Additionally, another individual suggested that FTS be offered in the first trimester at their institution. However, they noted that patients who have a low risk FTS are not offered NIPS if there are no other indications for further testing. This respondent also clarified that patients that do NIPS do not have to undergo a FTS.

Carrier screening

A large majority of respondents said that all patients are offered this screening test (26/30) with one respondent saying that based on other factors they may offer more than just a core 4 disease panel. A respondent practicing in the United States advised, "we only offer carrier screening for fragile x, cf, and sma unless there is a family history or consanguinity. I would like to have an expanded carrier screen be standard of care. I also wish we did nuchal measurements."

A large majority reported government coverage (22/30), private coverage (26/30), and out of pocket as reimbursement methods for carrier screening (26/30). It was much rarer for an institution/hospital (1/30) or a lab testing subsidy to be utilized (1/30). Comments included "60-70% of my patients are Medicaid. Whatever is not covered by Medicaid [my] institution eats."

Many respondents emphasized that expanded carrier screening should be offered to all patients as standard of care.

Biochemical marker screening

A majority of respondents said that all patients are offered this screening test (18/30). Three respondents said that this would be offered for low risk patients with another saying that now most patients are offered only NIPS, but that "some providers still use FTS/quad for non-AMA patients". A couple respondents indicated that this was not offered to everyone because it's not as accurate as other types of screening.

A majority of respondents from the United States indicated biochemical marker testing for PAPP-A (22/30), bHCG (22/30), and msAFP (19/30) were standard of care for all prenatal patients. One respondents noted quad screen and sequential screens to be standard of care at their practice. Another respondent elaborated that biochemical marker screening was only offered to women over 35 years old and this was due to ACOG guidelines and recommendations. A majority of respondents reported their decision to offer the testing was due to guidelines (20/25), citing ACMG, ACOG, Society for Maternal-Fetal Medicine (SMFM), and state-specific guidelines. Six respondents out of those who reported biochemical marker screening as standard of care at their clinic denied it was due to guidelines or recommendations. Most respondents advised that this test is offered as early as 11 weeks onwards. The earliest reported point of this test being offered was at 6 weeks. Biochemical marker screening reimbursement was indicated as government health insurance (19/22), private health insurance (21/22), as well as patient paying out of pocket (13/22).

Ultrasounds with nuchal translucency measurements

Majority of respondents said that all patients are offered this screening test (22/30). One respondent said "we do not offer NT ultrasound to women who had previous low risk NIPT screening unless they ask for it". Another said they would offer it for a "history of heart defect in self or prior pregnancy". As to why this isn't offered to everyone, someone said they "do not have ultrasound techs with proper certifications for nuchal measurements".

Ultrasounds with NT measurements were reported to be standard of care for a majority of respondents in the United States (19/30). A majority of respondents reported their decision to offer the screening test was based on recommendations or guidelines (16/19) from ACOG, ACMG, SMFM, The International Society of Ultrasound in Obstetrics and Gynecology (ISUOG), NSGC, Nuchal Translucency Quality Review Program (NTQR). Of these respondents reporting ultrasounds are standard of care to all patients, they indicated it was not due to guidelines or recommendations (3/19). Most respondents advised that this test is offered as early as 11 weeks onwards.

Reimbursement for ultrasound NT measurement was shown to be available through government health insurance (15/20), private health insurance (18/20), and at a cost to the patient out of pocket (12/20). Two respondents were unsure of specific ultrasound reimbursement methods (2/20).

Non-invasive prenatal screening (NIPS)

Majority of respondents said that all patients are offered this screening test (18/28). One respondent said this was offered “at discretion of OB”. Another two cited increased risk for aneuploidy as a reason to offer this. Reasons that were mentioned as to why this is not offered to everyone included “lack of clear statements from societies”, it’s “deemed not as accurate as other types of screening for the ‘low risk’ population”, and “lack of provider awareness/education”.

A majority of respondents indicated NIPS was offered as standard of care at their practice (19/30). Of the individuals that indicated the screening was standard of care, a majority of respondents reported their decision to offer it as a standard of care due to guidelines/recommendations (16/19) from ACOG, ACMG, and the Society for Maternal-Fetal Medicine (SMFM). The remaining respondents reported their offerings were not due to guidelines or recommendations (3/19). Most respondents advised that this test is offered as early as 10 weeks onwards. Respondents advised that NIPS reimbursement was possible through government health insurance (25/29), private health insurance (26/29), and at a cost to the patient out of pocket (24/29). It was also noted that a lab subsidy may be available to the patient for this cost (1/29).

Appendix 13. Initial email template to encourage participation or distribution of survey

Dear _____,

We are second year genetic counseling students at the Joan H. Marks Graduate Program in Human Genetics at Sarah Lawrence College looking for help in recruiting prenatal healthcare providers from around the world.

Our research study aims to identify and understand international prenatal genetic screening practices during the first trimester of pregnancy. We are interested in whether prenatal healthcare providers are adhering to established guidelines, what services are offered, to whom, by whom, when, and how they are reimbursed.

[Depending on Source of Contact]

Our thesis advisors, Laura Hercher and Lindsey Alico, provided us with your contact information since you expressed interest in either sharing your expertise as an international prenatal genetics professional or expressed willingness to help forward our survey to relevant colleagues within your professional network.

Participation in this research study consists of taking an anonymous, online survey. The survey explores various details surrounding prenatal genetic counseling practices and is designed to take less than 15 minutes to complete. Participation is completely voluntary, and participants may opt out at any time. This study was reviewed and approved by the Institutional Review Board at Sarah Lawrence College.

If you are not a prenatal care provider, would you please kindly forward this invitation to prenatal genetic healthcare professionals in your network and/or at your institution?

[If contact was distributing to society listserv platform]

Can you please advise us on whether it would be possible for our survey to be distributed on your professional society's listserv? If so, who should we be reaching out to?

We greatly appreciate your time and consideration.

To access the survey, please follow this link: https://s.surveyplanet.com/bTjG6jyu7

Please email any questions or concerns to: internationalprenatalgcsurvey@gmail.com

Warmest regards,

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Appendix 14. Two week follow-up survey email template

Dear _____,

Just a kind reminder that we are second year genetic counseling students at the Joan H. Marks Graduate Program in Human Genetics at Sarah Lawrence College and are recruiting prenatal healthcare providers from around the world.

Our current research study aims to identify and understand international prenatal genetic screening practices during the first trimester of pregnancy. More specifically, we are interested in whether prenatal healthcare providers are adhering to established guidelines, what services are offered, to whom, by whom, when, and how they are reimbursed.

If you haven't already completed the survey, it is open for responses until [date]. If you previously forwarded our international prenatal screening practice survey link, would you please kindly forward this reminder email to those same colleagues?

Thank you very much for your time. We greatly appreciate your assistance.

Warmest regards,

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Appendix 15. Consent form presented at the start of the survey

Thank you for your interest in our research study.

The purpose of this research study is to identify and understand differences in international prenatal genetic screening practices during the first trimester of pregnancy.

You are being asked to participate in this survey because you are currently a healthcare provider in a prenatal setting. This survey is designed to take at most 15 minutes to complete and consists of multiple choice and short answer questions.

Participating in this survey is completely voluntary. Your data will be kept confidential. Any identifying information except country of practice will be separated from the responses and you will not be identified in any reports produced by the study. You may stop taking the survey at any point by simply closing the survey window. In order to move through the survey, an answer is required for each question. If you do not wish to provide an answer, simply write 'N/A'. We appreciate any information that can be provided. Knowledge of your experiences will provide valuable insight on international prenatal practices.

There are no costs to you for participating in this survey and, to our knowledge, minimal risk. Your survey responses will remain confidential and will only be accessed by the researchers.

The principal investigators for this study are Masters degree candidates at the Sarah Lawrence College Joan H. Marks Program in Human Genetics. If you have any questions or concerns about this research study, you can contact us (Dharti Adhia, Ming Bauer, Rachel Lanning, Jenny Zhang) by email at internationalprenatalgcsurvey@gmail.com, or our mentors Lindsey Alico Ecker (lalico@sarahlawrence.edu) or Laura Hercher (lhercher@sarahlawrence.edu).

If you have questions about your rights as a research participant or want to speak to someone not connected to the study team, you may contact the Institutional Review Board co-chairs Professors Elizabeth Johnson (203-722-3287) and Claire Davis (914-395-2605) at irb@sarahlawrence.edu.

Appendix 16. Survey Questions

Respondent Demographics Information:

1) I understand the above information and understand that my participation in this survey is completely voluntary. By choosing "I agree" and continuing, I consent to having my responses included in the study.*

   I agree/ I wish to not participate *(If I wish to not participate selected, survey ends)*

2) What is your professional title? Select all that apply.

   Genetic Counselor
   Genetic Counseling Assistant
   Physician (e.g. obstetrician, gynaecologist, geneticist, surgeon, maternal fetal medicine specialists etc.)
   Physician Assistant
   Nurse (e.g. genetics nurse, midwife)
   Nurse practitioner
   Other: [Free text fill in]

3) What educational degrees do you hold?
   Select all that apply.

   Bachelors
   Masters
   Doctorate/ Ph.D
   M.D.
   Other: [Free text fill in]

4) What is your speciality? Select all that apply.
   Family Medicine
   Genetics
   Gynecologic Oncology
   Gynecology
   Internal Medicine
   Fertility
   Maternal Fetal Medicine
   Neurogenetics
   Obstetrics
   Obstetrics/Gynecology
   Pathology
   Pediatrics
   Pediatric oncology
   Prenatal

Primary Care
Surgery
Surgical Oncology
Other : [Free text fill in]

5) What, if any, professional organization(s) are you affiliated with? Select all that apply.
American Board of Genetic Counseling
Association of Genetic Nurses and Counselor
Australasian Society of Genetic Counselors
Australasia Board of Censors in Genetic Counseling
Canadian Association of Genetic Counselors
Chinese Board of Genetic Counseling
Dutch Association of Genetic Counselors
French Association of Genetic Counselors
Genetic Counseling Board of India
Health Professional Council of South Africa
Israeli Society of Genetic Counselors
Japanese Board of Genetic Counselors
Japanese Society for Genetic Counseling
Korea Society of Medical Genetics and Genomics
National Society of Genetic Counselors
Portuguese National Association of Genetic Counsellors (APPAcGen)
Professional Society of Genetic Counselors in Asia
Spanish Society of Genetic Counselors
Swedish Society of Genetic Counselors
Taiwan Association of Genetic Counseling
Other: [Free text fill in]

6) What best describes your primary work setting? Select all that apply.
[ ] Private hospital/medical facility
[ ] Physician private practice
[ ] Community hospital
[ ] Public hospital
[ ] Other [free text fill in]

7) In what country do you practice? [Free text fill in]

8) On average, how many prenatal patients do you see in a week?
[ ] 0 -> end of survey
[ ] 1-10
[ ] 11-20
[ ] More than 20

<u>Patient Prenatal Care:</u>

9) For what reason(s) are patients typically referred to you during the first trimester for genetic counseling? Check all referral indications.
   [ ] Advanced maternal age
   [ ] Carrier/suspected carrier of a genetic condition
   [ ] Personal medical history
   [ ] Abnormal first trimester screen (ultrasound or bloodwork)
   [ ] Pregnancy complications (either past or present)
   [ ] Exposures/Teratogen Counseling
   [ ] Family history of a genetic condition
   [ ] Consanguinity
   [ ] All prenatal patients are referred
   [ ] Other [free text fill in]

10) Would you consider yourself as part of the genetic counseling process? (Y/N)

11) As part of the genetic counseling process, do you provide pretest counseling to prenatal patients? (Y/N)
    If yes:
    - During pretest counseling, do you explain the conditions that may be identified by prenatal genetic screening tests? (Y/N)
    - During pretest counseling, is an individualized risk assessment based on medical and/or family history provided to patients? (Y/N)
    - During pretest counseling, is it within your scope of practice to obtain informed consent for screening tests? (Y/N)
    - During pretest counseling, is it within your scope of practice to counsel patients to help them understand the potential psychological implications of testing? (Y/N)

12) As part of the genetic counseling process, do you provide genetic screening test results? (Y/N)
    If yes:
    - When providing genetic screening test results, is it within your scope of practice to counsel patients to help them adapt to the psychological implications of testing and test results? (Y/N)

<u>Screening Tests:</u>

13) Who is offered carrier screening? Check all referral indications.
   [ ] Advanced maternal age
   [ ] Carrier/suspected carrier of a genetic condition
   [ ] Personal medical history
   [ ] Abnormal first trimester screen (ultrasound or bloodwork)
   [ ] Pregnancy complications (either past or present)
   [ ] Exposures
   [ ] Family history of a genetic condition

[ ] Consanguinity
[ ] All patients
[ ] At patient's request
[ ] No one is offered carrier screening
[ ] Other: [Free text fill in]

If "no one is offered carrier screening" is selected*:*

- Why do you think carrier screening is not offered to everyone? Select all that apply.
  [ ] Not deemed to be useful
  [ ] Not as accurate as other types of screening
  [ ] Reimbursement issues
  [ ] Cultural barriers
  [ ] Not sure
  [ ] Other: [free text fill in] (*please include other additional barriers you think contribute to this screening not being offered*)?

If any referral indication is selected:

- When is carrier screening offered? *Select all gestational age weeks that apply.*

  [Preconception] GA Weeks: [1] [2] [3] [4] [5] [6] [7] [8] [9] [10] [11] [12] [12+]

- Is carrier screening of any kind **standard of care** for all patients at your practice? (Y/N)

  If yes**:**

  - Is the decision to offer carrier screening as **standard of care** based on recommendations or guidelines formed by a regulatory body or professional association? (Y/N)

    If yes**:** Which regulatory body or professional association? [free text fill in]

- How is carrier screening paid for? *Select all that apply.*
  [ ] Covered by government health insurance
  [ ] Covered by private health insurance
  [ ] Patient out of pocket
  [ ] Other: [free text fill in]

14) Who is offered biochemical marker screening for chromosome abnormalities? Check all referral indications.
[ ] Advanced maternal age
[ ] Carrier/suspected carrier of a genetic condition

[ ] Personal medical history
[ ] Abnormal first trimester screen (ultrasound or bloodwork)
[ ] Pregnancy complications (either past or present)
[ ] Exposures
[ ] Family history of a genetic condition
[ ] Consanguinity
[ ] All patients
[ ] At patient's request
[ ] No one is offered biochemical marker screening
[ ] Other: [Free text fill in]

If "no one is offered biochemical marker screening" is selected*:*

- Why do you think biochemical marker screening for chromosome abnormalities is not offered to everyone? Select all that apply.
  [ ] Not deemed to be useful
  [ ] Not as accurate as other types of screening
  [ ] Reimbursement issues
  [ ] Cultural barriers
  [ ] Not sure
  [ ] Other: [free text fill in]

If any referral indication is selected:

- Which biochemical markers are screened for during the first trimester? Select all that apply
  [ ] PAPP-A
  [ ] bhCG
  [ ] msAFP
  [ ] Other: [free text fill in]

- When is biochemical marker screening for chromosome abnormalities offered? *Select all gestational age weeks that apply.*

  [Preconception] GA Weeks: [1] [2] [3] [4] [5] [6] [7] [8] [9] [10] [11] [12] [12+]

- Screening for which of the following biochemical markers are offered as **standard of care** for all patients at your practice? *Select all that apply*
  [ ] PAPP-A
  [ ] bhCG
  [ ] msAFP
  [ ] Other: [free text fill in]

  If any are selected**:**

- Is the decision to offer biochemical marker screening as **standard of care** based on recommendations or guidelines formed by a regulatory body or professional association? (Y/N)

If yes**:** Which regulatory body or professional association? [free text fill in]

- How is biochemical marker screening paid for? *Select all that apply.*
  [ ] Covered by government health insurance
  [ ] Covered by private health insurance
  [ ] Patient out of pocket
  [ ] Other:[free text fill in]

15) Who is offered ultrasounds with nuchal translucency measurements? Check all referral indications.
[ ] Advanced maternal age
[ ] Carrier/suspected carrier of a genetic condition
[ ] Personal medical history
[ ] Abnormal first trimester screen (ultrasound or bloodwork)
[ ] Pregnancy complications (either past or present)
[ ] Exposures
[ ] Family history of a genetic condition
[ ] Consanguinity
[ ] All patients
[ ] At patient's request
[ ] No one is offered ultrasounds with nuchal translucency measurements
[ ] Other: [Free text fill in]

If "no one is offered ultrasounds with nuchal translucency measurements" is selected*:*

- Why do you think ultrasounds with nuchal translucency measurements are not offered to everyone? Select all that apply.
  [ ] Not deemed to be useful
  [ ] Not as accurate as other types of screening
  [ ] Reimbursement issues
  [ ] Cultural barriers
  [ ] Not sure
  [ ] Other: [free text fill in]

If any referral indication is selected:

- When are ultrasounds with nuchal translucency measurements offered? *Select all gestational age weeks that apply.*

[Preconception] GA Weeks: [1] [2] [3] [4] [5] [6] [7] [8] [9] [10] [11] [12] [12+]

- Are ultrasounds with nuchal translucency measurements **standard of care** for all patients at your practice? (Y/N)

  If yes**:**

  - Is the decision to offer ultrasounds with nuchal translucency measurements as **standard of care** based on recommendations or guidelines formed by a regulatory body or professional association? (Y/N)

    If yes**:** Which regulatory body or professional association? [free text fill in]

- How are ultrasounds with nuchal translucency measurements paid for? *Select all that apply.*
  [ ] Covered by government health insurance
  [ ] Covered by private health insurance
  [ ] Patient out of pocket
  [ ] Other: [free text fill in]

16) Who is offered noninvasive prenatal screening (NIPS), also called cell-free fetal DNA testing? Check all referral indications.
[ ] Advanced maternal age
[ ] Carrier/suspected carrier of a genetic condition
[ ] Personal medical history
[ ] Abnormal first trimester screen (ultrasound or bloodwork)
[ ] Pregnancy complications (either past or present)
[ ] Exposures
[ ] Family history of a genetic condition
[ ] Consanguinity
[ ] All patients
[ ] At patient's request
[ ] No one is offered NIPS or cell-free fetal DNA testing
[ ] Other: [Free text fill in]

If "no one is offered NIPS or cell-free fetal DNA testing " is selected*:*

- Why do you think noninvasive prenatal screening (NIPS)/cell-free fetal DNA testing is not offered to everyone? Select all that apply.
  [ ] Not deemed to be useful
  [ ] Not as accurate as other types of screening
  [ ] Reimbursement issues
  [ ] Cultural barriers
  [ ] Not sure
  [ ] Other: [free text fill in]

If any referral indication is selected:

- When is the noninvasive prenatal screening (NIPS)/cell-free fetal DNA offered? *Select all gestational age weeks that apply.*

  [Preconception] GA Weeks: [1] [2] [3] [4] [5] [6] [7] [8] [9] [10] [11] [12] [12+]

- Is noninvasive prenatal screening (NIPS)/cell-free fetal DNA testing **standard of care** for all patients at your practice? Y/N

  If yes**:**

  - Is the decision to offer noninvasive prenatal screening (NIPS)/cell-free fetal DNA as **standard of care** based on recommendations or guidelines formed by a regulatory body or professional association? (Y/N)

  If yes**:** Which regulatory body or professional association? [free text fill in]

- How is the noninvasive prenatal screening (NIPS)/cell-free fetal DNA testing paid for? *Select all that apply.*
  [ ] Covered by government health insurance
  [ ] Covered by private health insurance
  [ ] Patient out of pocket
  [ ] Other: [free text fill in]

17) Are there any other screening tests offered during the first trimester? (Y/N)
    If yes:
    - If yes, which screening tests? [free text fill in]

18) Is there a screening test that you don't currently offer that you think would be beneficial to your current prenatal genetic screening program?
    If yes:
    - If yes, which screening tests? [free text fill in]

19) Please provide any additional comments. [free text fill in]