morbidities who receive a no-call result. Low fetal fraction has been associated with a number of adverse outcomes, but definitive rates of pregnancy complications and surveillance protocols have not been established.[47]

It should be noted that failure to obtain all elements of a traditional screening protocol can also occur. In the FASTER trial, failure to obtain the NT measurement occurred in 4.5% of pregnancies analyzed. Furthermore, 2.6% of the NT sonograms submitted as part of quality control were deemed unacceptable.[7]

There are reports of higher rates of no-call with NIPS in twin pregnancies than in singleton pregnancies that should be communicated as part of pretest counseling.[48] Different laboratories use proprietary algorithms to assess the sufficiency of fetal fraction and tend to use the lower of the 2 fetal fractions to determine the adequacy of the specimen to make a call. This is believed to be because of the placental mass differences between the 2 gestations, which may also be associated with aneuploidy in one of the twins.

Pretest and Post-test Counseling

As with all prenatal screening and diagnostic testing, appropriate pre- and post-test counseling is an integral aspect of informed decision-making. Multiple professional society statements addressing NIPS emphasize the importance of accurate and thorough pre- and post-test genetic counseling. We affirm the principles of counseling for NIPS that were highlighted in the 2016 position statement, including providing up-to-date, balanced, and accurate information and personalized, patient-centered counseling.

Other groups have similarly listed critical points to cover during pretest counseling.[49] Pretest counseling should include a discussion of the optional and screening nature of NIPS, the types of conditions that can and cannot be screened for, the types of test results (including no-call results and incidental findings) that can be received, information about positive and negative predictive values, and the recommendation for confirmation of any abnormal results. Previously unknown parental chromosome abnormalities may be uncovered in mosaic or complete states, eg, 22q11.2DS.

Post-test counseling for negative results should emphasize the reduction, but not elimination, of risk, and the fact that NIPS only screens for select conditions and does not reduce the risk for other genetic disorders. Recommendations for neural tube defect screening should be included in counseling as NIPS is not designed to detect fetal structural abnormalities. Post-test counseling for positive results should include a discussion of the PPV of the result, a balanced description of the condition for which the screen was positive, including information about the spectrum of outcomes associated with the particular condition, and the recommendation for prenatal or postnatal confirmation of the NIPS results. There should be particular emphasis on prenatal diagnostic confirmation before any decisions with respect to pregnancy termination are made. In addition, patients should be provided with access to educational materials that have been developed from collaborations between health care professional groups and advocacy organizations.

Benefits vs Harms

Timing of results from aneuploidy screening is a major consideration in assessing the benefits of the various options. Obtaining screening results during the first trimester provides the pregnant individual with either early reassurance, or in the event of a positive screen, the ability to pursue testing with ample time to consider reproductive options as warranted. Changes to delivery planning or transfer of care may be considerations. If pregnancy termination is elected, undertaking that earlier in pregnancy is associated with greater safety and lower costs.

Earlier screening in twin pregnancies is also beneficial. The diagnostic confirmation of aneuploidy in a twin gestation is more complex than in singletons and is impacted by the chorionicity and gestational age of the pregnancy. Most dizygotic twins will be discordant for a trisomy, with 1 affected fetus and 1 euploid fetus. Patients should be counseled about the availability of selective reduction if that is a consideration. Most studies indicate that this is safer when performed in the first trimester;[50] another clear advantage of earlier screening and diagnosis.

The SER found insufficient evidence to make conclusions about the psychosocial impact of NIPS. There is a potential for iatrogenic psychological harm such as anxiety and stress associated with a number of pregnancy-related screens, tests, or interventions, particularly with respect to fetal evaluation. Some of the anxiety and concern surrounding prenatal screening can be mitigated with appropriate pretest counseling.[51] The SER found no evidence that NIPS is more likely to result in those types of harms than other forms of screening. The noted potential harms are applicable to any type of prenatal screening for chromosome abnormalities. No studies have compared potential harms associated with NIPS in a head-to-head comparison with traditional screening methods.

A number of benefits and concerns have been raised in reviews of patient perspectives on pregnancy screening and NIPS in particular. The Ontario Health Technology Assessment[52] delineates several of them as listed in Table 4.

Screening pregnant individuals for fetal aneuploidy has been an established option for more than 5 decades.[54] The potential for stigmatization of individuals with chromosome disorders that can be detected via prenatal screening is not a new concern. There is no evidence that NIPS impacts that potential differently than traditional screening. Patient autonomy is deeply rooted within the professional medical genetics community. Providers should emphasize the informed and shared decision-making that surrounds screening and/or testing in a supportive environment.