

Comments and Reflections on Ethics in Screening for Biomarkers of Prenatal Alcohol Exposure

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Early identification of and intervention for fetal alcohol spectrum disorder (FASD) has been shown to optimize outcomes for affected individuals. Detecting biomarkers of prenatal alcohol exposure (PAE) in neonates may assist in the identification of children at risk of FASD enabling targeted early interventions. Despite these potential benefits, complicated ethical issues arise in screening for biomarkers of PAE and these must be addressed prior to the implementation of screening programs. Here, we identify and comment, based on a North American perspective, on concerns raised in the current ethical, social, and legal literature related to meconium screening for PAE. Major ethical concerns revolve around the targeting of populations for PAE screening, consent and respect for persons, stigma and participation rates, the cost—benefit analysis of a screening program, consequences of false-positive and false-negative test results, confidentiality and appropriate follow-up to positive screen results, and the use of screen results for criminal prosecution. We identify gaps in the literature on screening for PAE, most notably related to a lack of stakeholder perspectives (e.g., parents, healthcare providers) about screening and the ethical challenges it presents.

Key Words: Fetal Alcohol Spectrum Disorder, Meconium Screening, Prenatal Alcohol Exposure, Ethics, Stakeholders, Neuroethics.

FETAL ALCOHOL SPECTRUM disorder (FASD), a consequence of maternal alcohol consumption during pregnancy, is a leading known cause of preventable developmental disability and is implicated in a wide range of primary (e.g., birth defects, facial abnormalities, cognitive, and behavioral deficits) and secondary (e.g., mental health problems, alcohol and substance abuse, unemployment, involvement in criminal justice system) issues. Early identification and intervention significantly reduces the frequency of

secondary disabilities (Streissguth et al., 2004), but is fraught with ethical challenges (Caprara et al., 2007; Gifford et al., 2010; Zadunayski et al., 2006). Some are common to neonatal screening programs (e.g., parental consent, confidentiality, and third party disclosure), while others are related to the specific nature of FASD, where a positive result has implications for both the child and mother (e.g., both could be stigmatized) (Marcellus, 2007). Consequently, the value of developing an accurate biomarker screen to objectively identify individuals who have been exposed to alcohol in utero has been questioned. Ultimately, the desired outcome of such a screen would be to recognize children at risk of developing FASD and to monitor their development and determine whether medical treatment or early behavioral interventions are warranted. Here, we discuss and comment on ethical, social, and legal concerns in the literature. We focus on meconium screening, a prenatal alcohol exposure (PAE) detection technique that has been discussed in the scientific, ethical, and legal literature (Joya et al., 2012) and that has been recommended in some countries where FASD is recognized as an important health issue (Canadian Association of Paediatric Health Centres, 2012). Although meconium testing is only one of many different methods under investigation for PAE screening, we believe that the ethical issues raised with regard to its use also apply to other techniques. Moreover, it should be noted that the authors approach this topic within the North American context but expect that the issues and reflections raised are valuable broadly to other contexts. We also recognize that nonbiological screening methods (e.g., screening questionnaires) also lead to significant ethical questions.

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ETHICAL ISSUES OF MECONIUM TESTING FOR PAE

We identified 7 major ethical concerns in the ethical, social, and legal literature, upon which we comment at the end of each section (italicized sections). A detailed description of our literature review method is provided in Box 1.

Box 1

Details on Literature Review Methodology for This Commentary

We explored relevant literature in PubMed, Scopus, and the International Bibliography of Social Sciences (Proquest) using the keywords prenatal alcohol exposure (PAE), fetal alcohol syndrome, fetal alcohol spectrum disorder (FASD) and biomarkers, meconium testing and FASD, FASD and prevention, and FASD and intervention. Additional literature came from our personal library as well as consulting the reference lists of included articles. First, we reviewed the ethical, legal, and sociological literature on FASD and screening for detection of ethanol biomarkers in newborns. We identified the ethical issues discussed in these publications as well as recommendations put forward to address them. Second, a team analysis and discussion of the literature enabled us to identify further ethical issues of importance, which were not currently identified in the specific literature on biomarkers for PAE.

Targeted Populations for PAE Screening

A key concern in the literature is the debate over whether or not screening tests should be offered to all pregnant women (i.e., universal screening) or limited to those deemed at risk (i.e., targeted screening). Universal screening is most respectful of the principle of justice and minimizes the risk of stigmatizing and stereotyping population groups viewed as at risk (Dickens, 2011; Zadunayski et al., 2006). However, the ethical concerns that arise with universal screening include cost-effectiveness, the use of limited healthcare resources, and the lack of distinction between apparently high-risk and low-risk populations (Dickens, 2011; Zelner and Koren, 2009). In contrast, targeted screening is viewed as a more economically viable option (Hopkins et al., 2008; Zelner and Koren, 2009), but concerns have been raised over the potential for negative stereotyping (Zadunayski et al., 2006) and for over-identification of marginalized populations and under-identification of others (Marcellus, 2007). Targeted screens could be directed at populations known to be at a higher risk of alcohol abuse, such as those with low socioeconomic status and/or minority status, but again this may unfairly label these groups and ignore other populations that could be equally affected by FASD (Zadunayski et al., 2006). *Currently, a universal screening program is the most ethically advisable option (provided it could be made cost-effective) given the lack of definitive populations to screen and*

the potential negative social consequences of targeted screening.

Consent to a Screening Program and Respect for Persons

Informed consent is an important principle in bioethics and acknowledges the inherent personal worth and integrity of the other person, thereby demonstrating that the individual is valued and important in the decision-making process. In current medical practice, consent for medical testing or treatment involving children is sought from the mother or legal guardian, who is responsible for making decisions in the child's best interest. However, as a meconium screen is also a de facto test of the mother (Hicks et al., 2009), there may be a conflict of interest on the mother's part when asked to consent to the screen for her child. The screen may engender negative legal and social consequences (e.g., stigma and removal of the child from the mother's care) for both mother and child if test results are positive. Thus, where the best interests of the child lie may be contentious and depend on the type of outcome and follow-up care available (Dickens, 2011). For women at risk, fear of reprisals may decrease willingness to consent to meconium testing (Zelner et al., 2012b). Other reasons why some might not offer consent for testing include, a perceived lack of benefit of detection, perceived lack of risk of FASD (e.g., planned pregnancy in which alcohol was not consumed, nondrinker), and conceptions of truth and knowledge as private and personal (Hicks, 2007). *Given the numerous factors that influence willingness to consent, we suggest upholding a clear requirement of informed consent for PAE screening to ensure ongoing trust in health-care providers and to respect women's rights and autonomy.*

Stigma and Participation Rates in a PAE Screening Program

For screening to be effective and of clinical value in routine care, a high participation rate is necessary (Zelner et al., 2010). Recent work by Zelner and colleagues (2012b) examined the willingness of mothers in a high-risk obstetrics unit to participate in either an anonymous meconium screening study or in an open screening program involving voluntary testing and long-term developmental follow-up of positive cases through existing public health programs. They found significantly lower participation rates in the open screening program, regardless of the fact that the identification of children at risk was used to offer targeted services (Zelner et al., 2012b). This finding is surprising given earlier evidence indicating that mothers would support a universal alcohol and drug screening program, provided that screening would lead to effective treatments for the child and mother and that appropriate resources were made available (Hicks et al., 2009). Zelner and colleagues (2012b) concluded that fear, embarrassment, and guilt may have led to maternal unwillingness to participate. To help increase participation rates for open screening programs that provide follow-up services,

it has been suggested that an opt-out consent strategy be used. Here, screening would be conducted unless participants actively say “no.” This approach is ethically problematic, however, as women may hesitate to opt-out for fear that others may perceive this as an indication of guilt (Marcellus, 2007). Ultimately, participation can be maximized if stigma surrounding maternal alcohol consumption is minimized. *Currently, a traditional opt-in consent approach to participation is the most advisable option to protect the doctor–patient relationship. However, if stigma in general related to FASD and PAE was reduced, and the potential social risks of a positive screen were minimal, then an opt-out method may be preferable in an effort to increase participation and the success of a screening program.*

Cost-Effectiveness of a PAE Biomarker Screen

A prominent concern identified in the literature was the cost–benefit relationship associated with meconium testing and the appropriate use of healthcare resources. Hopkins and colleagues (2008) found that meconium screening can be cost-effective provided that it leads to early intervention and treatment services. This observation was based on findings that early intervention leads to improvements in literacy for affected children, which can enhance quality of life and increase adult lifetime earnings (Hopkins et al., 2008). Additionally, Gifford and colleagues (2010) determined that follow-up treatment for mothers which reduces drinking in future pregnancies was also cost-effective.

Parents, however, may be reluctant to participate in treatment programs due to possible feelings of guilt, shame, and fear (Marcellus, 2007). A previous study found that only 2 of 22 mothers who had babies with a positive meconium drug-screen agreed to use rehabilitative services (Zenewicz and Kuhn, 1998). Moreover, access to adequate treatment and health services may not be readily available or accessible to some families, especially those living in rural or remote communities (Hay et al., 2006). Finally, the efficacy of different early intervention programs and the emotional, psychological, and familial costs associated with a positive screen and subsequent labeling of the individual must be determined before true benefit can be established (Gifford et al., 2010; Marcellus, 2007; Zelner and Koren, 2009). *To ensure cost-effectiveness and appropriate use of resources, treatment strategies that demonstrate efficacy and that improve participation need to be set in place for both mother and child.*

Consequences of False-Positive and False-Negative Test Results

Ideally, screening tools for FASD need to have high sensitivity (i.e., the ability to correctly identify those who have been exposed to alcohol) and high specificity (i.e., the ability to correctly identify those who have not been exposed) to minimize the number of false-negatives and false-positives (Goh et al., 2008; Sarkar et al., 2009). The consequences of a

false-negative screen can result in a missed opportunity to provide intervention and treatment services (Marcellus, 2007). Alternatively, a false-positive result can cause undue guilt and parental anxiety, potentially harming the family (e.g., causing marital strife and damaging the parent–child relationship) and resulting in the use of unnecessary healthcare services (Marcellus, 2007). Another major consequence of a false-positive screen is stigma and marginalization from the community and from healthcare providers regarding future pregnancy (e.g., woman unnecessarily labeled as at risk). As priority in developing a screening tool is often placed on sensitivity (Hicks, 2003; Sarkar et al., 2009), these possible negative outcomes underscore the importance of ensuring that a screening tool is *both* sensitive and specific *before* it is put into practice. *Refinement of the meconium testing methods and the development of second-tier screening strategies, such as in-depth maternal interviews about alcohol consumption during pregnancy, are needed before screening is widely implemented.*

Confidentiality and Appropriate Follow-Up of Positive Screen Results

Once the positive screen is established, policies must be put in place to ensure that the sensitive nature of this information is always kept highly confidential, as the negative consequences resulting from labeling a child with PAE or the mother are unknown, but potentially significant (Marcellus, 2007). Care must be taken to ensure that this information does not significantly impact the mother–child relationship, create stigma or reinforce labels (Gareri et al., 2008). Hospitals and clinics would also need to develop comprehensive policies on the types of information, if any, that should be disclosed to social services and other third parties.

A positive result on a PAE screen is not a diagnosis, and it will therefore be important to emphasize that confirmed PAE does *not* equate with an FASD identification (Caprara et al., 2007). Nevertheless, appropriate follow-up should be provided. The infant’s health should be assessed and developmental progress should be monitored closely to identify any deficits requiring referral to service providers (Gareri et al., 2008). Due to the heterogeneous nature of FASD, treatment interventions will require a comprehensive multidisciplinary approach and will need to be customized to the child (Chudley et al., 2005; Gareri et al., 2008). The health of the family unit and the living environment of the child will need to be assessed to inform appropriate intervention and/or treatment programs (Zelner et al., 2010). A confirmation of PAE should also provide an opportunity to educate the mother and allow her to access appropriate healthcare services and supports.

Significant gaps in treatment services exist and are related to geography, social issues, and economic factors (Hicks, 2003; Marcellus, 2007). Without adequate follow-up capacity, the early detection of a disease is of no benefit to an individual (Gareri et al., 2008). Services need to be in place

before a screening program can be ethically implemented (Goh et al., 2008), ideally with prior demonstration of success through small-scale piloting (Zelner et al., 2012a). *Concerns related to the disclosure of sensitive information and inadequate availability or access to treatment services must be addressed prior to the implementation of a PAE screening program.*

Use of Screen Results for Criminal Prosecution

Last, a major ethical and legal consideration in the literature is the criminalization of maternal alcohol consumption and the use of positive PAE screens as evidence for prosecution of the mother. Criminalization of maternal alcohol consumption threatens a woman's autonomy and the status of women as equal citizens who are entitled to protection under the law (Armstrong, 2005; Moss, 1990). Moreover, legal coercion may further jeopardize infant well-being and does not prevent substance abuse among women (Foley, 2002). In fact, it may cause more harm as the perceived coupling of the healthcare and criminal justice systems may lead women to avoid obtaining prenatal care (Abel and Kruger, 2002; Armstrong, 2005; Miller et al., 1994), which can lead to negative medical consequences (Foley, 2002). Criminal prosecution could also adversely affect the clinician–patient relationship (Zadunayski et al., 2006), which relies on open communication, confidentiality and trust, and discounts the involvement of the father. The criminalization of prenatal alcohol use may also unfairly target the impoverished, medically and socially, marginalized groups (Zadunayski et al., 2006). Several challenges exist in using a positive PAE screen for legal prosecution of women including their right to confidentiality and privacy, and the fact that in some countries, women have no legally enforceable duty of care to their unborn child (Dickens, 2011). Hence, outcomes of PAE screening should not be used for criminal prosecution.

GAPS IN THE ETHICAL ANALYSIS: UNDERSTANDING AND PREPARING STAKEHOLDERS

The use of biomarker assays to test for PAE raises important questions for a wide array of stakeholders. However, we found very little literature about the values and perspectives of stakeholders regarding PAE screening, in spite of their importance (Potter, 2008). With respect to meconium screening, the perspectives of mothers have been evaluated to a limited extent (Hicks et al., 2009), but not the perspectives of other key stakeholders, such as families of affected and non-affected children, clinicians, addiction researchers, patient advocacy groups, women's rights groups, policy makers, and the broader public (Potter, 2008). As outlined in Table 1, we suggest more research is needed to further our understanding of the perspectives and values of stakeholders, especially for minorities and vulnerable populations, on issues such as third party disclosure and stigma, the latter being a major barrier in PAE screening.

Table 1. Recommendations for Further Stakeholder Research on Ethical, Legal, and Social Aspects of Prenatal Alcohol Exposure (PAE) Biomarkers in Fetal Alcohol Spectrum Disorder (FASD)

A deeper understanding of stakeholder perspectives and values
Third party disclosure: Whether or not to report a positive screen to third parties (e.g., child protection services) is a sensitive and complex topic not adequately addressed in the literature given significant consequences for the child, parents, healthcare providers, and social workers
Perspectives of minorities and vulnerable populations: Language and cultural factors need to be examined because they are important modulators of the perceived appropriateness of a screen and impact the communication of results (Goh et al., 2008) in multicultural societies and in aboriginal populations (The Aboriginal Healing Foundation, 2003)
Preparing stakeholders for FASD screening and developing strategies to reduce stigma and guilt
Public awareness: The notion of FASD as preventable and the general lack of understanding of social determinants that may cause women to consume alcohol during pregnancy can contribute to perceptions of guilt and social stigma of mothers (Armstrong, 1998). Strategies should be developed and trialed to reduce stigma and guilt subsequent to a positive test
Education and training: There are gaps in our knowledge and training about the sensitive issues surrounding PAE screening and nonjudgmental healthcare delivery. The impact a positive PAE test result can have on multiple relationships, including clinician–patient (mother or child), parent–child, and co-parents needs further attention

CONCLUSION

This commentary examined various ethical challenges associated with screening for PAE and offered perspectives on salient ethical, social, and legal issues for further debate. Although our focus was on meconium testing, similar questions would extend to other potential biomarkers of PAE. Currently, there is limited literature on best practices for PAE screening or on the establishment of strategies to prepare stakeholders for the emergence of PAE screening programs.

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