

Published in final edited form as:

*Birth Defects Res A Clin Mol Teratol.* 2010 October ; 88(10): 838–846. doi:10.1002/bdra.20731.

## Assessment of Benefits of a Universal Screen for Maternal Alcohol Use during Pregnancy

Anne E. Gifford<sup>1</sup>, Kathleen J. Farkas<sup>2</sup>, Leila W. Jackson<sup>3</sup>, Christopher D. Molteno<sup>4</sup>, Joseph L. Jacobson<sup>4,5,6</sup>, Sandra W. Jacobson<sup>4,5,6</sup>, and Cynthia F. Bearer<sup>7,\*</sup>

<sup>1</sup>International Society for Disease Surveillance, Boston, Massachusetts <sup>2</sup>Mandel School of Social Science, Case Western Reserve University, Cleveland, Ohio <sup>3</sup>Department of Epidemiology and Biostatistics, School of Medicine, Case Western Reserve University, Cleveland, Ohio

<sup>4</sup>Department of Psychiatry and Mental Health, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa <sup>5</sup>Department of Psychiatry and Behavioral Neurosciences, School of Medicine, Wayne State University, Detroit, Michigan <sup>6</sup>Department of Human Biology, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa <sup>7</sup>Department of Pediatrics, University of Maryland School of Medicine, Baltimore, Maryland

### Abstract

**INTRODUCTION**—The objective of this report is to estimate the benefits of universal meconium screening for maternal drinking during pregnancy. Fetal alcohol spectrum disorder (FASD), including its most severe manifestation fetal alcohol syndrome (FAS), is preventable and remains a public health tragedy. The incidences of FAS and FASD have been conservatively estimated to be 0.97 and 10 per 1000 births, respectively. Meconium testing has been demonstrated to be a promising at-birth method for detection of drinking during pregnancy.

**METHODS**—The current costs of FAS and FASD, alcohol treatment programs, and meconium screening were estimated by literature review. Monetary values were converted roughly to equal dollars in 2006.

**RESULTS**—Costs of adding meconium analysis to the current newborn screening program and of treatment for the identified mothers were estimated and compared to potential averted costs that may result from identification and intervention for mothers and affected infants. Three potential maternal treatment strategies are analyzed. Depending on the treatment type, the savings may range from \$6 to \$97 for every \$1 spent on screening and treatment.

**DISCUSSION**—It needs to be emphasized, however, that such screening is premature and that to be effective this screening can be implemented only if there is a societal willingness to institute prevention and intervention programs to improve both women's and children's health. Future research should be directed at improving detection and developing in-depth prevention and remedial intervention programs. A thorough consideration of the ethical issues involved in such a screening program is also needed.

### Keywords

fetal alcohol spectrum disorder; meconium; fatty acid ethyl esters; newborn screening; benefits; maternal alcohol use

## INTRODUCTION

Fetal alcohol spectrum disorder (FASD) represents a range of physical and developmental anomalies that result from exposure to ethanol during pregnancy. FASD is suspected to be present in 1% of all live births (Sampson et al., 1997). Fetal alcohol syndrome (FAS), the most severe manifestation of FASD, is the leading preventable cause of mental retardation in the Western world (Abel and Sokol, 1987), with the incidence conservatively estimated at 0.97 per 1000 births (Abel, 1995). The incidence of FAS among heavy drinkers has been estimated at 43 per 1000 (Abel, 1995).

Primary disabilities in children with FAS are identified as disabilities directly caused by prenatal alcohol exposure. These include low birth weight, growth retardation, neuro-behavioral problems, and physical anomalies (Stratton et al., 1996). Secondary disabilities arise throughout development and may be ameliorated through earlier diagnosis and appropriate interventions (Streissguth et al., 1996; Streissguth et al., 2004). Secondary disabilities include, but are not limited to, mental health problems, disrupted school experience, trouble with the law, imprisonment, inappropriate sexual behavior, alcohol and/or drug problems, dependent living, and problems with employment.

To reduce both primary and secondary disabilities, women who drink alcohol during pregnancy need to be identified. Programs need to be implemented to help these women reduce their alcohol intake, prevent future drinking during pregnancy, and provide remedial help for their children. Ideally, screening should occur early in pregnancy. Early screening could facilitate women's becoming more aware of their alcohol intake and the consequences of such drinking to the fetus. It may also influence their participation in programs to provide support for their stopping or reducing their alcohol consumption. However, it is common for health care professionals to be reticent or uncomfortable discussing alcohol use during pregnancy (Whaley and O'Connor, 1999). In one study of the Special Supplemental Food Program for Women, Infants and Children (WIC), 68% of WIC workers felt uncomfortable asking questions about patients' alcohol consumption, and 78% of workers expressed a need for better training in administration of questionnaires, assessment of results, and intervention (Whaley and O'Connor, 1999). Computer programs have been developed to enable a pregnant woman to assess her alcohol use and obtain feedback regarding how heavily she actually drinks relative to others and the potential risks she is incurring (Lapham et al., 1991; Kinzie et al., 1993). This type of intervention requires access to effective treatment programs and support for this information to be useful.

Current interview-based screenings conducted during pregnancy aim to identify problem drinkers and high-risk populations. But these screening tools potentially may leave the patient feeling threatened or judged and may, therefore, reduce the veracity of her responses (Barr and Streissguth, 2001). Stigma, shame, fear of legal repercussions, and fear of mandatory placement into detoxification programs lead many pregnant alcohol users to underreport alcohol use before, during, and after pregnancy, when interviewed by individuals not specifically trained to conduct such interviews. Furthermore, these considerations may lead women to avoid prenatal clinics and consistent care, leaving them off alcohol-related pregnancy studies entirely (Hankin et al., 2000). Use of biologic markers indicating maternal drinking may be useful in assessing alcohol use in combination with maternal interviews. One such biomarker, fatty acid ethyl esters (FAEEs), has shown some promise (Bearer et al., 2003; Chan et al., 2003; Bearer et al., 2005; Ismail et al., 2010). In our study of South African women, FAEEs identified women who reported drinking three or more drinks per occasion with 84.2% sensitivity and 83.3% specificity (Bearer et al., 2003). One previous study examined the cost-benefit ratio of universal and targeted newborn screening for FAEEs combined with early intervention for affected children (Hopkins et al.,

2008). Given the difficulties involved in estimating the true costs of intervention with the child (Zelner and Koren, 2009) and the limited evidence of the effectiveness of such interventions, we investigated the benefits of screening focusing on interventions to reduce maternal alcohol use and abuse during pregnancy in preventing FASD in future pregnancies. Thus, we examined whether a universal newborn screen based on meconium to identify women who drink during their pregnancies would be cost beneficial for primary prevention of future FASD births.

## METHODS

Cost of meconium analysis was determined by the current cost of this analysis in our laboratory.

A literature search was conducted using the PubMed and EBSCOHost databases including the following key words: maternal alcohol use, alcohol treatment for pregnant women, FASD, cost FASD, effects FASD, and substance abuse treatment pregnant women. All monetary values (US\$ only) were recalculated from their value in the year of publication into 2006 dollars using the Consumer Price Index inflation estimates available through the Bureau of Labor Statistics division of the U.S. Department of Labor.

## RESULTS

### Costs of Screening Program

Laboratory analysis of FAEEs in meconium is a newly developed research procedure, and its long-term cost has not been definitively determined. We estimated the cost of screening to consist of administrative, materials, and professional analysis costs. Since state-regulated newborn screening programs already require laboratory tests and a physician-parent reporting process, the administrative and reporting costs of adding a meconium screening are assumed to be 20% of the cost of the program for additional facilities, transport, training of personnel, and specimen collection. Table 1 shows assumptions/data gaps that require more research.

The cost of materials and analysis was calculated as one value because these costs may overlap. One full-time entry-level research assistant could analyze approximately 2000 samples per year (40/week 3 50 weeks) using current techniques. The salary of an entry-level researcher at our hospital is \$30,000 per year with benefits. We assumed that a laboratory would purchase a \$300,000 GC/MS/MS for analysis that can be used for 10 years. These calculations yield an annual materials and analysis cost of \$72,000 for analysis of 2000 samples, which comes to an estimated \$36 per sample. If we double this cost to account for chemical supplies and equipment, the analysis would be \$72 per sample. When this value is multiplied by the approximate cohort of newborns per year in the United States (4.09 million), we arrive at a total cost of approximately \$300 million for the meconium screening program nationwide (see Table 2).

### Estimate of Number of Women Identified as Drinkers

We estimated the number of women potentially affected by this screen. Final birth data for 2003 show 4.09 million total births to approximately 3,950,000 mothers nationwide [4,090,000 million (total births) –128,665 (no. of twins) –2 ×7,110 (no. of triplets) –3×468 (no. of quadruplets) –4 × 85 (no. of quintuplets and higher) ≈ 3.95 million total mothers] (Martin et al., 2005). If 2.0% of these 3950,000 mothers engaged in binge drinking during pregnancy (Centers for Disease Control and Prevention, 2004), then roughly 79,000 mothers would be considered true binge drinkers. Assuming the 84.2% sensitivity of the test (Bearer et al., 2003), approximately 66,500 women would be correctly identified as binge drinkers

by the meconium screen (Table 2). Assuming a 16.7% false-positive rate (Bearer et al., 2003), approximately 646,000 women would mistakenly be identified as binge drinkers in the total maternal population (Table 2).

### Costs of All Meconium Test-Positive Mothers

We analyzed three different maternal treatment options intended for different degrees of alcohol use. These treatment options were chosen because some data about short- and long-term efficacy are available. Each treatment option was analyzed based on the assumption that all meconium-positive women would receive the same treatment. This assumption allows the full range of treatment costs to be calculated, but it is doubtful that these treatment options would be ethical or appropriate for the many false positives found by this screen.

Brief interventions are useful for women who drink socially or occasionally during pregnancy but are not alcohol dependent. These women would benefit by learning about drinking patterns that could place the fetus at risk (Hankin et al., 2000; Ondersma et al., 2005). Brief intervention usually consists of one short session or a series of short sessions that help educate and motivate client change (Fleming and Manwell, 1999). Sessions may include four main components: assessment of the problem, setting goals, teaching behavioral modification, and distributing reinforcement materials (Chang, 2004). A brief intervention consisting of at least two separate visits to a counselor, social worker, or other substance abuse specialist would probably be more beneficial. Based on current data from our hospital, the maximum salary cost for a licensed independent social worker with previous hospital experience is \$32 per hour. When the patient cost (\$64 total for two sessions) is applied to the true-positive and false-positive binge drinkers, the cost of intervention is roughly \$4 million and \$41 million, respectively (see Table 2, column 3). Including the intervention as a routine part of postpartum care would utilize existing space and appointment time and would not incur additional costs associated with separate appointments. This calculation assumes that every newly delivered mother would accept the intervention; we recognize, however, that many women will refuse intervention or fail to complete it. To our knowledge, no literature has estimated the proportion of women who might take part voluntarily in a post-delivery alcohol intervention (Table 1).

Another recently published intervention includes pharmacotherapy, Medical Management (MM), and Combined Behavioral Intervention (CBI) (Anton et al., 2006). This approach is intended for patients who are alcohol dependent (Anton et al., 2006). Male and female patients in the study took 100 mg naltrexone per day for 16 weeks and had nine MM appointments spaced throughout the year (1 hour initial plus 8 half-hour sessions 5 total hours) and up to 20 CBI sessions with an alcoholism specialist or social worker (20 1-hour sessions = 20 total hours). Generic naltrexone costs approximately \$3 per 50 mg per dose, for a total cost for the course of naltrexone treatment of approximately \$672. An average counseling cost of \$32/hour is assumed for all 25 hours of the intervention, totaling \$800 for all counseling sessions. When the individual patient cost (\$1472 for counseling and prescription costs) is applied to the true-positive and false-positive binge drinking populations, the cost of this intervention is approximately \$98 million and \$951 million, respectively (see Table 2, column 3). Since naltrexone has not been approved by the FDA for use in pregnant or breast-feeding women, women utilizing this option would be advised to find alternatives to breast feeding. Additionally, health care providers would advise women to stop taking naltrexone if they are planning to or become pregnant while on their treatment regimen, and an alternative nonpharmacotherapy for the naltrexone would be recommended.

Given the potential risks associated with this treatment option (no breast feeding, potential exposure to future pregnancy), a second-stage screening strategy would be desirable to eliminate most of the false-positive women. If we hypothesize that an in-depth interview with the results of the meconium screen is theoretically able to reduce the number of false positives by 50% (Table 1), we can calculate the cost of this intervention with or without such a screen. The cost of the in-depth interview assuming 1 hour to conduct the interview with a licensed independent social worker with previous hospital experience is \$32 per hour. As can be seen in Table 2, a second-stage screen that lowers the false positives by 50% markedly reduces the cost of the intervention. Although not taken into account here, a secondary screen might also lower the number of true-positive women detected and reduce the benefit of screening.

Last, a residential treatment is considered. This treatment type is intended for women with severe alcohol dependence and would not be suitable for all identified drinkers. Nevertheless, it is included to estimate the most costly form of intervention. One reviewed program, the Johns Hopkins Bayview Center for Addiction and Pregnancy, provides residential (for mothers and their infants) and day services, medical care, and an intensive substance abuse treatment program at an estimated complete cost of \$6639 per person (Svikis et al., 1997), adjusted to roughly \$8365 per person in 2006 dollars. If this value were applied to the true-positive and false-positive binge drinking populations, the cost of residential treatment would be approximately \$420 million and \$4086 million, respectively (see Table 2, column 3). If one were to add a second-stage screen of an in-depth interview to reduce the numbers of false positives, the cost would drop to \$211 million and \$2.053 billion, respectively.

### Potential Benefit Gained through Prevention of Future FASD Births

Siblings (any children born after the first child) have a much greater chance of being born with FAS when an older sibling has already been diagnosed with this syndrome (Abel, 1988). Moreover, alcohol use increases with age during the childbearing years, and vulnerability to FAS and alcohol-related deficits increases as age of mother and parity increase (Masis and May, 1991; Jacobson et al., 1998; Jacobson et al., 2004; Jacobson et al., 2008). According to 2003 census information, women can be expected to give birth to an average of 2.04 children in their lifetimes (Martin et al., 2005); therefore, it is reasonable to suggest that women who receive effective interventions will engage in less drinking during subsequent pregnancies, which may significantly reduce the number of repeat cases of FASD.

In a large prospective longitudinal study of inner-city, African American women, timeline follow-back data were obtained regarding alcohol use at conception and across pregnancy from women at each prenatal visit and at 1 and 7.5 years postpartum (Jacobson et al., 2002). Alcohol levels reported at time of conception and during pregnancy predicted alcohol use at 1 year postpartum, both  $r = 0.49$ ,  $p < 0.001$ , and at 7.5 years after the pregnancy,  $r = 0.32$  and  $0.33$ ,  $p < 0.001$ . Among the 42 of 368 (11.4%) women who reported drinking at risk levels during pregnancy (0.5 oz absolute alcohol/day or the equivalent of one standard drink/day), 31 (73.8%) continued to drink at risk levels at 1 year postpartum,  $\chi^2 = 16.74$ ,  $p < 0.001$ . Among the 94 (25.5%) who reported binge drinking during pregnancy (2.0 oz absolute alcohol/occasion or the equivalent of four or more drinks/occasion), 60 (63.8%) continued to binge drink 1 year after the pregnancy,  $\chi^2 = 24.41$ ,  $p < 0.001$ . These levels of alcohol use have been found to place the fetus at risk for development of cognitive, behavioral, and growth deficits in infancy, childhood, and adolescence (Jacobson et al., 1994; Streissguth et al., 1994; Jacobson et al., 1998; Willford et al., 2006).

This same pattern of persistent drinking was seen in a cohort of heavy drinking Cape Colored (mixed ancestry) women in Cape Town, South Africa (Jacobson et al., 2008), where alcohol use during pregnancy predicted alcohol use at 1 and 5 years postpartum,  $r = 0.69$  and  $0.47$ ,  $p < 0.001$ , respectively. More than three-fourths of the women who drank at risk during pregnancy continued to drink at risk levels at 1 year (77.6%),  $\chi^2 = 61.34$ , and 5 years postpartum (78.4%),  $\chi^2 = 12.97$ , both  $p < 0.001$ . Ethyl oleate meconium levels were available for 25 of the newborns in this cohort. Using a cut-point of 0.032  $\mu\text{g}/\text{gram}$ , 84.6% of the mothers whose infants had positive ethyl oleate values drank at risk levels at 1 year postpartum,  $\chi^2 = 4.95$ ,  $p < 0.05$ . The findings from the U.S. and South African studies demonstrate that a large proportion of women who drink at levels that place the fetus at risk and could be identified using the meconium screening procedures would continue to drink at levels that would put the fetus in a subsequent pregnancy at risk unless they are identified and undergo an effective intervention.

Table 3 shows the estimates of averted costs potentially attainable by preventing cases of FASD in the subsequent pregnancies of women identified by meconium screening. Column 1 shows the potential savings in direct costs. These costs include medical, education, social services, and out-of-pocket costs. A recent Canadian study derived an annual direct cost of \$37,560 CA (\$36,000 USD) for each individual with FASD, with a lifetime direct cost of \$1,990,000 USD (Stade et al., 2009). Column 2 shows the potential savings in lifetime productivity. Patients with FASD are unlikely to achieve a level of productivity comparable to the general population (Harwood and Napolitano, 1985; Stade et al., 2009). It was estimated that the lifetime loss in productivity for each case of FASD is \$1430.65 CA (\$1400 USD) (Stade et al., 2009) annually, resulting in a savings of \$74,200 per lifetime (Table 3). By preventing future FAS births in the binge drinking population, a total of \$48 billion in direct costs and lifetime productivity losses may be saved (Table 3, column 4).

### Success Rates of Various Maternal Interventions

Table 4 shows the estimates of treatment effectiveness using conservative estimates obtained from the literature. For brief antenatal interventions, one study found up to 70% abstinence in follow-up reports that were given approximately 2 months after delivery (Chang et al., 2000). Unfortunately, the long-term effect of brief interventions is yet unknown, so the 70% success rate that we assumed is likely an overly optimistic estimate (see Tables 1 and 4).

Patients who received MM, CBI, and naltrexone treatment showed a 59–68% increase in days abstinent after 1 year of completion of the treatment regimen (Anton et al., 2006). In the absence of long-term effectiveness data, the lower limit of 59% effectiveness will be assumed in the calculations (see Table 4).

For residential treatment, 68% of women who completed their treatment reported using no alcohol or any other drugs in the 6 months following discharge (Clark, 2001). A similar study reported that 68–71% of postpartum women who completed more than 6 months of treatment reported using no alcohol or any other drug at follow-up (Greenfield et al., 2004). The long-term effect of residential treatments is yet unknown, so the lower estimate of 68% treatment effectiveness is assumed for the residential treatment program (Table 4).

### Cost Effectiveness of Screening and Intervention

Table 5 summarizes the total costs and savings potentially attainable through each of the different treatment types. The greatest potential cost savings could be as high as \$97 per every \$1 spent on screening and brief intervention for identified mothers (Table 5). The pharmacotherapy and medical management treatment and residential treatment options are

cost-effective in the long run, yielding as much as \$20 and \$6, respectively, for every \$1 spent even in the absence of a second-stage screen (Table 5).

## DISCUSSION

A universal meconium analysis of newborns and subsequent intervention for the identified mothers could be a cost-effective intervention strategy to reduce the incidence of FAS and FASD. Conservatively estimated, savings could range from \$97 to \$6 per every dollar spent depending on the type of intervention strategy.

The estimate of potential benefit presented here does not include several benefits that we could not estimate financially. It has been suggested that the burden of secondary disabilities can be lessened by early diagnosis and appropriate interventions (Streissguth et al., 1996; Streissguth et al., 2004). We expect there to be potential cost savings and increases to quality of life for these children that would result from early diagnosis and placement into specialized programs. A recent article by Hopkins et al. (2008) has found a positive cost benefit of universal meconium screening for this reason alone. However, the costs associated with these interventions were not included in this model and are unknown (Table 1) (Zelner and Koren, 2009). Because positive results on a universal meconium screen could potentially be used as evidence to support the separation of a child from the mother, hospitals and providers would need to implement procedures that ensure the privacy of the patient and the confidentiality of the test results. Steps would also need to be taken to ensure that a patient's insurance status and legal child custody status are not called into question before any screening program could be implemented. The need for consent for drug testing is a hospital-by-hospital decision, with some hospitals requiring universal screening. (Zellman et al., 2002).

The benefit figures presented here may be underestimates because most of the existing literature uses FAS as an outcome measure without including other forms of FASD; the recognition of other forms of FASD became commonplace in the field only beginning in the late 1990s (Stratton et al., 1996). The overall financial impact of FASD is difficult to estimate because of the range of effects that may be evident in the individual. Thus, economic values available for FAS cases most likely underestimate the full impact of FASD. More attention is needed to incorporate individuals with other forms of FASD into ongoing research.

This report does not take into account the psychosocial trauma and psychological burden of disease for either FASD or alcoholism or for the labeling of individuals as FASD or alcohol dependent. Although measures of quality of life are not included, an additional potential benefit of meconium screening and effective intervention might include improved health and well-being for identified mothers and children. Alcohol-dependent women may also be expected to experience an increase in economic productivity following treatment, but these potential benefits are not estimated in this study. Reduction in the false-positive rate would be required before a screening program could be implemented. Reduction in false positives could occur only with refinement of the meconium analysis and the development of a more specific second-tier screening, such as an in-depth maternal interview by a qualified interviewer. Identification of women who tested false-positive by an in-depth interview may provide the opportunity to inform them and thereby alleviate some of the emotional impact of being falsely identified. The in-depth interview would also potentially provide an opportunity for true positives to discuss their alcohol use and to be referred for intervention. Refinement of the meconium test may include defining different cutoff values to indicate different degrees of drinking and hence direct women to intervention appropriate to the level of drinking. The in-depth interview could also determine the level and dependency of

drinking and make appropriate referrals to specific interventions. Meconium results may also need to be validated with respect to maternal drinking in premature or post-dates infants (Table 1).

There are several limitations to this study. First, it is not clear how many women who binge drink during pregnancy meet criteria for alcohol-dependent drinking, making it difficult to estimate the effect of treatment on these mothers. Moreover, the effectiveness values of different substance abuse treatments are debated in the literature. Drop-out rates from treatment and relapse rates for addiction would decrease the estimated benefits. Few studies follow subjects for a long period, making it difficult to assess the long-term impact of these programs. Multiple-drug use is common. It is unclear how multiple-drug use affects success rates of alcohol use intervention. In addition, given that women for whom treatment is not effective may have multiple children, some women may utilize alcohol intervention more than once, making the lifetime costs per child and per woman higher than for a one-time intervention.

Second, the sensitivity and specificity of the meconium test used here were for binge drinking mothers and raises the questions regarding the ability of the test to identify and benefit social drinkers. To address this issue, we reran the data from our 2003 study (Bearer et al., 2003) and found a sensitivity/specificity of 80 and 81% to identify women who reported drinking one drink per drinking day. More research is necessary to define the utility of the meconium test to identify social drinkers. Thus it is feasible to use the meconium test to identify social drinkers, and with both improvement in the assay as well as a second-stage screen, this test may lead to better sensitivity and specificity to identify such women.

Third, the numerical values used in this analysis are mostly estimates collected from research over the past 20 years, and as costs have undoubtedly changed with the economic changes during that period, cost values need to be taken as estimates rather than exact figures. The cost estimates that are used, therefore, do not necessarily represent true economic value (Johns et al., 2003). The results are also based on assumptions of incidence, compliance, and treatment effectiveness, as well as availability and quality of services, whose accuracy is difficult to determine.

Fourth, false negatives are estimated at roughly 12,000 using a false missed detection of 15.8% (Bearer et al., 2003). There is no proposed follow-up for test negatives, so these cases may go unnoticed at birth. Additional research is needed to attempt to improve the accuracy of meconium screening. One way to improve the specificity of the test would be to require two positive tests. This option should be considered in the future as more knowledge is gained about the precision and accuracy of meconium analysis. In the future, multiple assays of the same sample or analyses of separate meconium segments may be useful in reducing false negatives. Even though this practice may double the cost, the ratio would still remain favorable.

Fifth, the program is based on U.S. figures. The recent paper by Hopkins et al. (2008) relates specifically to Canada, and the commentary by Zelner and Koren (2009) emphasizes that cost-effectiveness analysis of disease is country- and population-specific. The incidence and economic burden of disease of FASD in the Cape Colored population in South Africa are described in this report, but any universal screening and treatment program would need to be designed to take into account the unique sociodemographic, economic, and governmental context of South Africa, which has other compelling high-priority public health problems.

Sixth, the cost estimate of the meconium analysis is a prediction because the analysis is still continuing to be developed in its research stages. Implementation of universal screening is premature at this time, particularly given the number of false positives detected using the



current test. With time and development, the long-term cost of this kind of analysis will become clearer. However, when added to the numerous newborn screens already performed, the costs of materials, training, and reporting are expected to be minimal in relation to the potential benefits.

This report estimates the benefit of universal intervention; costs and benefits assume 100% participation in treatment (Table 1). More research is needed to estimate the willingness of pregnant women and new mothers to participate voluntarily in treatment programs. The intervention type, in practice, needs to be chosen by the patient, based on the physician's recommendation. Our analysis suggests that even the most expensive universal intervention (residential treatment) would be cost effective, and tailoring treatment type to individual patient circumstances may further maximize benefit and reduce cost.

There is considerable ethical controversy about whether or not an FAS or FASD diagnosis, or the identification of an alcohol-using mother, should warrant an automatic intervention by health care providers or social services. We and others view mandatory intervention as an infringement of the mother's right to privacy (Hankin et al., 2000). Moreover, there is good reason to suspect that many women who would benefit from intervention will hesitate to seek it if they believe that admitting to drinking will increase the risk of their infant's being taken from them. There is also both an emotional and possibly economic cost to identifying false positives. Women may feel shame or stigma at being falsely identified, and this may impact their health, mindset, and productivity. Falsely identified mothers may also incur undeserved critical judgment by their health care providers and family and friends.

In sum, a universal meconium analysis of newborns and subsequent intervention for the identified mothers may be a cost-effective method for the prevention of FAS and FASD. However, there are several reasons why we believe that it would be premature to institute universal screening at this time: (1) the need to conduct more research on analysis of meconium and refine the measure further and (2) the need to improve the specificity of the meconium test currently available and the development of a second-tier screening strategy. The high number of false positives (10 times the number of true positives) is a major problem, and funding for treatment of such a high number of false positives is unrealistic and unnecessary. (3) The need to put in place confidential computerized screening/feedback of women during pregnancy and (4) the need to develop more effective interventions and treatments for alcohol-using women and affected children. The long-term costs and benefits of the programs described here have not been demonstrated. The benefits of the current interventions are likely overstated, and truly effective treatment and prevention are likely to cost more than the programs described here and need to be further developed. (5) The need for data from a pilot program or other clinical trial to evaluate the effectiveness of a the type of screening program described here. Thus, more funding needs to be allocated to further refine meconium testing and improve the effectiveness of intervention with women at risk and their affected children.

## Acknowledgments

We would like to thank Joseph White and Sybil Marsh for their thoughtful suggestions and comments and Robert Sokol, who collaborated on the Detroit longitudinal cohort study.

This paper was supported by grants from the National Institute on Alcohol Abuse and Alcoholism/(NIAAA) NIH (R01 AA16398 and R03 AA12618) (C.F.B.), the National Institute on Environmental Health Science/NIH/EPA (P01 ES11261) (C.F.B.), AAMC/CDC/ATSDR Cooperative Agreement, MM-0122-02/02 (C.F.B.), and the Mary Ann Swetland Center for Environmental Health (A.G., C.F.B.). This paper used data collected in our longitudinal research in Cape Town, South Africa, funded by two administrative supplements to NIAAA grant R01 AA09524 (S.W.J.), NIAAA U01 AA014790 (S.W.J.) in conjunction with the NIAAA Collaborative Initiative on Fetal Alcohol Spectrum Disorder, and a grant from the Joseph Young, Sr., Fund from the State of Michigan (S.W.J.)

## REFERENCES

- Abel EL. Fetal alcohol syndrome in families. *Neurotoxicol Teratol.* 1988; 10(1):1–2. [PubMed: 3352564]
- Abel EL. An update on incidence of FAS: FAS is not an equal opportunity birth defect. *Neurotoxicol Teratol.* 1995; 17:437–443. [PubMed: 7565490]
- Abel EL, Sokol RJ. Incidence of fetal alcohol syndrome and economic impact of FAS-related anomalies. *Drug Alcohol Depend.* 1987; 19:51–70. [PubMed: 3545731]
- Anton RF, O'Malley SS, Ciraulo DA, et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. *JAMA.* 2006; 295(17): 2003–2017. [PubMed: 16670409]
- Barr HM, Streissguth AP. Identifying maternal self-reported alcohol use associated with fetal alcohol spectrum disorders. *Alcohol Clin Exp Res.* 2001; 25(2):283–287. [PubMed: 11236844]
- Bearer CF, Jacobson JL, Jacobson SW, et al. Validation of a new bio-marker of fetal exposure to alcohol. *J Pediatr.* 2003; 143(4):463–469. [PubMed: 14571221]
- Bearer CF, Santiago LM, O'Riordan MA, et al. Fatty acid ethyl esters: quantitative biomarkers for maternal alcohol consumption. *J Pediatr.* 2005; 146:824–830. [PubMed: 15973326]
- Centers for Disease Control, and Prevention. Alcohol consumption among women who are pregnant or might become pregnant: United States, 2002. *Morb Mortal Wkly Rep.* 2004; 53(50):1178–1181.
- Chan D, Bar-Oz B, Pellerin B, et al. Population baseline of meconium fatty acid ethyl esters among infants of nondrinking women in Jerusalem and Toronto. *Ther Drug Monit.* 2003; 25:271–278. [PubMed: 12766552]
- Chang G. Screening and brief intervention in prenatal care settings. *Alcohol Res Health.* 2004; 28(2): 80–84. [PubMed: 19006995]
- Chang G, Goetz MA, Wilkins-Haug L, et al. A brief intervention for prenatal alcohol use: an in-depth look. *J Subst Abuse Treat.* 2000; 18(4):365–369. [PubMed: 10812310]
- Clark HW. Residential substance abuse treatment for pregnant and postpartum women and their children: treatment and policy implications. *Child Welf.* 2001; 80(2):179–198.
- Fleming MF, Manwell LB. Brief intervention in primary care settings: a primary treatment method for at-risk, problem and dependent drinkers. *Alcohol Res Health.* 1999; 23:128–137. [PubMed: 10890807]
- Greenfield L, Burgdorf K, Chen X, et al. Effectiveness of long-term residential substance abuse treatment for women: findings from three national studies. *Am J Drug Alcohol Abuse.* 2004; 30(3):537–550. [PubMed: 15540492]
- Hankin J, McCaul ME, Heussner J, et al. Pregnant, alcohol-abusing women. *Alcohol Clin Exp Res.* 2000; 24(8):1276–1285. [PubMed: 10968668]
- Harwood HJ, Napolitano DM. Economic implications of the fetal alcohol syndrome. *Alcohol Health Res World.* 1985; 10:38–43.
- Hopkins RB, Paradis J, Roshankar T, et al. Universal or targeted screening for fetal alcohol exposure: a cost-effectiveness analysis. *J Stud Alcohol Drugs.* 2008; 69(4):510–519. [PubMed: 18612566]
- Ismail S, Buckley S, Budacki R, et al. Screening, diagnosing and prevention of fetal alcohol syndrome: is this syndrome treatable? *Dev Neurosci.* 2010; 32(2):91–100. [PubMed: 20551645]
- Jacobson JL, Jacobson SW, Sokol RJ, Ager JW Jr. Relation of maternal age and pattern of pregnancy drinking to functionally significant cognitive deficit in infancy. *Alcohol Clin Exp Res.* 1998; 22(2):345–351. [PubMed: 9581639]
- Jacobson SW, Chiodo LM, Sokol RJ, et al. Validity of maternal report of prenatal alcohol, cocaine, and smoking in relation to neuro-behavioral outcome. *Pediatrics.* 2002; 109(5):815–825. [PubMed: 11986441]
- Jacobson SW, Jacobson JL, Sokol RF, et al. Effects of alcohol exposure on infant reaction time. *Alcohol Clin Exp Res.* 1994; 18:1125–1132. [PubMed: 7847594]
- Jacobson SW, Jacobson JL, Sokol RJ, et al. Maternal age, alcohol abuse history, and quality of parenting as moderators of the effects of prenatal alcohol exposure on 7.5-year intellectual function. *Alcohol Clin Exp Res.* 2004; 28(11):1732–1745. [PubMed: 15547461]

- Jacobson SW, Stanton ME, Moltano CD, et al. Impaired eyeblink conditioning in children with fetal alcohol syndrome. *Alcohol Clin Exp Res*. 2008; 32(2):365–372. [PubMed: 18162064]
- Johns B, Baltussen R, Hutubessy R, et al. Programme costs in the economic evaluation of health interventions. *Cost Eff Resour Alloc*. 2003; 1(1):1. [PubMed: 12773220]
- Kinzie MB, Schorling JB, Siegel M, et al. Prenatal alcohol education for low-income women with interactive multimedia. *Patient Educ Couns*. 1993; 21(1–2):51–60. [PubMed: 8337205]
- Lapham SC, Kring MK, Skipper B, et al. Prenatal behavioral risk screening by computer in a health maintenance organization-based prenatal care clinic. *Am J Obstet Gynecol*. 1991; 165(3):506–14. [PubMed: 1892174]
- Martin JA, Hamilton BE, Sutton PD, et al. Births: final data for 2003. *National Vital Statistics Reports*. CDC. 2005; 54(2):1–116.
- Masis KB, May PA. A comprehensive local program for the prevention of fetal alcohol syndrome. *Public Health Rep*. 1991; 106(5):484–489. [PubMed: 1910181]
- Ondersma SJ, Chase SK, Svikis DS, Schuster CR. Computer-based brief motivational intervention for perinatal drug use. *J Subst Abuse Treat*. 2005; 28(4):305–312. [PubMed: 15925264]
- Sampson PD, Streissguth AP, Bookstein FL, et al. Incidence of fetal alcohol syndrome and prevalence of alcohol-related neurodevelopmental disorder. *Teratology*. 1997; 56(5):317–326. [PubMed: 9451756]
- Stade B, Ali A, Bennett D, et al. The burden of prenatal exposure to alcohol: revised measurement of cost. *Can J Clin Pharmacol*. 2009; 16(1):e91–e102. [PubMed: 19168935]
- Stratton, K.; Howe, C.; Battaglia, F. Summary. Fetal alcohol syndrome: diagnosis, epidemiology, prevention, and treatment. Washington, DC: National Academy Press; 1996.
- Streissguth, AP.; Barr, HM.; Kogan, J.; Bookstein, FL. Final report. Seattle: University of Washington School of Medicine Department of Psychiatry and Behavioral Sciences; 1996. Understanding the occurrence of secondary disabilities in clients with fetal alcohol syndrome (FAS) and fetal alcohol effects (FAE).
- Streissguth AP, Bookstein FL, Barr HM, et al. Risk factors for adverse life outcomes in fetal alcohol syndrome and fetal alcohol effects. *J Dev Behav Pediatr*. 2004; 25:228–238. [PubMed: 15308923]
- Streissguth AP, Sampson PD, Olson HC, et al. Maternal drinking during pregnancy: attention and short-term memory in 14-year-old offspring—a longitudinal prospective study. *Alcohol Clin Exp Res*. 1994; 18(1):202–218. [PubMed: 8198221]
- Svikis DS, Golden AS, Huggins GR, et al. Cost-effectiveness of treatment for drug-abusing pregnant women. *Drug Alcohol Depend*. 1997; 45(1–2):105–113. [PubMed: 9179512]
- Whaley SE, O'Connor MJ. Barriers to effective FAS prevention. *Alcohol Clin Exp Res*. 1999; 23:111A.
- Willford J, Leech S, Day N. Moderate prenatal alcohol exposure and cognitive status of children at age 10. *Alcohol Clin Exp Res*. 2006; 30(6):1051–1059. [PubMed: 16737465]
- Zellman GL, Fair CC, Hoube J, et al. A search for guidance: examining prenatal substance exposure protocols. *Matern Child Health J*. 2002; 6(3):205–212. [PubMed: 12236668]
- Zelner I, Koren G. Universal or targeted screening for fetal alcohol exposure: a cost-effectiveness analysis. *Ther Drug Monit*. 2009; 31(2):170–172. [PubMed: 19258931]

**Table 1****Critical Data Gaps That Affect Ability to Accurately Estimate Costs and Benefits of Universal Screening**


---

Cost of including meconium screening in the established newborn screening system
Number of women who would voluntarily participate in interventions
Long-term effectiveness of each intervention
Development of a second-stage screen that substantially reduces false positives
Impact of gestational age on the sensitivity/specificity of the meconium test
Refinement of the meconium test to indicate level of drinking
Ability of the meconium test to identify social drinkers
Inclusion of FASD children into primary research
Relation between binge drinking during pregnancy and alcohol dependence
Strategy to reduce false negatives
Interventions that reduce secondary disabilities in infants identified as FASD
Cross-country generalizability
Effect of multiple-drug use on effectiveness of intervention

---

Table 2

Direct Cost Estimates for Potential Universal Meconium Screening and Possible Subsequent Interventions for Test Positives

Maternal intervention strategy	Column 1: Direct cost (\$ spent per individual)	Column 2: Population size	Column 3: Estimated cost of program per population (million \$) (column 1 × column 2)	Column 4: Estimated total cost screening plus intervention per population (sum total of column 3 costs)
Universal meconium analysis	\$72 <sup>d</sup> /sample	4,090,000 <sup>b</sup>	\$300	I. \$345 million
I. Brief intervention	\$64/patient <sup>c</sup>	True positives: 3,950,000 <sup>d</sup> × 0.02 <sup>e</sup> × 0.842 <sup>f</sup> = 66,518	\$4	
	\$64/patient <sup>c</sup>	False positives: 3,950,000 × 0.98 <sup>e</sup> × 0.167 <sup>f</sup> = 646,457	\$41	
Universal meconium analysis	\$72 <sup>d</sup> /sample	4,090,000 <sup>b</sup>	\$300	IIA. \$1.4 billion or IIB.
IIA. Pharmacotherapy, medical management, and combined behavioral intervention	\$1472 <sup>g</sup> /patient	True positives: 3,950,000 <sup>d</sup> × 0.02 <sup>e</sup> × 0.842 <sup>f</sup> = 66,518	\$98	\$0.9 billion
	\$1472 <sup>g</sup> /patient	False positives: 3,950,000 × 0.98 <sup>e</sup> × 0.167 <sup>f</sup> = 646,457	\$952	
IIB. Pharmacotherapy, medical management, and combined behavioral intervention with second-stage screen	\$1472 <sup>g</sup> + 32 <sup>h</sup> /patient	True positives: 3,950,000 <sup>d</sup> × 0.02 <sup>e</sup> × 0.842 <sup>f</sup> = 66,518	\$100	
	\$1472 <sup>g</sup> + 32 <sup>h</sup> /patient	False positives: 3,950,000 × 0.98 <sup>e</sup> × 0.167 <sup>f</sup> = 646,457 × 0.5 <sup>i</sup>	\$486	
Universal meconium analysis	\$72 <sup>d</sup> /sample	4,090,000 <sup>b</sup>	\$300	IIIA. \$4.8 billion or IIIB.
IIIA. Comprehensive/residential treatment	\$6321 <sup>j</sup> /patient	True positives: 3,950,000 <sup>d</sup> × 0.02 <sup>e</sup> × 0.842 <sup>f</sup> = 66,518	\$420	\$2.6 billion
	\$6321 <sup>j</sup> /patient	False positives: 3,950,000 × 0.98 <sup>e</sup> × 0.167 <sup>f</sup> = 646,457	\$4086	
IIIB. Comprehensive/residential treatment with second-stage screen	\$6321 <sup>j</sup> + 32 <sup>h</sup> /patient	True positives: 3,950,000 <sup>d</sup> × 0.02 <sup>e</sup> × 0.842 <sup>f</sup> = 66,518 × 0.5 <sup>i</sup>	\$211	
	\$6321 <sup>j</sup> + 32 <sup>h</sup> /patient	False positives: 3,950,000 × 0.98 <sup>e</sup> × 0.167 <sup>f</sup> × 0.5 <sup>i</sup> = 646,457 × 0.5 <sup>i</sup>	\$2053	

<sup>a</sup> see text.

<sup>b</sup> Total births screened (Martin et al. 2005).

<sup>c</sup> Theoretical salary cost for two 1-hour sessions.

<sup>d</sup> Total mothers with screened children (Martin et al. 2005).

<sup>e</sup> Maternal binge drinking rate (Centers for Disease Control and Prevention 2004).

<sup>f</sup> Sensitivity of meconium analysis (Bearer et al. 2003).

<sup>g</sup> Cost of 16 weeks of naltrexone, 9 sessions MM, 20 sessions CBI (Anton et al. 2006).

<sup>h</sup>Cost of 1-hour in-depth interview with licensed social worker.

<sup>i</sup>Reduction in false positives by secondary screening (estimate).

<sup>j</sup>Average cost of residential alcohol treatment (Svikis et al. 1997; Hankin et al. 2000).

<sup>k</sup>False identification rate for meconium analysis (Bearer et al. 2003).

**Table 3**

Direct Benefits of Prevention of Future FASD Births as a Result of Meconium Screening, Assuming Perfect Effectiveness

Factor	Column 1: Lifetime direct benefit (\$ saved per individual)	Column 2: Lifetime productivity gains (\$ gained per individual)	Column 3: Population size	Column 4: Lifetime benefit (estimated total \$ saved per population assuming 100% effectiveness treatment (column 1 + 2) × column 3)
Subsequent FASD birth prevention	\$1,990,000 <sup>a</sup>	\$74,200 <sup>b</sup>	1.04 <sup>c</sup> × test positives [3,950,000 <sup>d</sup> × 0.02 <sup>e</sup> × 0.842 <sup>f</sup> × 0.40 <sup>g</sup> × 0.846 <sup>h</sup> ] -23410	\$48 billion

<sup>a</sup>Expected lifetime costs of FASD individual (Stade et al. 2009).

<sup>b</sup>Expected lifetime productivity loss in FASD individual (Stade et al. 2009).

<sup>c</sup>Average expected future births after first child per mother (Martin et al. 2005).

<sup>d</sup>Total mothers of screened children (Martin et al. 2005).

<sup>e</sup>Prevalence binge drinking (Centers for Disease Control and Prevention 2004).

<sup>f</sup>Sensitivity meconium analysis (Bearer et al. 2003).

<sup>g</sup>Estimated percentage of alcohol exposed infants affected by FASD (Streissguth et al. 1996).

<sup>h</sup>Refer to text.

**Table 4**

## Benefits by Treatment Program Factoring Effectiveness

Treatment type	Column 1: Benefit estimate before effectiveness: prevention future FASD (Table 2)	Column 2: Average effectiveness of treatment	Benefit estimate factoring effectiveness: (column 1 × column 2)
Brief intervention	\$48 billion	70% <sup>a</sup>	\$33.6 billion
Pharmacotherapy with medical management	\$48 billion	59% <sup>b</sup>	\$28 billion
Residential facility treatment	\$48 billion	68% <sup>c</sup>	\$32.6 billion

<sup>a</sup>Chang (2004).

<sup>b</sup>Anton et al. (2006).

<sup>c</sup>Clark (2001); Greenfield et al. (2004).



**Table 5**

## Benefit-to-Cost Ratios for Each Treatment Type

<b>Treatment type</b>	<b>Column 1: Total cost of screening and treatment type for all test positives (\$) (Table 2)</b>	<b>Column 2: Benefit estimate for prevention future FASD births (Table 4)</b>	<b>Column 3: Total benefit-to-cost ratio (column 2: column 1) (\$)</b>
I. Brief intervention	\$.35 billion	\$34 billion	97:1
IIA. Pharmacotherapy with medical management	\$1.4 billion	\$28 billion	20:1
IIB. Pharmacotherapy with medical management	\$0.9 billion	\$32.6 billion	37:1
IIIA. Residential facility treatment	\$4.8 billion	\$28 billion	6:1
IIIA. Residential facility treatment	\$2.6 billion	\$32.6 billion	12:1