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Decreasing smoking during pregnancy: Potential economic benefit of reducing sudden unexpected infant death

Stephen T. Higgins[a,b,*], Eric P. Slade[a,c], Donald S. Shepard[a,d]

[a] Vermont Center on Behavior and Health, Department of Psychiatry, University of Vermont, United States of America
[b] Department of Psychological Science, University of Vermont, United States of America
[c] Johns Hopkins University School of Nursing, United States of America
[d] Heller School for Social Policy and Management, Brandeis University, United States of America

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ABSTRACT

Sudden Unexpected Infant Death (SUID) remains the leading cause of death among U.S. infants age 1–12 months. Extensive epidemiological evidence documents maternal prenatal cigarette smoking as a major risk factor for SUID, but leaves unclear whether quitting reduces risk. This Commentary draws attention to a report by Anderson et al. (*Pediatrics.* 2019, 143[4]) that represents a breakthrough on this question and uses their data on SUID risk reduction to delineate potential economic benefits. Using a five-year (2007–11) U.S. CDC Birth Cohort Linked Birth/Infant Death dataset, Anderson et al. demonstrated that compared to those who continued smoking, women who quit or reduced smoking by third trimester decreased the adjusted odds of SUID risk by 23% (95% CI, 13%–33%) and 12% (95% CI, 2%–21%), respectively. We applied these reductions to the U.S. Department of Health and Human Services' recommended value of a statistical life in 2020 ($10.1 million). Compared to continued smoking during pregnancy, the economic benefits per woman of quitting or reducing smoking are $4700 (95% CI $2700–$6800) and $2500 (95% CI, $400–$4300), respectively. While the U.S. obtained aggregate annual economic benefits of $0.58 (95% CI, 0.35–0.82) billion from pregnant women who quit or reduced smoking, it missed an additional $1.16 (95%CI 0.71–1.60) billion from the women who continued smoking. Delineating the health and economic impacts of decreasing smoking during pregnancy using large epidemiological studies like Anderson et al. is critically important for conducting meaningful economic analyses of the benefits-costs of developing more effective interventions for decreasing smoking during pregnancy.

Sudden Unexpected Infant Death (SUID) remains a significant public health problem globally and the leading cause of death among infants age 1–12 months in the U.S. (Pretorius and Rew, 2020; Tanabe and Hauck, 2018). SUID, which includes Sudden Infant Death Syndrome (SIDS), is defined as the sudden and unexpected death of an infant less than 1 year of age in which the cause was not obvious before investigation (AAP TASK FORCE ON SUDDEN INFANT DEATH SYNDROME, 2016; Centers for Disease Control and Prevention, 2020a, 2020b). Extensive epidemiological evidence documents maternal prenatal cigarette smoking as a major risk factor for SUID, including evidence sufficient to support causal inference (Anderson and Cook, 1997; Mitchell and Milerad, 2006; U.S. Department of Health and Human Services (USDHHS), 2004, 2014, 2018). Maternal smoking during pregnancy followed by bed sharing increases SUID risk even further (Mitchell et al., 2017). However, the evidence had previously been inconclusive on whether decreasing maternal smoking during pregnancy decreases SUID risk (USDHHS, 2018). The purpose of this Commentary is to (1) draw attention to a report by Anderson et al. (2019) that we believe represents a breakthrough on this question and (2) use their data on SUID risk reduction from decreasing smoking during pregnancy to delineate resulting economic benefits.

1. Epidemiological studies are important to estimating the economic impact of smoking cessation

Considering economic implications of epidemiological studies like Anderson et al. is of critical importance to delineating and quantifying the economic benefits-costs of clinical (e.g., Higgins and Solomon, 2016) and population (e.g., England et al., 2017) interventions designed to decrease smoking during pregnancy. Anderson et al. (2019) used a five-year (2007–11) U.S. CDC Birth Cohort Linked Birth/Infant Death dataset to examine relationships between maternal self-reported

* Corresponding author at: University of Vermont, University Health Center 1 S. Prospect St., Burlington, VT 05401, United States of America.
E-mail address: stephen.higgins@uvm.edu (S.T. Higgins).

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smoking status during pregnancy and SUID risk controlling for multiple potential confounders (i.e., parental race/ethnicity, age, mother's marital status and education, live birth order, number of prenatal visits, gestational length, delivery method, infant sex and birth weight). They examined 20,685,463 births and 19,127 cases of SUID. Confirming prior evidence, maternal smoking during pregnancy was associated with twice the adjusted odds ratio (aOR) of SUID compared to not smoking (aOR = 2.44; 95% CI, 2.31–2.57). Adding important new information, Anderson et al. demonstrated that compared to those who continued smoking, women who (1) quit or (2) reduced smoking by the third trimester decreased the adjusted odds (aOR) of SUID risk by 23% (95% CI 13%–33%) and 12% (95% CI 2%–21%), respectively. They also detailed how smoking even as little as 1 cigarette per day through pregnancy increased the risk of SUID by 98% (aOR = 1.98; 95 CI, 1.73–2.28), with odds increasing linearly thereafter by 0.07 for every additional cigarette smoked per day before flattening out at 20+. Anderson et al. (2019) concluded appropriately, in our opinion, that these relationships met criteria for inferring causality in that there was (1) a strong empirical association; (2) a dose-response relationship; (3) a logical temporal order to the relationships (i.e., smoking preceded SUID); (4) findings consistent with an extant scientific literature (smoking is a well-established risk factor for SUID—see USDHHS, 2018, Chapter 4); 5) biological plausibility (plausible accounts of the pathophysiology underpinning smoking and SUID risk have been detailed–see Horne et al., 2002; Mitchell and Milerad, 2006; Mitchell, 2009; Parsiow et al., 2004); and (6) decreases in risk when smoking is reduced or discontinued (i.e., if smoking is the cause, then decreasing or eliminating it should reduce risk).

Like all studies, the Anderson et al. (2019) study has limitations common in this area of investigation. The most substantive, in our opinion, is the exclusive reliance on maternal self-reported smoking status, which is common in epidemiological studies but nevertheless problematic as pregnant women often fail to disclose ongoing smoking. Nondisclosure of smoking during pregnancy is well established (Dietz et al., 2011; England et al., 2007; Tong et al., 2015), with rates among U.S. pregnant women when queried on quitting during the current pregnancy estimated at ~30% (England et al., 2007). This pattern of nondisclosure leads to categorizing women who are continuing to smoke as quitters, thereby diminishing the estimated benefit of quitting on SUID risk. Nondisclosure is more common among lighter than heavier smokers, but when dealing with SUID where risk increases substantially even among light smokers, the impact on risk estimation is nevertheless likely to be diminished.

An additional limitation was not controlling for maternal alcohol or illicit drug use. We are unaware of quantitative parsing of the effects of other substance use during pregnancy on SUID risk comparable to what we have described above for nondisclosure of smoking. Adjustment for alcohol use during pregnancy did not significantly influence estimated smoking risk for stillbirth or infant mortality in the one prior study we know of on this topic (Wisborg et al., 2001), although in a later study both were demonstrated to be independent risk factors for infant death, with the greatest level of risk compared to nonusers being seen among women who continued using both substances (Elliott et al., 2020). Combined use of cigarette smoking and illicit drug use is well documented (e.g., Oga et al., 2019), but less is known about their independent contributions to SUID. The likely impact of these two limitations on estimated smoking-attributable risk would likely be in opposite directions. While they merit mention they certainly do not undermine the importance of the Anderson et al. findings on the benefits of decreasing smoking during pregnancy on SUID risk.

Epidemiological studies of this type provide critically important information for examining the comparative benefits and costs of interventions to reduce smoking during pregnancy. The reason is that while catastrophic in nature, many serious adverse health effects of smoking are relatively rare (e.g., SUID) or sufficiently delayed in time (e.g., smoking attributable lung and other cancers) to be impractical to include in smoking-cessation intervention studies be they randomized controlled trials or population-level interventions. As such, programs have been established such as the CDC's Smoking-Attributable Morbidity, Mortality, and Economic Costs (SAMMEC) model to link changes in smoking status and health impacts in large epidemiological studies (CDC, 2020a, 2020b). Indeed, decades of data from epidemiological studies comparing former smokers to continuing smokers has fostered development of the various health related quality of life (HRQoL) measures that are key to evaluations of the comparative effectiveness of smoking-cessation interventions in the general population of smokers (e.g., USDHHS, 2018, Chapter 5). Unfortunately, comparable measures are not yet available for examining the economic benefits of decreasing smoking during pregnancy, although there have been some notable efforts in that direction mostly around how changes in smoking status during treatment impact use of neonatal intensive care services (e.g., Ayadi et al., 2006).

In a fiscal climate in which U.S. federal and state funding for public health has been generally declining since the 2008 economic crisis (Trust for America's Health, 2018) or directed to COVID-19 in 2020, the paucity of economic information will likely stall efforts to increase the scope and intensity of smoking-cessation services for pregnant women. That is not a minor problem as there is broad consensus regarding the need for more effective interventions for smoking cessation during pregnancy (Higgins and Solomon, 2016; Scherman et al., 2018; USDHHS, 2018). A programmatic series of meta-analyses from Cochrane Reviews on interventions for smoking cessation among pregnant women, which now include more than 77 RCTS and 25,000 women, provide compelling evidence that these interventions increase cessation rates (Chamberlain et al., 2013; Chamberlain et al., 2017; Lumley et al., 2009). However, cessation rates across the different interventions examined in these comprehensive meta-analyses are quite modest. They are generally only about 6 percentage points better than control levels. That effect size is too modest to be satisfactory when dealing with a problem that causes catastrophic outcomes such as SUID and a wide range of other serious adverse pregnancy (e.g., ectopic pregnancy, placental abruption, premature rupture of membranes) and birth outcomes (fetal growth restriction, oral-facial deformities) and greater later-in-life disease risk (e.g., metabolic disorders) (Franco et al., 1999; USDHHS, 2004, 2014, 2018; Weese-Mayer et al., 2008).

There are many reasons why smoking during pregnancy is difficult to treat (e.g., maternal socioeconomic disadvantage, stigma, concerns regarding potential adverse effects of smoking-cessation medications), but to obtain larger effect sizes among pregnant women, more intensive and hence more expensive interventions are likely necessary (Clinical Practice Guideline Treating Tobacco Use and Dependence 2008 Update Panel, Liaisons, and Staff, 2008; Higgins and Solomon, 2016). For example, as early as 2009 a meta-analysis noted that financial incentives usually offered in combination with routine care were significantly more successful in achieving late-pregnancy cessation than other approaches (Lumley et al., 2009). Instead of the overall average 6% increase, financial incentives were shown to increase late-pregnancy cessation rates by an average of approximately 23% or an aOR of late-pregnancy cessation of 3.79 (95% CI, 2.74–5.25) compared to control interventions (Cahill et al., 2015; Higgins and Solomon, 2016; Lumley et al., 2009). Nevertheless, financial incentives are not used in routine care for smoking during pregnancy, with cost concerns being a common explanation offered for ignoring that evidence (Higgins et al., 2019). Hence, the need for and importance of epidemiological studies like Anderson et al., 2019 that are sufficiently powered statistically to delineate the health impacts of decreasing smoking during pregnancy on health outcomes. In addition to supporting the rationale for developing more intensive and likely more costly interventions, this information can also support efforts to increase use of existing evidence-based interventions.

2. Estimating economic impacts

As a step towards examining the economic value of preventing SUID through smoking cessation or reductions in smoking intensity during pregnancy, we used the SUID risk estimates from Anderson et al., 2019 to estimate the total monetary value of economic benefits from preventing SUID deaths attributed to smoking during pregnancy and economic costs of SUID deaths. By putting a monetary value on smoking-attributable SUID deaths, we hope to draw attention to the potential economic benefit of greater efforts to reduce smoking during pregnancy and the economic cost that results from not doing so.

Anderson et al.'s five-year (2007–11) data set contained an average of approximately 4.14 million births per year. Of these, an estimated 368,000 women who reported smoking during pregnancy using the 8.9% smoking prevalence in the final year of their 5-year data set served as a conservative estimate. Among these pregnant smokers, approximately 77,322 (21%) reported quitting by the third trimester, 88,368 (24%) reported reducing smoking intensity by the third trimester, while the remaining 202,511 (55%) reported continued smoking with no reduction in intensity. Compared to women who continued smoking at same intensity, SUID risk was reduced by 23% (aOR = 0.77; 95% CI, 0.67–0.87) among women who quit and 12% (aOR = 0.88; 95% CI, 0.79–0.98) among those who reduced smoking intensity. These differences in SUID rates by smoking status and associated CIs provided the resulting estimates and CIs in deaths averted discussed below and in Table 1.

The economic value of life has been conceptualized as including both the value of an individual's contribution to economic production over their remaining lifetime plus the additional value people place on the enjoyment of life (for reviews see Robinson et al., 2017; Shillcutt et al., 2009). Although the literature on valuing life is extensive, few prior methodological studies offer specific guidance on valuing infant lives. Here we apply the 2020 value of a statistical life of $10.1 million using guidelines from the U.S. Department of Health and Human Services for making health policy (USDHHS, 2020). Using that 2020 value, we estimate (see Table 1) that the values gained from the reduced SUIDS risk per pregnant smoker who quits or reduces by the start of the third trimester compared to continued smoking are $4700 (95% CI $2700–$6800) and $2500 ($400–$4300), respectively. We derived these values by starting with the rate of SUID in woman who continued smoking and translating the relative reductions from reducing or abstaining into the absolute reduction in SUID risk per 1000 pregnancies. We then multiplied these absolute reductions in deaths averted times the aforementioned value of a statistical life. Just these benefits alone would exceed the combined costs of smoking-cessation counseling, a 10-week course of nicotine replacement therapy, and financial incentives (e.g., see Boyd et al., 2016).

Using these figures, we then estimated the monetary benefit the United States likely realizes each year from current smoking reductions and quits by third trimester compared to all pregnant smokers continuing to smoke throughout pregnancy without reducing or quitting, and found this was around $0.58 (95% CI $0.35–$0.82) billion. We also estimated the value to be gained each year of further reducing the prevalence of smoking during the third trimester of pregnancy from current prevalence levels to 0 prevalence. We estimate that if all pregnant smokers quit and remained abstinent in the third trimester, the additional aggregate economic benefits would be $1.16 (95% CI, $0.71–$1.60) billion per year. If all pregnant smokers who were continuing at their initial rate simply reduced their smoking, the aggregate economic benefits would be $0.50 (95%CI 0.08–0.87) billion per year. We calculated each of these national amounts (and CIs) by summing of products of the actual values per woman (with associated CIs, before rounding) times the national numbers of women in each smoking subcategory (e.g., $4737 × 202,511 + [$4737 − $2475] × 88,368 = $1.16 billion).

3. Conclusions

The Anderson et al. report provides compelling empirical evidence that quitting or reducing smoking before the 3rd trimester can significantly reduce SUID risk with quantitative estimates of the magnitude of risk reduction associated with each compared to women who continued smoking through pregnancy without altering smoking rate. Epidemiological studies of this type are critical to quantifying the benefits and costs of decreasing smoking. By monetizing the observed risk reductions from quitting or reducing smoking, we have attempted to interpret the importance of their results in terms of economic impact. By any standard that we are familiar with, the potential per smoker savings of $4700 and $2500 from smoking abstinence and reductions, respectively, are significant in light of evidence that as a rule-of thumb more intensive interventions produce better outcomes in smoking cessation generally (Clinical Practice Guideline Treating Tobacco Use and Dependence 2008 Update Panel, Liaisons, and Staff, 2008) and, as discussed above, also among pregnant smokers at least with regard to clinical interventions involving financial incentives (e.g., Cahill et al., 2015; Higgins and Solomon, 2016; Tappin et al., 2015).

While the focus of the Anderson et al. report and this Commentary is SUID, there are many additional outcomes to be examined with regard to the economic benefits of quitting or reducing smoking during pregnancy. For example, there is already sufficient evidence to conclude that smoking cessation during pregnancy attenuates the adverse effects of maternal smoking on fetal growth including risk of delivering a small-for-gestational-age infant (< 10th percentile) (USDHHS, 2018, Chapter 4). What are needed now regarding those outcomes, however, are studies that monetize the benefits of those reductions in risk and that examine the cost-effectiveness of more effective, but also more

Table 1
Reductions in SUIDS rates and associated economic benefits related to smoking among pregnant women in the U.S.

	Women who smoked just prior to pregnancy	Women who continued smoking at same or greater level into 3rd trimester	Women who reduced smoking before 3rd trimester	Women who abstained from smoking before 3rd trimester
Fraction of pregnant smokers (%)	100%	55%	24%	21%
Live births per year	368,201	202,511	88,368	77,322
Cases of SUID per year	690	411	158	121
Estimated annual rate of SUID cases*		2.031	1.786	1.562
Reduction in SUIDS rate compared to continued smoker (95% CI)*			0.245 (0.041–0.426)	0.468 (0.264–0.670)
Reduction in SUIDS rate compared to reduced smoker (95% CI)*				0.223 (0.037–0.389)
Economic benefit per woman compared to continued smoker (95% CI)			$2500 ($400–$4300)	$4700 ($2700–$6800)
Economic benefit per woman compared to reduced smoker (95% CI)				$2300 ($400–$3900)

*per 1000 live births.

expensive, interventions. Besides SUID, there are additional adverse outcomes where the smoking-attributable risk has been established but where it is not known whether reducing smoking or quitting during pregnancy alters that risk. Preterm delivery and infant facial birth defects (e.g., oral clefts) are two relevant examples (Little et al., 2004; USDHHS, 2018, Chapter 4). For these outcomes, we need studies like Andersen et al. that have sufficient statistical power to answer the important question of whether smoking cessation or reductions during pregnancy significantly reduce risk coupled with efforts like the present one to monetize any risk reductions that are demonstrated. In short, there is an unmet need for the equivalent of a SAMMEC model for maternal/infant tobacco-attributable morbidity, mortality, and economic benefits, an effort evident in Ayadi et al. (2006) that appears to have stalled. We hope the present Commentary may represent a step towards rekindling interest in that direction.

Lastly, while the dataset examined in Anderson et al., was from 2007 to 11, there is no question that smoking during pregnancy remains a significant U.S. public health problem. For example, our group conducted a recent study examining differences across three U.S. national data sets on prevalence during pregnancy (Population Assessment of Tobacco and Health (PATH), National Survey on Drug Use and Health [NSDUH], and Pregnancy Risk Assessment Monitoring System [PRAMS] surveys) (Nighbor et al., 2020). The most recent year examined in that study was 2016, five years beyond the last year (2011) in the Anderson et al. dataset where prevalence was reported to be 8.9%. Prevalence rates across the three surveys were at or above that 2011 rate (PATH: 13.8%, 9.8–17.7%; NSDUH: 10.2%, 7.2–13.2%; PMAMS: 7.7%, 7.2–8.1%). There is little question that smoking during pregnancy remains a substantial U.S. public health problem. There is broad agreement on the need for more effective interventions to reduce this problem (Chamberlain et al., 2013; Chamberlain et al., 2017; Higgins and Solomon, 2016; Lumley et al., 2009). To conduct the type of comparative benefit-cost analyses of interventions to decrease smoking among pregnant women that are now a well-established part of smoking-cessation research in the general population, we believe that additional epidemiological studies of the type reported by Anderson et al. coupled with economic-impact costing information of the type that we have attempted to provide in this Commentary will be essential.

CRediT authorship contribution statement

Stephen T. Higgins: Conceptualization, Writing - original draft, Writing - review & editing, Supervision, Funding acquisition.**Eric P. Slade:**Data curation, Visualization, Writing - review & editing.**Donald S. Shepard:**Data curation, Visualization, Writing - review & editing.

Declaration of competing interest

Dr. Shepard reports grant support from Takeda Vaccines, Inc. and Sanofi Pasteur not related to this study. Drs. Higgins and Slade have nothing to declare.

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